# Malignant disease

## 1 Antibody responsive malignancy

ANTINEOPLASTIC DRUGS › MONOCLONAL ANTIBODIES

### Amivantamab 17-Feb-2022

I DRUG ACTION Amivantamab is a human monoclonal antibody that targets and disrupts signalling in epidermal growth factor receptor (EGFR) and mesenchymalepithelial transition factor (MET) receptor pathways, thereby preventing tumour cell progression and also causing immune-mediated tumour cell death.

I INDICATIONS AND DOSE

Non-small cell lung cancer [with activating epidermal growth factor receptor (EGFR) exon 20 insertion mutations] (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

I CAUTIONS Pre-medication must be administered to minimise the development of infusion-related reactions

CAUTIONS, FURTHER INFORMATION

▶ Infusion-related reactions gInfusion-related reactions can occur and amivantamab should only be administered when appropriately trained staff and resuscitation facilities are immediately available; pre-medication with an antipyretic, antihistamine, and corticosteroid is recommended—consult product literature. M

I SIDE-EFFECTS

▶ Common or very common Appetite decreased . asthenia . constipation . diarrhoea . dizziness . dry eye . electrolyte imbalance . eye discomfort . eye disorders . eye inflammation . facial swelling . gastrointestinal discomfort . hypoalbuminaemia . increased risk of infection . infusion related reaction . mucositis . myalgia . nail disorders . nausea . oedema . onycholysis . oral disorders . perineal rash . peripheral swelling . respiratory disorders . skin reactions . vertigo . vision disorders . vomiting

▶ Uncommon Toxic epidermal necrolysis

▶ Frequency not known Back pain . dyspnoea . fever . muscle weakness . pulmonary embolism

I CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception during treatment and for at least 3 months after last treatment. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY gAvoid unless potential benefit outweighs risk—limited information available. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING gAvoid during treatment and for 3 months after last treatment—no information available. M

I PRESCRIBING AND DISPENSING INFORMATION

Amivantamab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

The manufacturer of Rybrevant ◦ has provided a Risk minimisation materials document for healthcare professionals.

I HANDLING AND STORAGE Store in a refrigerator (2-8°C) and protect from light—consult product literature for storage conditions after preparation of the infusion.

I PATIENT AND CARER ADVICE Patients should be advised to limit sun exposure during treatment and for 2 months after last treatment; protective clothing and use of sunscreen are advisable. Patients should be advised to discontinue contact lens use until worsening eye symptoms are evaluated.

Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of dizziness and visual impairment.

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Edetic acid (edta), polysorbates

▶ Amivantamab (non-proprietary) A

Amivantamab 50 mg per 1 ml Rybrevant 350mg/7ml concentrate for solution for infusion vials | 1 vialP £1,079.00 (Hospital only)



## Atezolizumab 24-Nov-2021

I DRUG ACTION Atezolizumab is a monoclonal antibody, which binds to the programmed death-ligand 1 (PD-L1), thereby reactivating the immune response to tumour cells.

I INDICATIONS AND DOSE

Urothelial carcinoma (specialist use only) | Non-small cell lung cancer (specialist use only) | Small cell lung cancer (specialist use only) | Breast cancer (specialist use only) | Hepatocellular carcinoma (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ◆) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)

Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic drugs, such as atezolizumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, atezolizumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Atezolizumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of atezolizumab in patients with a history of severe or lifethreatening SCAR associated with other immunostimulant antineoplastic drugs.

I CAUTIONS Abnormal thyroid function—consider appropriate treatment . history of severe cutaneous adverse reactions—see Important safety information for details . patients may need pre-medication to minimise the development of infusion-related reactions—consult product literature

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Abdominal pain . appetite decreased . arthralgia . ascites . asthenia . chills . cough . cystitis . cytokine release syndrome . diarrhoea . dysphagia . dyspnoea . electrolyte imbalance . euthyroid sick syndrome . eye disorders . fever . gastrointestinal disorders . goitre . hepatic disorders . hyperglycaemia . hypersensitivity . hypotension . hypothyroidism . hypoxia . increased risk of infection . influenza like illness . infusion related reaction . myalgia . myxoedema . nasal congestion . nausea . oesophageal varices . oesophageal varices haemorrhage . oropharyngeal complaints . pain . radiation pneumonitis . respiratory disorders . skin reactions . skin ulcer . throat irritation . thrombocytopenia . thyroid disorder . thyroiditis . ulcerative colitis . vomiting

▶ Uncommon Adrenal hypofunction . connective tissue disorders . diabetes mellitus . diabetic ketoacidosis . hyperthyroidism . ketoacidosis . meningitis . muscle abscess . myopathy . nerve disorders . pancreatitis . photophobia . severe cutaneous adverse reactions (SCARs)

▶ Rare or very rare Hypophysitis . myocarditis . nephritis . neuromuscular dysfunction . temperature regulation disorder

SIDE-EFFECTS, FURTHER INFORMATION Immune-related reactions Manufacturer advises most immune-related adverse reactions are reversible and managed by temporarily stopping treatment and administration of a corticosteroid—consult product literature.

Infusion-related reactions Manufacturer advises permanently discontinue treatment in patients with severe infusion reactions.

I CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in women of childbearing

potential, during treatment and for 5 months after stopping treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**PREGNANCY** Manufacturer advises avoid unless essential—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**BREAST FEEDING** Manufacturer advises avoid—no information available.

**MONITORING REQUIREMENTS** Manufacturer advises monitor for signs and symptoms of infusion- and immunerelated reactions—consult product literature.

**PRESCRIBING AND DISPENSING INFORMATION**

Manufacturer advises to record the brand name and batch number after each administration.

All prescribers should be familiar with the Physician Information and Management Guidelines provided by the manufacturer.

**HANDLING AND STORAGE** Manufacturer advises store in a refrigerator (2–8°C); consult product literature for storage conditions after dilution.

**PATIENT AND CARER ADVICE** An alert card should be provided.

Driving and skilled tasks Manufacturer advises patients should be counselled on the effects on driving and performance of skilled tasks—increased risk of drowsiness.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (June 2018) NICE TA525 Recommended with restrictions

▶ Atezolizumab for untreated PD-L1-positive advanced urothelial cancer when cisplatin is unsuitable (October 2021) NICE TA739 Recommended

▶ Atezolizumab for treating locally advanced or metastatic nonsmall-cell lung cancer after chemotherapy (May 2018) NICE TA520 Recommended with restrictions

▶ Atezolizumab in combination for treating metastatic nonsquamous non-small-cell lung cancer (June 2019) NICE TA584 Recommended with restrictions

▶ Atezolizumab monotherapy for untreated advanced nonsmall-cell lung cancer (June 2021) NICE TA705 Recommended

▶ Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer (July 2020) NICE TA638 Recommended with restrictions

▶ Atezolizumab with nab-paclitaxel for untreated PDL1-positive, locally advanced or metastatic, triple-negative breast cancer (July 2020) NICE TA639 Recommended

▶ Atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma (December 2020) NICE TA666 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Atezolizumab (Tecentriq ◦) for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy. Patients with EGFR activating mutations or ALK-positive tumour mutations should also have received targeted therapy before receiving Tecentriq ◦ (July 2018) SMC No. 1336/18 Recommended with restrictions

▶ Atezolizumab (Tecentriq ◦), in combination with bevacizumab, paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC) (November 2019) SMC No. SMC2208 Not recommended



▶ Atezolizumab (Tecentriq ◦) as monotherapy for the first-line treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumours have a PD-L1 expression on 50% or more tumour cells (TC) or 10% or more tumourinfiltrating immune cells (IC) and who do not have epidermal growth factor receptor (EGFR) mutant or anaplastic lymphoma kinase (ALK)-positive NSCLC (November 2021) SMC No. SMC2379 Recommended

▶ Atezolizumab (Tecentriq ◦) in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (November 2020) SMC No. SMC2279 Recommended

▶ Atezolizumab (Tecentriq ◦) as monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma: after prior platinum-containing chemotherapy, or who are considered cisplatin ineligible (November 2018) SMC No. SMC2103 Not recommended

▶ Atezolizumab (Tecentriq ®) in combination with nab-paclitaxel for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer whose tumours have PD-L1 expression at a level of 1% or more and who have not received prior chemotherapy for metastatic disease (November 2020) SMC No. SMC2267 Recommended

▶ Atezolizumab (Tecentriq ®) in combination with bevacizumab for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma who have not received prior systemic therapy (July 2021) SMC No. SMC2349 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates, sucrose

▶ Tecentriq (Roche Products Ltd) A

Atezolizumab 60 mg per 1 ml Tecentriq 840mg/14ml concentrate for solution for infusion vials | 1 vialP £2,665.38 (Hospital only)

Tecentriq 1200mg/20ml concentrate for solution for infusion vials | 1 vialP £3,807.69 (Hospital only)

## Avelumab 10-Sep-2021

I DRUG ACTION Avelumab is a human monoclonal antibody, which binds to the programmed death-ligand 1 (PD-L1), thereby reactivating the immune response to tumour cells.

I INDICATIONS AND DOSE

Merkel cell carcinoma (specialist use only) | Renal cell carcinoma (specialist use only) | Urothelial carcinoma (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 800 mg every 2 weeks, for information on dose delay or discontinuation due to side-effects and infusion-related reactions—consult product literature

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ®) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)

Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic drugs, such as avelumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, avelumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Avelumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of avelumab in patients with a history of severe or life-threatening SCAR associated with other immunostimulant antineoplastic drugs.

I CAUTIONS Patients should receive pre-medication to minimise the development of adverse reactions (consult product literature)

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Anaemia . appetite decreased . arthralgia . asthenia . back pain . chills . constipation . cough . diarrhoea . dizziness . dry mouth . dyspnoea . fever . gastrointestinal discomfort . headache . hypertension . hyperthyroidism . hyponatraemia . hypothyroidism . influenza like illness . infusion related reaction . lymphopenia . myalgia . nausea . nerve disorders . peripheral oedema . respiratory disorders . skin reactions . thrombocytopenia . vomiting . weight decreased

▶ Uncommon Adrenal hypofunction . arthritis . eosinophilia . flushing . gastrointestinal disorders . hepatic disorders . hyperglycaemia . hypersensitivity . hypotension . myositis . nephritis . neuromuscular dysfunction . renal failure . thyroiditis

▶ Rare or very rare Cardiac inflammation . diabetes mellitus . hypopituitarism . pancreatitis . systemic inflammatory response syndrome . uveitis

▶ Frequency not known Endocrine disorders

SIDE-EFFECTS, FURTHER INFORMATION Infusion-related reactions For treatment modifications in patients with grade 1 or 2 infusion-related reactions, consult product literature. Manufacturer advises permanently discontinue treatment in patients with grade 3 or 4 infusion-related

reaction.
Immune-related reactions Most immune-related adverse reactions are reversible and managed by temporarily stopping treatment and administration of a corticosteroid—consult product literature for further information.
I CONCEPTION AND CONTRACEPTION Manufacturer advises women of child-bearing potential should use effective contraception during treatment and for at least 1 month after stopping treatment.
I PREGNANCY Manufacturer advises avoid unless essential—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
I BREAST FEEDING Manufacturer advises avoid during treatment and for at least 1 month after stopping treatment—no information available.
I MONITORING REQUIREMENTS Manufacturer advises monitor for signs and symptoms of infusion- and immunerelated reactions.
I DIRECTIONS FOR ADMINISTRATION Manufacturer advises for intermittent intravenous infusion (Bavencio ®), dilute requisite dose with Sodium Chloride 0.9%; give over 60 minutes via a separate line using a low-protein binding 0.2 micron filter.
I PRESCRIBING AND DISPENSING INFORMATION Avelumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.
I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8 °C)—consult product literature for storage conditions after preparation of the infusion.
I PATIENT AND CARER ADVICE Patients should be provided with an alert card. A patient information brochure highlighting important safety information to minimise the risk of immune-related side-effects is also available.



Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.
I NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Avelumab for treating metastatic Merkel cell carcinoma (updated April 2021) NICE TA517 Recommended with restrictions
▶ Avelumab for untreated metastatic Merkel cell carcinoma (April 2021) NICE TA691 Recommended with restrictions
▶ Avelumab with axitinib for untreated advanced renal cell carcinoma (September 2020) NICE TA645 Recommended
Scottish Medicines Consortium (SMC) decisions
▶ Avelumab (Bavencio ®) as monotherapy for the treatment of adult patients with metastatic Merkel cell carcinoma (May 2018) SMC No. 1315/18 Recommended
▶ Avelumab (Bavencio ®) in combination with axitinib for the first-line treatment of adult patients with advanced renal cell carcinoma (October 2020) SMC No. SMC2248 Recommended
▶ Avelumab (Bavencio ®) as monotherapy for the first-line maintenance treatment of adult patients with locally advanced or metastatic urothelial carcinoma who are progression-free following platinum-based chemotherapy (August 2021) SMC No. SMC2359 Recommended
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for infusion
▶ Bavencio (Merck Serono Ltd) A
Avelumab 20 mg per 1 ml Bavencio 200mg/10ml concentrate for solution for infusion vials | 1 vialP £768.00

## Belantamab mafodotin 05-Jul-2021

I DRUG ACTION Belantamab mafodotin is an antibody-drug conjugate that contains belantamab linked to mcMMAF, a cytotoxic microtubule disrupting agent.
I INDICATIONS AND DOSE
Multiple myeloma (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: 2.5 mg/kg every 3 weeks, for dose adjustments, interruption, and discontinuation due to side-effects and infusion-related reactions—consult product literature
I CAUTIONS History of dry eyes
I SIDE-EFFECTS
▶ Common or very common Anaemia . decreased leucocytes .

diarrhoea . dry eye . eye discomfort . eye inflammation . fever . increased risk of infection . infusion related reaction . nausea . neutropenia . thrombocytopenia . vision disorders . vomiting

▶ Frequency not known Eye disorders . fatigue . lethargy

I CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception during treatment and for 4 months after last treatment; male patients should use effective contraception during treatment and for 6 months after last treatment if their partner is of childbearing potential. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY gAvoid unless potential benefit outweighs risk—embryotoxic in animal studies. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING gDiscontinue breast-feeding before starting treatment and for 3 months after last treatment. M

I MONITORING REQUIREMENTS

▶gOphthalmic examination is advised at baseline, before the first 3 treatment cycles, and as clinically indicated during treatment—consult product literature.

▶ Obtain complete blood counts at baseline and monitor during treatment as clinically indicated—consult product literature. M

I PRESCRIBING AND DISPENSING INFORMATION Belantamab mafodotin is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in a refrigerator (2–8 °C)—consult product literature for storage conditions after preparation of the infusion.

I PATIENT AND CARER ADVICE Patients should be advised to administer preservative-free artificial tears at least four times daily during treatment and to avoid wearing contact lenses until treatment is completed.

Driving and skilled tasks Patients and their carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of vision disorders.

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

EXCIPIENTS: May contain Disodium edetate, polysorbates

▶ Blenrep (GlaxoSmithKline UK Ltd) A

Belantamab mafodotin 100 mg Blenrep 100mg powder for concentrate for solution for infusion vials | 1 vialP £5,707.83 (Hospital only)

## Bevacizumab 19-May-2021

I DRUG ACTION Bevacizumab is a monoclonal antibody that inhibits vascular endothelial growth factor.

I INDICATIONS AND DOSE

Colorectal cancer (specialist use only) | Breast cancer (specialist use only) | Renal cell carcinoma (specialist use only) | Non-small cell lung cancer (specialist use only) | Epithelial ovarian cancer (specialist use only) | Fallopian tube cancer (specialist use only) | Primary peritoneal cancer (specialist use only) | Carcinoma of the cervix (specialist use only) | Hepatocellular carcinoma (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: BEVACIZUMAB AND SUNITINIB: RISK OF OSTEONECROSIS OF THE JAW (JANUARY 2011)

Treatment with bevacizumab or sunitinib may be a risk factor for the development of osteonecrosis of the jaw. Patients treated with bevacizumab or sunitinib, who have previously received bisphosphonates, or are treated concurrently with bisphosphonates, may be particularly at risk.

Dental examination and appropriate preventive dentistry should be considered before treatment with bevacizumab or sunitinib.

If possible, invasive dental procedures should be avoided in patients treated with bevacizumab or sunitinib who have previously received, or who are currently receiving, intravenous bisphosphonates.

MHRA/CHM ADVICE: SYSTEMICALLY ADMINISTERED VEGF PATHWAY INHIBITORS: RISK OF ANEURYSM AND ARTERY DISSECTION (JULY 2020)

A European review of worldwide data concluded that systemically administered VEGF pathway inhibitors may lead to aneurysm and artery dissection in patients with

or without hypertension. Some fatal cases have been reported, mainly in relation to aortic aneurysm rupture and aortic dissection. The MHRA advises healthcare professionals to carefully consider the risk of aneurysm and artery dissection in patients with risk factors before initiating treatment with bevacizumab; any modifiable risk factors (such as smoking and hypertension) should be reduced as much as possible. Patients should be monitored and treated for hypertension as required.

**CAUTIONS** Elective surgery (withhold treatment and avoid for at least 28 days after major surgery or until wound fully healed) . history of cardiovascular disease (increased risk of cardiovascular events, especially in the elderly) . history of hypertension (increased risk of proteinuria—discontinue if nephrotic syndrome) . increased risk of fistulas (discontinue permanently if tracheo-oesophageal or grade 4 fistula develops) . increased risk of haemorrhage . increased risk of tumour-associated haemorrhage . intraabdominal inflammation (risk of gastro-intestinal perforation and gall bladder perforation) . risk factors for aneurysm or artery dissection . risk factors for arterial thromboembolism . uncontrolled hypertension . untreated CNS metastases

**CAUTIONS, FURTHER INFORMATION**

▶ Monitoring of blood pressure The MHRA advises to monitor blood pressure regularly—consult product literature if hypertension occurs during treatment.

**INTERACTIONS** → Appendix 1: monoclonal antibodies

**SIDE-EFFECTS**

▶ Common or very common Abscess . anaemia . appetite decreased . arthralgia . asthenia . congestive heart failure . constipation . cough . decreased leucocytes . dehydration . diarrhoea . drowsiness . dysarthria . dysphonia . dyspnoea . electrolyte imbalance . embolism and thrombosis . eye disorders . fever . fistula . gastrointestinal discomfort . gastrointestinal disorders . haemorrhage . headache . healing impaired . hypersensitivity . hypertension . hypoxia . increased risk of infection . infusion related reaction . mucositis . muscle weakness . myalgia . nausea . neutropenia . ovarian failure . pain . pelvic pain . peripheral neuropathy . proteinuria . rectovaginal fistula . sepsis . skin reactions . stomatitis . stroke . supraventricular tachycardia . syncope . taste altered . thrombocytopenia . vomiting . weight decreased

▶ Rare or very rare Encephalopathy . necrotising fasciitis (discontinue and initiate treatment promptly)

▶ Frequency not known Aneurysm . artery dissection . chest pain . chills . flushing . gallbladder perforation . hyperglycaemia . hypotension . nasal septum perforation . osteonecrosis of jaw . pulmonary hypertension . renal thrombotic microangiopathy

**CONCEPTION AND CONTRACEPTION** Effective contraception required during and for at least 6 months after treatment in women.

**PREGNANCY** Avoid—toxicity in animal studies. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**BREAST FEEDING** Manufacturer advises avoid breastfeeding during and for at least 6 months after treatment.

**MONITORING REQUIREMENTS**

▶ Monitor for necrotising fasciitis (usually secondary to wound healing complications, gastro-intestinal perforation or fistula formation)—discontinue and initiate treatment promptly.

▶ Monitor for congestive heart failure.

▶ Monitor for posterior reversible encephalopathy syndrome (presenting as seizures, headache, altered mental status, visual disturbance or cortical blindness, with or without hypertension).

▶ Consider dental check-up before initiating treatment (risk of osteonecrosis of the jaw).

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions
▶ Bevacizumab and cetuximab for the treatment of metastatic colorectal cancer (January 2007) NICE TA118 Not recommended
▶ Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer (December 2010) NICE TA212 Not recommended
▶ Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy (January 2012) NICE TA242 Not recommended
▶ Bevacizumab (first-line), sorafenib (first and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma (August 2009) NICE TA178 Not recommended
▶ Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer (February 2011) NICE TA214 Not recommended
▶ Bevacizumab in combination with capecitabine for the firstline treatment of metastatic breast cancer (August 2012) NICE TA263 Not recommended
▶ Bevacizumab in combination with paclitaxel and carboplatin for the first-line treatment of advanced ovarian cancer (May 2013) NICE TA284 Not recommended
▶ Bevacizumab in combination with gemcitabine and carboplatin for the treatment of the first recurrence of platinum-sensitive advanced ovarian cancer (May 2013) NICE TA285 Not recommended
▶ Atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma (December 2020) NICE TA666 Recommended with restrictions
▶ Olaparib plus bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer (April 2021) NICE TA693 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Bevacizumab (Avastin ®) in combination with capecitabine for first-line treatment of metastatic breast cancer (May 2012) SMC No. 778/12 Not recommended
▶ Bevacizumab (Avastin ®) in combination with paclitaxel, topotecan, or pegylated liposomal doxorubicin for the treatment of platinum-resistant recurrent ovarian, fallopian tube, or primary peritoneal cancer (September 2015) SMC No. 1063/15 Recommended with restrictions
▶ Bevacizumab (Avastin ®) in combination with carboplatin and paclitaxel, for the front-line treatment of advanced (International Federation of Gynaecology and Obstetrics (FIGO) stages IIIB, IIIC and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer (November 2015) SMC No. 806/12 Recommended with restrictions
All Wales Medicines Strategy Group (AWMSG) decisions
▶ Bevacizumab (Avastin ®) in combination with paclitaxel and cisplatin, or, alternatively, paclitaxel and topotecan in patients who cannot receive platinum therapy, for the treatment of adult patients with persistent, recurrent, or metastatic carcinoma of the cervix (September 2017) AWMSG No. 2166 Not recommended
MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug. Forms available from special-order manufacturers include: solution for injection
Solution for infusion
▶ Alymsys (Zentiva Pharma UK Ltd) A
Bevacizumab 25 mg per 1 ml Alymsys 400mg/16ml concentrate for solution for infusion vials | 1 vialP £810.10 (Hospital only)
Alymsys 100mg/4ml concentrate for solution for infusion vials | 1 vialP £205.55 (Hospital only)



▶ Avastin (Roche Products Ltd)
Bevacizumab 25 mg per 1 ml Avastin 400mg/16ml solution for infusion vials | 1 vialP £924.40 (Hospital only)
Avastin 100mg/4ml solution for infusion vials | 1 vialP £242.66 (Hospital only)
▶ Aybintio (Organon Pharma (UK) Ltd) A
Bevacizumab 25 mg per 1 ml Aybintio 100mg/4ml solution for infusion vials | 1 vialP £218.39 (Hospital only)
Aybintio 400mg/16ml solution for infusion vials | 1 vialP £831.96 (Hospital only)
▶ Oyavas (Thornton & Ross Ltd) A
Bevacizumab 25 mg per 1 ml Oyavas 400mg/16ml concentrate for solution for infusion vials | 1 vialP £877.80 (Hospital only)
Oyavas 100mg/4ml concentrate for solution for infusion vials | 1 vialP £230.00 (Hospital only)
▶ Zirabev (Pfizer Ltd) A

Bevacizumab 25 mg per 1 ml Zirabev 400mg/16ml solution for infusion vials | 1 vial P £902.70 (Hospital only)
Zirabev 100mg/4ml solution for infusion vials | 1 vial P £225.67 (Hospital only)

## Blinatumomab 17-May-2021

I DRUG ACTION The anti-lymphocyte monoclonal antibodies cause lysis of B lymphocytes.

I INDICATIONS AND DOSE

Relapsed or refractory Philadelphia chromosomenegative acute lymphoblastic leukaemia (initiated by a specialist)

▶ BY CONTINUOUS INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

Philadelphia chromosome-negative acute lymphoblastic leukaemia in complete remission with minimal residual disease (initiated by a specialist)

▶ BY CONTINUOUS INTRAVENOUS INFUSION

▶ Adult (body-weight 45 kg and above): (consult product literature)

I CAUTIONS Aphasia . brain injuries (severe) . cerebellar disease . dementia . elderly—limited information available . epilepsy . paresis . Parkinson's disease . patients may need pre-medication to minimise adverse reactions . psychosis . seizure . severe hepatic impairment . severe renal impairment . stroke

CAUTIONS, FURTHER INFORMATION

▶ Pre-medication Manufacturer advises pre-medication with a corticosteroid and an anti-pyretic—consult product literature.

▶ Neurological events There is potentially a higher risk of neurological events in patients with clinically relevant CNS pathology—manufacturer advises caution.

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Abdominal pain . anaemia . arrhythmias . ataxia . chest discomfort . chills . cognitive disorder . confusion . constipation . cough . cranial nerve disorder . decreased leucocytes . diarrhoea . dizziness . drowsiness . dyspnoea . encephalopathy . facial swelling . fever . flushing . headache . hyperbilirubinaemia . hypersensitivity . hypertension . hypogammaglobulinaemia . hypoglobulinaemia . hypotension . immune disorder . increased risk of infection . infusion related reaction . insomnia . leucocytosis . memory loss . nausea . neutropenia . oedema . pain . respiratory disorders . seizure . sensation abnormal . sepsis . skin reactions . speech impairment . thrombocytopenia . tremor . tumour lysis syndrome . vomiting . weight increased

▶ Uncommon Capillary leak syndrome . haemophagocytic lymphohistiocytosis . lymphadenopathy . pancreatitis

▶ Frequency not known Consciousness impaired . psychiatric disorder . viral infection reactivation

SIDE-EFFECTS, FURTHER INFORMATION Pancreatitis Lifethreatening or fatal cases of pancreatitis have been reported; manufacturer advises monitor for signs and symptoms of pancreatitis during treatment—temporary interruption or discontinuation may be required (consult product literature).

Cytokine release syndrome, infusion-reactions and tumour lysis syndrome Life-threatening (including fatal) cases of cytokine release syndrome and tumour lysis syndrome have been reported in patients taking blinatumomab. Manufacturer advises monitor signs and symptoms of cytokine release syndrome and infusion reactions during treatment; temporary interruption or discontinuation may be required—consult product literature.

I CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception during treatment and for at least 48 hours after treatment in women of child-bearing potential. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—no information available; if exposed during pregnancy, monitor infant for B-cell depletion. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING Manufacturer advises avoid during and for at least 48 hours after treatment—no information available.
I HEPATIC IMPAIRMENT Manufacturer advises caution in severe impairment (no information available).
I RENAL IMPAIRMENT gCaution in severe impairment (no information available). M
I MONITORING REQUIREMENTS Manufacturer advises neurological examination prior to the initiation of treatment and continued monitoring during treatment—consult product literature.
I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C); consult product literature for storage conditions after reconstitution and dilution.
I PATIENT AND CARER ADVICE A patient alert card should be provided. Educational materials should be provided to patients, carers and healthcare professionals to ensure blinatumomab is used in a safe and effective way, and to prevent the risk of medication errors and neurological events—consult product information.
Driving and skilled tasks Manufacturer advises patients and carers should be counselled about the effects on driving and performance of skilled tasks—increased risk of confusion, disorientation, co-ordination and balance disorders, seizures and disturbances in consciousness.
I NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Blinatumomab for previously treated Philadelphiachromosome-negative acute lymphoblastic leukaemia (June 2017) NICE TA450 Recommended
▶ Blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity (July 2019) NICE TA589 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Blinatumomab (Blincyto ®) as monotherapy for the treatment of adults with Philadelphia chromosome-negative CD19 positive B-precursor acute lymphoblastic leukaemia in first or second complete remission with minimal residual disease greater than or equal to 0.1% (March 2020) SMC No. SMC2234 Recommended with restrictions



I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Powder for solution for infusion
EXCIPIENTS: May contain Polysorbates
▶ Blincyto (Amgen Ltd) A
Blinatumomab 38.5 microgram Blincyto 38.5micrograms powder for concentrate and solution for solution for infusion vials | 1 vialP £2,017.00 (Hospital only)

## Brentuximab vedotin 03-Feb-2021

I INDICATIONS AND DOSE
CD30 positive Hodgkin lymphoma (specialist use only) | Systemic anaplastic large cell lymphoma (specialist use only) | CD30 positive cutaneous T-cell lymphoma (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: (consult product literature)
I CAUTIONS Elevated BMI—risk of hyperglycaemia . high tumour burden—risk of tumour lysis syndrome . rapidly proliferating tumours—risk of tumour lysis syndrome
I INTERACTIONS → Appendix 1: monoclonal antibodies
I SIDE-EFFECTS
▶ Common or very common Abdominal pain . alopecia . anaemia . arthralgia . back pain . chills . constipation . cough . diarrhoea . dizziness . dyspnoea . fatigue . fever . hyperglycaemia . increased risk of infection . infusion related reaction . myalgia . nausea . nerve disorders . neutropenia . skin reactions . thrombocytopenia . vomiting . weight decreased
▶ Uncommon Anaphylactic reaction . cytomegalovirus infection reactivation . pancreatitis acute . sepsis . severe cutaneous adverse reactions (SCARs) . tumour lysis syndrome
▶ Frequency not known Disease recurrence . gastrointestinal disorders . gastrointestinal haemorrhage . progressive multifocal leukoencephalopathy (PML) . respiratory disorders

I CONCEPTION AND CONTRACEPTION Effective contraception required during treatment and for 6 months after treatment in men and women.
I PREGNANCY Avoid unless potential benefit outweighs risk (toxicity in animal studies).
I BREAST FEEDING Avoid—no information available.
I MONITORING REQUIREMENTS
▶ Monitor for symptoms of progressive multifocal leucoencephalopathy (presenting as new or worsening neurological, cognitive or behavioural signs or symptoms).
▶ Monitor for new or worsening abdominal pain—investigate and withhold treatment if acute pancreatitis suspected and discontinue if confirmed (fatal cases reported).
▶ Monitor for pulmonary toxicity—treat symptoms promptly.
▶ Routinely monitor hepatic function.
▶ Monitor for infusion-related (including anaphylactic) reactions.
▶ Monitor for signs of peripheral neuropathy—consult product literature for treatment adjustment.
I NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma (October 2017) NICE TA478 Recommended with restrictions
▶ Brentuximab vedotin in combination for untreated systemic anaplastic large cell lymphoma (August 2020) NICE TA641 Recommended
▶ Brentuximab vedotin for treating CD30-positive Hodgkin lymphoma (June 2018) NICE TA524 Recommended with restrictions
▶ Brentuximab vedotin for treating CD30-positive cutaneous Tcell lymphoma (April 2019) NICE TA577 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Brentuximab vedotin (Adcetris ®) for the treatment of adult patients with CD30-positive cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy (January 2020) SMC No. SMC2229 Recommended with restrictions
▶ Brentuximab vedotin (Adcetris ®) in combination with cyclophosphamide, doxorubicin and prednisone for adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) (January 2021) SMC No. SMC2310 Recommended
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Powder for solution for infusion
EXCIPIENTS: May contain Polysorbates
ELECTROLYTES: May contain Sodium
▶ Adcetris (Takeda UK Ltd) A
Brentuximab vedotin 50 mg Adcetris 50mg powder for concentrate for solution for infusion vials | 1 vialP £2,500.00 (Hospital only)

## Cemiplimab 19-Jul-2021

I DRUG ACTION Cemiplimab is a human immunoglobulin G4 monoclonal antibody, which binds to the programmed death-1 (PD-1) receptor thereby potentiating an immune response to tumour cells.
I INDICATIONS AND DOSE
Cutaneous squamous cell carcinoma (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: 350 mg every 3 weeks, for dose interruption or discontinuation of treatment due to side-effects or infusion-related reactions—consult product literature
IMPORTANT SAFETY INFORMATION
MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ®) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)
Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic drugs, such as cemiplimab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, cemiplimab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Cemiplimab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of cemiplimab in patients with a history of severe or lifethreatening SCAR associated with other immunostimulant antineoplastic drugs.
I CAUTIONS For full details consult product literature.

I INTERACTIONS → Appendix 1: monoclonal antibodies
I SIDE-EFFECTS
▶ Common or very common Arthralgia . arthritis . asthenia . colitis . diarrhoea . hepatic disorders . hyperthyroidism . hypothyroidism . infusion related reaction . myalgia . pain . pneumonitis . skin reactions . stomatitis
▶ Uncommon Adrenal insufficiency . cardiac inflammation . diabetic ketoacidosis . encephalitis . hypophysitis . immune thrombocytopenic purpura . keratitis . meningitis . muscle weakness . myasthenia gravis . nephritis . nerve disorders . nervous system disorders . Sjögren's syndrome . thyroiditis . type 1 diabetes mellitus . vasculitis
▶ Frequency not known Encephalitis non-infective . severe cutaneous adverse reactions (SCARs)
I CONCEPTION AND CONTRACEPTION Manufacturer advises females of childbearing potential should use effective contraception during treatment and for at least 4 months after the last dose. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
I PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
I BREAST FEEDING Manufacturer advises discontinue breast-feeding during treatment and for at least 4 months after stopping—no information available.
I MONITORING REQUIREMENTS Manufacturer advises monitor for signs and symptoms of infusion- and immunerelated side-effects—consult product literature.
I DIRECTIONS FOR ADMINISTRATION Manufacturer advises for intermittent intravenous infusion, dilute to a concentration between 1 mg/mL and 20 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 30 minutes through a low-protein binding in-line or add-on filter (pore size 0.2–5 micron).
I PRESCRIBING AND DISPENSING INFORMATION Cemiplimab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; manufacturer advises to record the brand name and batch number after each administration.
The manufacturer of Libtayo ® has provided a Risk minimisation materials document for healthcare professionals.
I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C) and protect from light—consult product literature about storage after preparation of the infusion.
I PATIENT AND CARER ADVICE
Risk of immune-related side-effects A patient alert card and patient guide should be provided.
I NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Cemiplimab for treating metastatic or locally advanced cutaneous squamous cell carcinoma (August 2019) NICE TA592 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Cemiplimab (Libtayo ®) as monotherapy for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma (CSCC) who are not candidates for curative surgery or curative radiation (February 2020) SMC No. SMC2216 Recommended
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for infusion
EXCIPIENTS: May contain L-proline, polysorbates, sucrose
▶ Libtayo (Sanofi) A
Cemiplimab 50 mg per 1 ml Libtayo 350mg/7ml concentrate for solution for infusion vials | 1 vialP £4,650.00 (Hospital only)

## Cetuximab 20-May-2021

I INDICATIONS AND DOSE
Metastatic colorectal cancer with a BRAF V600E mutation (in combination with encorafenib) | Treatment of wildtype RAS metastatic colorectal cancer in patients with tumours expressing epidermal growth factor receptor, as combination therapy, or as monotherapy if oxaliplatin- and irinotecan-based therapy has failed or if

irinotecan is not tolerated | Treatment of locally advanced squamous cell cancer of the head and neck (in combination with radiotherapy) | Treatment of recurrent or metastatic squamous cell cancer of the head and neck (in combination with platinum-based chemotherapy)

▶ BY INTRAVENOUS INFUSION

▶ Adult (initiated by a specialist): (consult product literature or local protocols)

IMPORTANT SAFETY INFORMATION

Patients must receive an antihistamine and a corticosteroid at least one hour before infusion. Resuscitation facilities should be available and treatment should be initiated by a specialist.

MHRA/CHM ADVICE: EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITORS: SERIOUS CASES OF KERATITIS AND ULCERATIVE KERATITIS (MAY 2012)

Keratitis and ulcerative keratitis have been reported following treatment with epidermal growth factor receptor (EGFR) inhibitors for cancer (cetuximab, erlotinib, gefitinib and panitumumab). In rare cases, this has resulted in corneal perforation and blindness. Patients undergoing treatment with EGFR inhibitors who present with acute or worsening signs and symptoms suggestive of keratitis should be referred promptly to an ophthalmology specialist. Treatment should be interrupted or discontinued if ulcerative keratitis is diagnosed.

l CONTRA-INDICATIONS

▶ When used for treatment of wild-type ras metastatic colorectal cancer in patients with tumours expressing epidermal growth factor receptor, in combination therapy with oxaliplatin-containing chemotherapy RAS mutated colorectal tumours (or if RAS tumour status unknown)

l CAUTIONS Cardiopulmonary disease . cardiovascular disease . history of keratitis . pulmonary disease—discontinue if interstitial lung disease . risk factors for keratitis . risk factors for ulcerative keratitis (including contact lens use) . severe dry eye

l INTERACTIONS → Appendix 1: monoclonal antibodies

l SIDE-EFFECTS

▶ Common or very common Appetite decreased . cytokine release syndrome . dehydration . diarrhoea . electrolyte imbalance . eye inflammation . fatigue . headache . hypersensitivity . infusion related reaction . mucositis . nausea . skin eruption . vomiting

▶ Uncommon Embolism and thrombosis . interstitial lung disease

▶ Rare or very rare Severe cutaneous adverse reactions (SCARs)

▶ Frequency not known Meningitis aseptic . superinfection of skin lesions

l CONCEPTION AND CONTRACEPTION Contraceptive advice required, see Pregnancy and reproductive function in Cytotoxic drugs p. 962.

l PREGNANCY Use only if potential benefit outweighs risk—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

l BREAST FEEDING Avoid breast-feeding during and for 2 months after treatment—no information available.



l PRE-TREATMENT SCREENING

▶ When used for Treatment of wild-type RAS metastatic colorectal cancer in patients with tumours expressing epidermal growth factor receptor, as combination therapy, or as monotherapy if oxaliplatin- and irinotecan-based therapy has failed or if irinotecan is not tolerated gEvidence of non-mutated (wild-type) RAS status (at exons 2, 3, and 4 of KRAS and NRAS) is required before cetuximab is initiated, and should be determined by an experienced laboratory using a validated test method. M

l MONITORING REQUIREMENTS

▶gMonitor serum electrolyte levels prior to therapy and periodically during treatment.

▶ Monitor for signs and symptoms of infusion-related reactions—consult product literature. M

l DIRECTIONS FOR ADMINISTRATION Manufacturer advises resuscitation facilities should be available.

l NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck (June 2008) NICE TA145 Recommended
▶ Cetuximab for treating recurrent or metastatic squamous cell cancer of the head and neck (August 2017) NICE TA473 Recommended
▶ Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy (January 2012) NICE TA242 Not recommended
▶ Cetuximab and panitumumab for previously untreated metastatic colorectal cancer (updated September 2017) NICE TA439 Recommended with restrictions
▶ Encorafenib plus cetuximab for previously treated BRAF V600E mutation-positive metastatic colorectal cancer (January 2021) NICE TA668 Recommended

ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

▶ Erbitux (Merck Serono Ltd)

Cetuximab 5 mg per 1 ml Erbitux 100mg/20ml solution for infusion vials | 1 vialP £178.10 (Hospital only)

Erbitux 500mg/100ml solution for infusion vials | 1 vialP £890.50 (Hospital only)

## Daratumumab 04-May-2022

ı DRUG ACTION Daratumumab is a monoclonal antibody that binds to CD38, a cell-surface protein, resulting in tumour cell death by immune-mediated actions and apoptosis.

ı INDICATIONS AND DOSE

Multiple myeloma (specialist use only)

▶ BY INTRAVENOUS INFUSION, OR BY SUBCUTANEOUS INJECTION

▶ Adult: (consult product literature or local protocols)

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: DARATUMUMAB (DARZALEX ▪): RISK OF REACTIVATION OF HEPATITIS B VIRUS (AUGUST 2019)

An EU cumulative review of worldwide data has identified reports of hepatitis B virus (HBV) reactivation in patients treated with daratumumab, including several fatal cases. Healthcare professionals are advised to screen all patients for hepatitis B before starting treatment; patients with unknown serology already being treated with daratumumab should also be screened. Those with positive serology should be monitored for signs of HBV reactivation during, and for at least 6 months after, treatment; immediate medical attention should be sought if signs and symptoms of HBV reactivation develop. Daratumumab should be stopped in patients with HBV reactivation and appropriate treatment initiated, based on expert advice. Experts should be consulted before resuming daratumumab in patients with adequately controlled viral reactivation.

ı CAUTIONS History of obstructive pulmonary disorder (consider additional post-medication—consult product literature) . patients may need pre-medication tominimise adverse reactions . risk of herpes zoster reactivation (consider antiviral prophylaxis)

CAUTIONS, FURTHER INFORMATION

▶ Infusion-related reactions Serious infusion-related reactions can occur following either intravenous or subcutaneous injection, and daratumumab should only be administered by appropriately trained staff where resuscitation facilities are available; manufacturer advises pre-medication with a corticosteroid, an antihistamine and an anti-pyretic and post-medication with oral corticosteroids—consult product literature. Manufacturer advises patients should be closely monitored for signs of infusion-related reactions during and after administration; in the event of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated.

ı INTERACTIONS → Appendix 1: monoclonal antibodies

ı SIDE-EFFECTS

▶ Common or very common

▶ With intravenous use Pruritus

▶ With parenteral use Anaemia . appetite decreased . arthralgia . asthenia . atrial fibrillation . chills . constipation . cough . decreased leucocytes . dehydration . diarrhoea . dizziness . dyspnoea . fever . headache . hyperglycaemia . hypertension . hypocalcaemia . increased risk of infection . infusion related reaction . insomnia . muscle spasms . nausea . neutropenia . pain . pancreatitis . paraesthesia . peripheral neuropathy . peripheral oedema . pulmonary oedema . rash . sepsis . thrombocytopenia .

vomiting
▶ Uncommon
▶ With parenteral use Hepatitis B reactivation
SIDE-EFFECTS, FURTHER INFORMATION Manufacturer advises treatment should be immediately interrupted if an infusion-related reaction of any grade or severity occurs—consult product literature for specific management recommendations.
CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in women of childbearing potential during treatment and for 3 months after stopping treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
BREAST FEEDING Manufacturer advises avoid—no information available.
EFFECT ON LABORATORY TESTS Possible positive indirect Coombs test (may affect antibody screening).
HANDLING AND STORAGE Manufacturer advises store in a refrigerator at 2–8°C; consult product literature for storage advice following dilution.
NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (April 2019) NICE TA573 Recommended with restrictions



▶ Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable (February 2022) NICE TA763 Recommended
▶ Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (April 2022) NICE TA783 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Daratumumab (Darzalex ®) as monotherapy, for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and have demonstrated disease progression on the last therapy (October 2017) SMC No. 1205/17 Recommended with restrictions
▶ Daratumumab (Darzalex ®) in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (July 2019) SMC No. SMC2180 Recommended with restrictions
▶ Daratumumab subcutaneous injection (Darzalex ®) in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy (October 2020) SMC No. SMC2301 Recommended with restrictions
▶ Daratumumab subcutaneous injection (Darzalex ®) as monotherapy, for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and have demonstrated disease progression on the last therapy (October 2020) SMC No. SMC2304 Recommended with restrictions
▶ Daratumumab (Darzalex ®) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (January 2021) SMC No. SMC2302 Recommended
▶ Daratumumab subcutaneous injection (Darzalex ®) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant (January 2021) SMC No. SMC2326 Recommended
MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for injection
EXCIPIENTS: May contain Polysorbates, sorbitol
▶ Darzalex (Janssen-Cilag Ltd) A
Daratumumab 120 mg per 1 ml Darzalex 1800mg/15ml solution for injection vials | 1 vialP £4,320.00 (Hospital only)
Solution for infusion
EXCIPIENTS: May contain Polysorbates
ELECTROLYTES: May contain Sodium

▶ **Darzalex** (Janssen-Cilag Ltd) A

Daratumumab 20 mg per 1 ml Darzalex 100mg/5ml concentrate for solution for infusion vials | 1 vial P £360.00 (Hospital only)
Darzalex 400mg/20ml concentrate for solution for infusion vials | 1 vial P £1,440.00 (Hospital only)

## Dinutuximab beta 04-Nov-2020

I DRUG ACTION Dinutuximab beta is a chimeric monoclonal antibody; it specifically targets the carbohydrate moiety of disialoganglioside 2, which is overexpressed on neuroblastoma cells.

I INDICATIONS AND DOSE

High-risk neuroblastoma (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

I CONTRA-INDICATIONS Acute grade 3 or 4, or extensive chronic graft-versus-host disease

I CAUTIONS Avoid vaccinations during and for at least 10 weeks after treatment cessation (increased risk of immune stimulation and neurological toxicity) . ensure absence of systemic infection—any other infection should be controlled before treatment initiation . pre-medication must be administered tominimise the risk of infusionrelated reactions and neuropathic pain

CAUTIONS, FURTHER INFORMATION

▶ Pre-medication Severe infusion-related reactions can occur and dinutuximab beta should only be administered when appropriately trained staff and resuscitation facilities are immediately available; manufacturer advises premedication with an antihistamine, and to monitor closely, particularly during the first and second treatment course; discontinue immediately if reaction occurs and treat as indicated—consult product literature.
Manufacturer advises pre-medication with non-opioid analgesics, gabapentin and opioids—consult product literature.

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Anaemia . anxiety . appetite decreased . arthralgia . ascites . capillary leak syndrome . chest pain . chills . constipation . cough . cytokine release syndrome . decreased leucocytes . device related infection . diarrhoea . dizziness . dyspnoea . electrolyte imbalance . eye disorders . eye inflammation . fever . fluid imbalance . gastrointestinal discomfort . gastrointestinal disorders . haematuria . headache . heart failure . hyperhidrosis . hypersensitivity . hypertension . hypertriglyceridaemia . hypoalbuminaemia . hypotension . hypoxia . increased risk of infection . left ventricular dysfunction . muscle spasms . nausea . neutropenia . oedema . oral disorders . pain . paraesthesia . pericardial effusion . peripheral neuropathy . photosensitivity reaction . pulmonary oedema . renal impairment . respiratory disorders . seizure . sepsis . skin reactions . tachycardia . thrombocytopenia . tremor . urinary retention . urine abnormalities . vision disorders . vomiting . weight changes

▶ Uncommon Disseminated intravascular coagulation . eosinophilia . hepatocellular injury . hypovolaemic shock . intracranial pressure increased . peripheral vascular disease . posterior reversible encephalopathy syndrome (PRES)

▶ Frequency not known Erythropenia

I CONCEPTION AND CONTRACEPTION Manufacturer advises women of childbearing potential should use contraception during and for 6 months after stopping treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY Manufacturer advises avoid—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING Manufacturer advises avoid during treatment and for 6 months after the last dose—no information available.

I MONITORING REQUIREMENTS

▶ Manufacturer advises pre-treatment evaluation of pulse oximetry, bone marrow function, liver function and renal function—consult product literature for values required for treatment initiation.

▶ Manufacturer advises monitor circulatory and respiratory function—risk of capillary leak syndrome.
▶ Manufacturer advises monitor liver function and electrolytes regularly.
ı HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C)—consult product literature for further information regarding storage conditions outside refrigerator and after preparation of the infusion.



ı PATIENT AND CARER ADVICE
Driving and skilled tasks Manufacturer advises patients should not use or drive machines during treatment.
ı NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Dinutuximab beta for treating neuroblastoma (August 2018) NICE TA538 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Dinutuximab beta (Qarziba ®) for the treatment of high-risk neuroblastoma in patients aged 12 months and above, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and stem cell transplantation, as well as patients with history of relapsed or refractory neuroblastoma, with or without residual disease (November 2018) SMC No. SMC2105 Recommended
ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for infusion
▶ Qarziba (EUSA Pharma (UK) Ltd) A
Dinutuximab beta 4.5 mg per 1 ml Qarziba 20mg/4.5ml concentrate for solution for infusion vials | 1 vialP £7,610.00 (Hospital only)

## Dostarlimab 01-Apr-2022

ı DRUG ACTION Dostarlimab is a humanised monoclonal antibody which binds to the programmed death-1 (PD-1) receptor, thereby potentiating an immune response to tumour cells.
ı INDICATIONS AND DOSE
Endometrial cancer (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: 500 mg every 3 weeks for 4 doses on weeks 1, 4, 7, and 10, followed by 1 g every 6 weeks from week 13 onwards, for dose delay or discontinuation due to sideeffects and infusion-related reactions—consult product literature
ı CAUTIONS History of severe or life-threatening cutaneous adverse reactions associated with other immunostimulant antineoplastic drugs . risk of transplant-related complications
CAUTIONS, FURTHER INFORMATION
▶ Transplant-related complications gPatients who receive an allogeneic haematopoietic stem cell transplant before or after dostarlimab treatment may be at an increased risk of transplant-related complications, and should be closely monitored. There may also be an increased risk of rejection in solid organ transplant recipients. M
ı INTERACTIONS → Appendix 1: monoclonal antibodies
ı SIDE-EFFECTS
▶ Common or very common Adrenal insufficiency . anaemia . arthralgia . autoimmune haemolytic anaemia . chills . diarrhoea . enterocolitis haemorrhagic . fever . gastrointestinal disorders . hyperthyroidism . hypertransaminasaemia . hypothyroidism . infusion related reaction . myalgia . nausea . pancreatitis . respiratory disorders . skin reactions . vomiting
▶ Uncommon Diabetic ketoacidosis . eye inflammation . hepatic disorders . hypophysitis . nephritis . thyroiditis . type 1 diabetes mellitus
▶ Frequency not known Hypersensitivity
SIDE-EFFECTS, FURTHER INFORMATION Immune-related reactions Manufacturer advises most immune-related adverse reactions are reversible and managed by temporarily stopping treatment and administration of a corticosteroid—consult product literature.
Infusion-related reactions Manufacturer advises permanently discontinue treatment in patients with severe infusion reactions.
ı CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception

during treatment and for 4 months after last treatment. M See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY g Avoid—limited information available. M See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING g Avoid during treatment and for at least 4 months after last treatment—no information available. M

I MONITORING REQUIREMENTS g Monitor for signs and symptoms of infusion- and immune-related reactions—consult product literature. M

I DIRECTIONS FOR ADMINISTRATION g For intravenous infusion, dilute to a concentration of 2–10 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 30 minutes via an infusion pump. M

I PRESCRIBING AND DISPENSING INFORMATION Dostarlimab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after dilution.

I PATIENT AND CARER ADVICE A patient card should be provided.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (March 2022) NICE TA779 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Dostarlimab (Jemperli ®) as monotherapy for the treatment of adult patients with recurrent or advanced mismatch repair deficient or microsatellite instability-high endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen (March 2022) SMC No. SMC2404 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Dostarlimab (non-proprietary) A

Dostarlimab 50 mg per 1 ml Jemperli 500mg/10ml concentrate for solution for infusion vials | 1 vial P £5,887.33 (Hospital only)



## Durvalumab 19-Jul-2021

I DRUG ACTION Durvalumab is a human monoclonal antibody that selectively binds to programmed cell death ligand-1 (PD-L1), blocking its interaction with the programmed death-1 (PD-1) receptor and with CD80, and thereby potentiating an immune response to tumour cells.

I INDICATIONS AND DOSE

Non-small cell lung cancer (initiated by a specialist)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 10 mg/kg every 2 weeks, consult product literature for information on dose adjustments based on individual patient safety and tolerability

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ®) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)

Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunotimulant antineoplastic drugs, such as durvalumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, durvalumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Durvalumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of durvalumab in patients with a history of severe or lifethreatening SCAR associated with other immunostimulant antineoplastic drugs.

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Cough . diarrhoea . dysphonia . dysuria . fever . flank pain . gastrointestinal discomfort . gastrointestinal disorders . hyperthyroidism . hypothyroidism . increased risk of infection . infusion related reaction . myalgia . night sweats . peripheral oedema . respiratory disorders . skin reactions . thyroiditis

▶ Uncommon Adrenal insufficiency . glomerulonephritis . hepatic disorders . myopathy . nephritis . type 1 diabetes mellitus

▶ Rare or very rare Diabetes insipidus . hypophysitis . hypopituitarism . myocarditis

SIDE-EFFECTS, FURTHER INFORMATION Immune-related reactions Manufacturer advises that most immunerelated adverse reactions resolved with appropriate management, including initiation of immunosuppressive treatment and treatment modifications—consult product literature.

Infusion-related reactions Manufacturer advises to permanently discontinue treatment in patients with severe infusion reactions.

I CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in women of childbearing potential during treatment and for at least 3 months after stopping treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY Manufacturer advises avoid—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING Manufacturer advises avoid—no information available.

I MONITORING REQUIREMENTS Manufacturer advises monitor for signs and symptoms of infusion- and immunerelated reactions—consult product literature.

I DIRECTIONS FOR ADMINISTRATION Manufacturer advises for intravenous infusion, dilute to a concentration between 1 mg/mL and 15 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 60 minutes through a low-protein binding in-line filter (pore size 0.2 or 0.22 micron).

I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after preparation of the infusion.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Durvalumab for treating locally advanced unresectable nonsmall-cell lung cancer after platinum-based chemoradiation (May 2019) NICE TA578 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Durvalumab (Imfinzi ®) for locally advanced, unresectable non-small cell lung cancer after platinum-based chemoradiation in adults (June 2019) SMC No. SMC2156 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Imfinzi (AstraZeneca UK Ltd) A

Durvalumab 50 mg per 1 ml Imfinzi 120mg/2.4ml concentrate for solution for infusion vials | 1 vialP £592.00 (Hospital only)

Imfinzi 500mg/10ml concentrate for solution for infusion vials | 1 vialP £2,466.00 (Hospital only)

## Elotuzumab 12-Apr-2019

I DRUG ACTION Elotuzumab is a monoclonal antibody that targets the signalling lymphocytic activation molecule family member 7 (SLAMF7) protein, thereby activating natural killer cells and mediating myeloma cell death.

I INDICATIONS AND DOSE

Multiple myeloma in patients who have received at least one prior therapy (in combination with lenalidomide and dexamethasone) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 10 mg/kg every week, on days 1, 8, 15 and 22 of cycles 1 and 2, then 10 mg/kg every 2 weeks, on days 1 and 15 of subsequent cycles

I CAUTIONS Pre-medication must be administered to minimise the development of infusion-related reactions—consult product literature . secondary primary malignancies

CAUTIONS, FURTHER INFORMATION

▶ Secondary primary malignancies Manufacturer advises to monitor for the development of secondary primary malignancy before and during treatment with elotuzumab.

INTERACTIONS → Appendix 1: monoclonal antibodies

SIDE-EFFECTS

▶ Common or very common Chest pain . cough . decreased leucocytes . deep vein thrombosis . diarrhoea . fatigue . fever . headache . hypersensitivity . increased risk of infection . infusion related reaction . mood altered . night sweats . numbness . oropharyngeal pain . weight decreased

▶ Frequency not known Second primary malignancy

SIDE-EFFECTS, FURTHER INFORMATION Side-effects reported when used in combination with lenalidomide and dexamethasone, bortezomib and dexamethasone, or pomalidomide and dexamethasone.



Infusion-related reactions Manufacturer advises for mild-to-moderate infusion reactions interrupt treatment or reduce infusion rate, and monitor closely (consult product literature); permanently discontinue therapy in severe infusion reactions.

CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in men and women of childbearing potential; male patients should continue effective contraceptive measures for 180 days after stopping treatment if their partner is pregnant or of childbearing potential. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

PREGNANCY Manufacturer advises avoid unless essential—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C); consult product literature for storage conditions after preparation of the infusion.

MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

EXCIPIENTS: May contain Polysorbates, sucrose

▶ Empliciti (Bristol-Myers Squibb Pharmaceuticals Ltd)
Elotuzumab 300 mg Empliciti 300mg powder for concentrate for solution for infusion vials | 1 vialP £1,085.00 (Hospital only)
Elotuzumab 400 mg Empliciti 400mg powder for concentrate for solution for infusion vials | 1 vialP £1,446.00 (Hospital only)

## Gemtuzumab ozogamicin 06-Nov-2020

DRUG ACTION Gemtuzumab ozogamicin is a monoclonal antibody that binds to CD33-expressing tumour cells to induce cell cycle arrest and apoptotic cell death.

INDICATIONS AND DOSE

CD33-positive acute myeloid leukaemia (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

CAUTIONS Adverse-risk cytogenetics (consider benefits and risks of treatment, consult product literature) . haematopoietic stem cell transplantation (increased risk of hepatotoxicity) . pre-medication recommended to minimise adverse reactions

CAUTIONS, FURTHER INFORMATION

▶ Pre-medication Serious infusion-related reactions can occur and gemtuzumab ozogamicin should only be administered when appropriately trained staff and resuscitation facilities are immediately available; manufacturer advises pre-medication with a corticosteroid, paracetamol and antihistamine 1 hour prior to dosing, and to take appropriate measures to help prevent the development of tumour lysis-related hyperuricaemia—consult product literature.

INTERACTIONS → Appendix 1: gemtuzumab ozogamicin

SIDE-EFFECTS

▶ Common or very common Anaemia . appetite decreased . ascites . chills . constipation . decreased leucocytes . diarrhoea . dyspnoea . fatigue . fever . gastrointestinal discomfort . gastrointestinal disorders . haemorrhage . headache . hepatic disorders . hyperbilirubinaemia . hyperglycaemia . hypertension . hypotension . infection . infusion related reaction (including fatal cases) . multi organ failure . nausea . neutropenia . oedema . pancytopenia . sinusoidal obstruction syndrome . skin reactions . stomatitis . tachycardia . thrombocytopenia . tumour lysis syndrome (including fatal cases) . vomiting

▶ Frequency not known Interstitial pneumonia

SIDE-EFFECTS, FURTHER INFORMATION Infusion-related reactions (including fatal cases) can occur during the first 24 hours after administration. Manufacturer advises interrupt treatment immediately and treat as clinically indicated (consult product literature); permanent discontinuation should be strongly considered in patients who develop signs and symptoms of anaphylaxis.

I CONCEPTION AND CONTRACEPTION Manufacturer advises women of childbearing potential should use 2 methods of effective contraception during treatment and for at least 7 months after the last dose; male patients should use 2 methods of effective contraception during treatment and for at least 4 months after the last dose if their partner is of childbearing potential. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—toxicity in animal studies. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING Manufacturer advises avoid during treatment and for at least one month after the last dose—no information available.

I HEPATIC IMPAIRMENT Manufacturer advises caution in moderate-to-severe impairment—increased risk of developing hepatotoxicity; postpone treatment if serum transaminases (ALT or AST) greater than 2.5 times the upper limit of normal or total bilirubin greater than 2 times the upper limit of normal.

I MONITORING REQUIREMENTS

▶ Manufacturer advises monitor complete blood counts prior to each dose as well as signs and symptoms of infection, bleeding and other effects of myelosuppression during treatment; dose interruption or discontinuation of treatment may be required—consult product literature.

▶ Manufacturer advises monitor for signs and symptoms of infusion-related reactions—close clinical monitoring, including pulse, blood pressure and temperature, should be performed during infusion; monitor for signs and symptoms of tumour lysis syndrome.

▶ Manufacturer advises monitor for signs and symptoms of hepatotoxicity (including hepatic veno-occlusive disease); liver tests should be monitored prior to each dose—consult product literature.

I PRESCRIBING AND DISPENSING INFORMATION

Gemtuzumab ozogamicin is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1.

I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after reconstitution and dilution.

I PATIENT AND CARER ADVICE

Driving and skilled tasks Manufacturer advises patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue and headache.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Gemtuzumab ozogamicin for untreated acute myeloid leukaemia (November 2018) NICE TA545 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Gemtuzumab ozogamicin (Mylotarg ⁎) as combination therapy with daunorubicin and cytarabine for the treatment of patients age 15 years and above with previously untreated, de novo CD33-positive acute myeloid leukaemia, except acute promyelocytic leukaemia (October 2018) SMC No. SMC2089 Recommended with restrictions



I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

▶ Mylotarg (Pfizer Ltd) A

Gemtuzumab ozogamicin 5 mg Mylotarg 5mg powder for concentrate for solution for infusion vials | 1 vial P £6,300.00 (Hospital only)

## Inotuzumab ozogamicin 09-Nov-2020

I DRUG ACTION Inotuzumab ozogamicin is a monoclonal antibody that binds to CD22-expressing tumour cells to induce cell cycle arrest and apoptotic cell death.

I INDICATIONS AND DOSE

Monotherapy for relapsed or refractory CD22-positive B cell precursor acute lymphoblastic leukaemia (under expert supervision)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

CONTRA-INDICATIONS Prior confirmed severe or ongoing sinusoidal obstruction syndrome

CAUTIONS History of, or predisposition to QT-interval prolongation (e.g. electrolyte disturbances, concomitant use of drugs that prolong the QT interval) . patients may need pre-medication to minimise adverse reactions . patients undergoing haematopoietic stem cell transplantation (increased risk of hepatotoxicity)

CAUTIONS, FURTHER INFORMATION

▶ Pre-medication Manufacturer advises pre-medication with a corticosteroid, antipyretic and antihistamine prior to dosing in all patients and pre-medication to reduce uric acid levels and hydration in patients with a high tumour burden (increased risk of tumour lysis syndrome)—consult product literature.

INTERACTIONS → Appendix 1: monoclonal antibodies

SIDE-EFFECTS

▶ Common or very common Anaemia . appetite decreased . ascites . bone marrow disorders . central nervous system haemorrhage . chills . constipation . decreased leucocytes . diarrhoea . fatigue . fever . gastrointestinal discomfort . haemorrhage . headache . hyperbilirubinaemia . hypersensitivity . hyperuricaemia . increased risk of infection . infusion related reaction . nausea . neutropenia . QT interval prolongation . sepsis . sinusoidal obstruction syndrome . stomatitis . thrombocytopenia . tumour lysis syndrome . vomiting

▶ Frequency not known Hepatotoxicity

SIDE-EFFECTS, FURTHER INFORMATION Manufacturer advises interrupt treatment if an infusion related reaction occurs; depending on the severity, discontinuation of the infusion or administration of steroids and antihistamines should be considered (consult product literature); permanently discontinue treatment in severe or lifethreatening infusion reactions.

CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in women of childbearing potential during treatment and for at least 8 months after the last dose; male patients should use effective contraception during treatment and for at least 5 months after the last dose if their partner is of childbearing potential. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—toxicity in animal studies.

BREAST FEEDING Manufacturer advises avoid during treatment and for at least two months after the last dose—no information available.

HEPATIC IMPAIRMENT Manufacturer advises caution if bilirubin and transaminase levels are raised (limited information available); avoid in serious ongoing impairment.

Dose adjustments Manufacturer advises dose interruption or discontinuation according to bilirubin and transaminase levels.

PRE-TREATMENT SCREENING Manufacturer advises baseline CD22 positivity of greater than 0% is required prior to initiating treatment.

MONITORING REQUIREMENTS

▶ Manufacturer advises monitor complete blood counts prior to each dose as well as signs and symptoms of infection, bleeding and other effects of myelosuppresion during treatment; dose reduction or interruption or discontinuation of treatment may be required—consult product literature.

▶ Manufacturer advises monitor for signs of infusion related-reactions during and for at least 1 hour after infusion; monitor for signs and symptoms of tumour lysis syndrome.

▶ Manufacturer advises ECG and electrolytes should be monitored prior to the start of treatment and periodically during treatment; monitor for increases in serum amylase and lipase.

▶ Manufacturer advises monitor for signs and symptoms of sinusoidal obstruction syndrome; liver tests should be monitored prior to and following each dose—consult product literature.

DIRECTIONS FOR ADMINISTRATION Manufacturer advises

resuscitation facilities should be available during administration.

**PRESCRIBING AND DISPENSING INFORMATION** Inotuzumab ozogamicin is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; manufacturer advises to record the brand name and batch number after each administration.

**HANDLING AND STORAGE** Manufacturer advises store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after reconstitution and dilution.

**PATIENT AND CARER ADVICE**

Driving and skilled tasks Manufacturer advises patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Inotuzumab ozogamicin for treating relapsed or refractory Bcell acute lymphoblastic leukaemia (September 2018) NICE TA541 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Inotuzumab ozogamicin (Besponsa ◆) as monotherapy for the treatment of adults with relapsed or refractory CD22-positive B cell precursor acute lymphoblastic leukaemia (ALL). Adult patients with Philadelphia chromosome positive relapsed or refractory B cell precursor ALL should have failed treatment with at least 1 tyrosine kinase inhibitor (June 2018) SMC No. 1328/18 Recommended with restrictions

**MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

ELECTROLYTES: May contain Sodium

▶ Besponsa (Pfizer Ltd) A

Inotuzumab ozogamicin 1 mg Besponsa 1mg powder for concentrate for solution for infusion vials | 1 vial P £8,048.00 (Hospital only)



## Ipilimumab 08-Apr-2022

**DRUG ACTION** Ipilimumab is a monoclonal antibody which causes T-cell activation resulting in tumour cell death.

**INDICATIONS AND DOSE**

Melanoma (as monotherapy) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 3 mg/kg every 3 weeks for 4 doses, for dose interruption or discontinuation of treatment due to immune-related side-effects—consult product literature

Melanoma (in combination with nivolumab) (specialist use only) | Renal cell carcinoma (in combination with nivolumab) (specialist use only) | Non-small cell lung cancer (in combination with nivolumab and platinumbased chemotherapy) (specialist use only) | Malignant pleural mesothelioma (in combination with nivolumab) (specialist use only) | Colorectal cancer (in combination with nivolumab) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

**IMPORTANT SAFETY INFORMATION**

MHRA/CHM ADVICE: IPILIMUMAB (YERVOY ◆): REPORTS OF CYTOMEGALOVIRUS (CMV) GASTROINTESTINAL INFECTION OR REACTIVATION (JANUARY 2019)

There have been post-marketing cases of gastrointestinal CMV infection or reactivation in ipilimumab-treated patients reported to have corticosteroid-refractory immune-related colitis, including fatal cases.

Patients should be advised to contact their healthcare professional immediately at the onset of symptoms of colitis. Possible causes, including infections, should be investigated; a stool infection work-up should be performed and patients screened for CMV. For patients with corticosteroid-refractory immune-related colitis, use of an additional immunosuppressive agent should only be considered if other causes are excluded using viral PCR on biopsy, and eliminating other viral, bacterial, and parasitic causes.

MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ◆) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)

Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic

drugs, such as ipilimumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, ipilimumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Ipilimumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of ipilimumab in patients with a history of severe or lifethreatening SCAR associated with other immunostimulant antineoplastic drugs.

ı CAUTIONS For full details consult product literature.

ı INTERACTIONS → Appendix 1: monoclonal antibodies

ı SIDE-EFFECTS

▶ Common or very common Alopecia . anaemia . appetite decreased . arthralgia . asthenia . cancer pain . chills . confusion . constipation . cough . dehydration . diarrhoea . dizziness . dyspnoea . electrolyte imbalance . eye discomfort . fever . gastrointestinal discomfort . gastrointestinal disorders . haemorrhage . headache . hepatic disorders . hypophysitis . hypopituitarism . hypotension . hypothyroidism . influenza like illness . lethargy . lymphopenia . mucositis . muscle complaints . musculoskeletal discomfort . nausea . nerve disorders . night sweats . oedema . pain . skin reactions . vasodilation . vision disorders . vomiting . weight decreased

▶ Uncommon Adrenal hypofunction . alkalosis . allergic rhinitis . amenorrhoea . arrhythmias . arthritis . brain oedema . depression . dysarthria . eosinophilia . eye inflammation . glomerulonephritis . haemolytic anaemia . hair colour changes . hypersensitivity . hyperthyroidism . hypogonadism . increased risk of infection . infusion related reaction . libido decreased . meningitis aseptic . movement disorders . multi organ failure . muscle weakness . myopathy . nephritis autoimmune . neutropenia . pancreatitis . paraneoplastic syndrome . peripheral ischaemia . polymyalgia rheumatica . psychiatric disorder . pulmonary oedema . renal failure . renal tubular acidosis . respiratory disorders . sepsis . severe cutaneous adverse reactions (SCARs) . stomatitis . syncope . systemic inflammatory response syndrome . thrombocytopenia . tremor . tumour lysis syndrome . vascular disorders . vasculitis

▶ Rare or very rare Myasthenia gravis . proteinuria . serous retinal detachment . thyroiditis

▶ Frequency not known Cytomegalovirus infection reactivation . haemophagocytic lymphohistiocytosis . solid organ transplant rejection

SIDE-EFFECTS, FURTHER INFORMATION A corticosteroid can be used after starting ipilimumab, to treat immunerelated reactions.

ı CONCEPTION AND CONTRACEPTION Use effective contraception.

ı PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—toxicity in animal studies.

ı BREAST FEEDING Manufacturer advises avoid—present in milk in animal studies.

ı HEPATIC IMPAIRMENT Manufacturer advises caution if bilirubin greater than 3 times upper limit of normal range or if transaminases equal to or greater than 5 times upper limit of normal range (limited information available).

ı MONITORING REQUIREMENTS

▶$_g$Monitor liver function tests and thyroid function prior to initiation of treatment and before each dose.

▶ Monitor for electrolyte disturbances before and periodically during treatment.

▶ Monitor for signs and symptoms of gastrointestinal perforation, immune-related reactions, and cardiac and pulmonary reactions during treatment—consult product literature. Patients should be monitored for adverse reactions for at least 5 months after the last dose. M

ı DIRECTIONS FOR ADMINISTRATION $_g$For intravenous infusion, give undiluted or dilute to a concentration of

1–4 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 30 or 90 minutes (depending on dose—consult product literature) through an in-line filter (pore size 0.2–1.2 micron). M

I PRESCRIBING AND DISPENSING INFORMATION Ipilimumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

Infusion-related side-effects have been reported. If mild or moderate reactions occur, premedication is recommended; treatment should be discontinued for severe reactions.

I HANDLING AND STORAGE Manufacturer advises store in a refrigerator (2–8 °C) and protect from light—consult product literature for further information regarding



storage conditions outside refrigerator and after preparation of the infusion.

I PATIENT AND CARER ADVICE A patient information guide and alert card should be provided.

Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma (December 2012) NICE TA268 Recommended with restrictions

▶ Ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma (July 2014) NICE TA319 Recommended with restrictions

▶ Nivolumab in combination with ipilimumab for treating advanced melanoma (July 2016) NICE TA400 Recommended with restrictions

▶ Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (July 2021) NICE TA716 Recommended

▶ Nivolumab with ipilimumab and chemotherapy for untreated metastatic non-small-cell lung cancer (September 2021) NICE TA724 Not recommended

▶ Nivolumab with ipilimumab for untreated advanced renal cell carcinoma (March 2022) NICE TA780 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Ipilimumab (Yervoy *) for the treatment of advanced (unresectable or metastatic) melanoma in adults who have received prior therapy (April 2013) SMC No. 779/12 Recommended

▶ Ipilimumab (Yervoy *) for the treatment of advanced (unresectable or metastatic) melanoma in adults (first-line use) (November 2014) SMC No. 997/14 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

ELECTROLYTES: May contain Sodium

▶ Yervoy (Bristol-Myers Squibb Pharmaceuticals Ltd)

Ipilimumab 5 mg per 1 ml Yervoy 50mg/10ml concentrate for solution for infusion vials | 1 vialP £3,750.00 (Hospital only)

Yervoy 200mg/40ml concentrate for solution for infusion vials | 1 vialP £15,000.00 (Hospital only)

## Isatuximab 10-Feb-2022

I DRUG ACTION Isatuximab is a monoclonal antibody that binds to CD38, a cell-surface protein, resulting in tumour cell death by immune-mediated actions and apoptosis.

I INDICATIONS AND DOSE

Multiple myeloma (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 10 mg/kg every week on days 1, 8, 15 and 22 of the first 28-day cycle, then 10 mg/kg every 2 weeks on days 1 and 15 of subsequent 28-day cycles until disease progression or unacceptable toxicity, for dose interruption, adjustment of infusion rate or discontinuation of treatment due to infusion-related reactions or side-effects—consult product literature

I CAUTIONS Pre-medication must be administered to minimise the development of infusion-related reactions—consult product literature . secondary primary malignancies

CAUTIONS, FURTHER INFORMATION

▶ Infusion-related reactions Serious infusion-related reactions

can occur and isatuximab should only be administered when appropriately trained staff and resuscitation facilities are immediately available; manufacturer advises pre-medication with dexamethasone, an antihistamine, and an anti-pyretic—consult product literature. Manufacturer advises patients should be closely monitored for signs of infusion-related reactions during and after administration; in the event of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated—consult product literature.

▶ Secondary primary malignancies Manufacturer advises to monitor for the development of secondary primary malignancy before and during treatment with isatuximab and initiate treatment as indicated.

**SIDE-EFFECTS**

▶ Common or very common Appetite decreased . atrial fibrillation . diarrhoea . dyspnoea . fatigue . increased risk of infection . infusion related reaction . nausea . neoplasms . neutropenia . vomiting . weight decreased

▶ Uncommon Anaphylactic reaction

**CONCEPTION AND CONTRACEPTION** Manufacturer advises effective contraception in female patients of childbearing potential during treatment and for 5 months after last treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**PREGNANCY** Manufacturer advises avoid—no information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**BREAST FEEDING** Manufacturer advises avoid during first few days after birth—possible risk from transfer of antibodies to infant. After this time, use during breastfeeding only if clinically needed.

**EFFECT ON LABORATORY TESTS** Manufacturer advises may cause false positive indirect Coombs test—consult product literature. Manufacturer advises may affect accuracy of both serum protein electrophoresis (SPE) and immunofixation (IFE) assays—consult product literature.

**PRESCRIBING AND DISPENSING INFORMATION** The manufacturer of Sarclisa ∗ has provided a Prescriber Brochure.

Isatuximab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; manufacturer advises to record the brand name and batch number after each administration.

**HANDLING AND STORAGE** Store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after preparation of the infusion.

**PATIENT AND CARER ADVICE** A patient alert card should be provided.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (November 2020) NICE TA658 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Isatuximab (Sarclisa ∗) in combination with pomalidomide and dexamethasone for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor, and have demonstrated disease progression on the last therapy (April 2021) SMC No. SMC2303 Recommended with restrictions

**MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates, sucrose

▶ Sarclisa (Sanofi Genzyme) A

Isatuximab 20 mg per 1 ml Sarclisa 500mg/25ml concentrate for solution for infusion vials | 1 vialP £2,534.69 (Hospital only)



Sarclisa 100mg/5ml concentrate for solution for infusion vials | 1 vialP £506.94 (Hospital only)

## Mogamulizumab 04-Jan-2022

**DRUG ACTION** Mogamulizumab is a monoclonal antibody, which binds to the CCR4 receptor, thereby potentiating an immune response to cancer cells.

**INDICATIONS AND DOSE**

Mycosis fungoides (initiated by a specialist) | Sézary syndrome (initiated by a specialist)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 1 mg/kg every week on days 1, 8, 15 and 22 of the first 28-day cycle, followed by 1 mg/kg every 2 weeks on days 1 and 15 of subsequent 28-day cycles, dose to be administered within 2 days of the scheduled day, for treatment interruption or discontinuation due to side-effects and infusion-related reactions—consult product literature

**CAUTIONS** Patients may need pre-medication to minimise infusion-related reactions . risk factors for cardiac disorders . risk of serious infection and/or viral reactivation such as hepatitis B . risk of transplant-related complications

**CAUTIONS, FURTHER INFORMATION**

▶ Pre-medication Manufacturer advises pre-medication with an antihistamine and an anti-pyretic—consult product literature.

▶ Hepatitis B infection Manufacturer advises patients should be tested for hepatitis B infection before treatment initiation; expert advice on measures against hepatitis B reactivation should be sought for patients with positive hepatitis B serology.

▶ Transplant-related complications Manufacturer advises patients who receive an allogeneic haematopoietic stem cell transplant within 50 days of mogamulizumab treatment are at higher risk of complications, such as severe graft-versus-host disease, and should be closely monitored.

**INTERACTIONS** → Appendix 1: monoclonal antibodies

**SIDE-EFFECTS**

▶ Common or very common Anaemia . constipation . diarrhoea . fatigue . fever . headache . hypothyroidism . increased risk of infection . infusion related reaction . leucopenia . nausea . neutropenia . peripheral oedema . sepsis . skin reactions . stomatitis . thrombocytopenia . vomiting

▶ Uncommon Hepatic disorders . tumour lysis syndrome

▶ Frequency not known Cardiomyopathy . myocardial infarction . polymyositis . severe cutaneous adverse reactions (SCARs) . viral infection reactivation

**CONCEPTION AND CONTRACEPTION** Manufacturer advises effective contraception in male and female patients of childbearing potential during treatment and for at least 6 months after last treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**PREGNANCY** Manufacturer advises avoid—limited information available. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**BREAST FEEDING** Manufacturer advises avoid during first few days after birth—possible risk from transfer of antibodies to infant. After this time, use during breastfeeding only if clinically needed.

**MONITORING REQUIREMENTS** Manufacturer advises monitor electrolytes, hydration status and renal function, particularly in the first month of treatment—risk of tumour lysis syndrome.

**DIRECTIONS FOR ADMINISTRATION** Manufacturer advises for intravenous infusion (Poteligeo ®), dilute to a concentration between 0.1 mg/mL to 3 mg/mL with Sodium Chloride 0.9%; give over at least 60 minutes through a low-protein binding 0.22 micron in-line filter. Resuscitation facilities should be available.

**HANDLING AND STORAGE** Store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after preparation of the infusion.

**PATIENT AND CARER ADVICE**

Driving and skilled tasks Manufacturer advises patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Mogamulizumab for previously treated mycosis fungoides and Sézary syndrome [in adults with mycosis fungoides] (December 2021) NICE TA754 Recommended with restrictions

▶ Mogamulizumab for previously treated mycosis fungoides and Sézary syndrome [in adults with Sézary syndrome] (December 2021) NICE TA754 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Mogamulizumab (Poteligeo ®) for the treatment of adult patients with mycosis fungoides or Sézary syndrome who have received at least one prior systemic therapy (June 2021) SMC No. SMC2336 Recommended with restrictions

ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Poteligeo (Kyowa Kirin Ltd) A

Mogamulizumab 4 mg per 1 ml Poteligeo 20mg/5ml concentrate for solution for infusion vials | 1 vialP £1,329.00 (Hospital only)

## Nivolumab 01-Apr-2022

ı DRUG ACTION Nivolumab is a human immunoglobulin G4 monoclonal antibody, which binds to the programmed death-1 (PD-1) receptor thereby potentiating an immune response to tumour cells.

ı INDICATIONS AND DOSE

Melanoma (in combination with ipilimumab) (specialist use only) | Renal cell carcinoma (in combination with cabozantinib or ipilimumab) (specialist use only) | Nonsmall cell lung cancer (in combination with ipilimumab and platinum-based chemotherapy) (specialist use only) | Malignant pleural mesothelioma (in combination with ipilimumab) (specialist use only) | Colorectal cancer (in combination with ipilimumab) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

Melanoma (as monotherapy) (specialist use only) | Renal cell carcinoma (as monotherapy) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 240 mg every 2 weeks, for dose delay or discontinuation due to side-effects and infusionrelated reactions—consult product literature, alternatively 480 mg every 4 weeks, for dose delay or discontinuation due to side-effects and infusionrelated reactions—consult product literature



Non-small cell lung cancer (as monotherapy) (specialist use only) | Urothelial carcinoma (as monotherapy) (specialist use only) | Squamous cell cancer of the head and neck (as monotherapy) (specialist use only) | Classical Hodgkin lymphoma (as monotherapy) (specialist use only) | Oesophageal squamous cell carcinoma (as monotherapy) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 240 mg every 2 weeks, for dose delay or discontinuation due to side-effects and infusionrelated reactions—consult product literature

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: NIVOLUMAB (OPDIVO ▪): REPORTS OF ORGAN TRANSPLANT REJECTION (JULY 2017)

A European review of worldwide data concluded that nivolumab may increase the risk of rejection in organ transplant recipients. The MHRA recommends considering the benefit of treatment with nivolumab versus the risk of possible organ transplant rejection for each patient.

MHRA/CHM ADVICE: NIVOLUMAB (OPDIVO ▪): REPORTS OF CYTOMEGALOVIRUS (CMV) GASTROINTESTINAL INFECTION OR REACTIVATION (OCTOBER 2019)

A European review of worldwide data identified cases suggestive of gastrointestinal CMV infection or reactivation in nivolumab-treated patients, including fatal cases.

Patients should be advised to contact their healthcare professional immediately at the onset of symptoms of colitis. Possible causes, including infections, should be investigated; a stool infection work-up should be performed and patients screened for CMV. For patients with corticosteroid-refractory immune-related colitis, use of an additional immunosuppressive agent should only be considered if other causes are excluded using viral PCR on biopsy, and eliminating other viral, bacterial, and parasitic causes.

MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ▪) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)

Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic drugs, such as nivolumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, nivolumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Nivolumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution

is recommended when considering the use of nivolumab in patients with a history of severe or life-threatening SCAR associated with other immunostimulant antineoplastic drugs.

**CAUTIONS** Haematopoietic stem cell transplant in patients with classical Hodgkin lymphoma . rapidly progressing or aggressive disease (delayed onset of effect)

**CAUTIONS, FURTHER INFORMATION**

▶ Haematopoietic stem cell transplant

▶ When used for classical Hodgkin lymphoma gNivolumab may increase the risk of severe and potentially fatal graftversus-host disease when used in patients with classical Hodgkin lymphoma who have undergone allogeneic haematopoietic stem cell transplant, particularly if there is a history of graft-versus-host disease. M

**INTERACTIONS** → Appendix 1: monoclonal antibodies

**SIDE-EFFECTS**

▶ Common or very common Abdominal pain . alopecia . anaemia . appetite decreased . arthralgia . constipation . cough . decreased leucocytes . diarrhoea . dizziness . dry eye . dry mouth . dyspnoea . electrolyte imbalance . fatigue . fever . gastrointestinal disorders . haemolytic anaemia . headache . hyperglycaemia . hypersensitivity . hypertension . hyperthyroidism . hypoglycaemia . hypothyroidism . increased risk of infection . inflammation . infusion related reaction . muscle complaints . musculoskeletal discomfort . nausea . nerve disorders . neutropenia . oedema . pain . respiratory disorders . skin reactions . stomatitis . thrombocytopenia . vomiting . weight decreased

▶ Uncommon Adrenal hypofunction . arrhythmias . arthritis . cardiac inflammation . chest pain . dehydration . diabetes mellitus . eosinophilia . eye inflammation . hepatic disorders . hypophysitis . hypopituitarism . metabolic acidosis . nephritis . pancreatitis . paresis . pericardial disorders . renal impairment . sarcoidosis . thyroiditis . vision blurred

▶ Rare or very rare Connective tissue disorders . demyelination . diabetic ketoacidosis . histiocytic necrotising lymphadenitis . myopathy . neuromuscular dysfunction . severe cutaneous adverse reactions (SCARs) . vasculitis

▶ Frequency not known Cytomegalovirus infection reactivation . haemophagocytic lymphohistiocytosis . hypoparathyroidism. meningitis aseptic . solid organ transplant rejection . tumour lysis syndrome

**SIDE-EFFECTS, FURTHER INFORMATION** Immune-related reactions Manufacturer advises that most immunerelated adverse reactions improved or resolved with appropriate management, including initiation of corticosteroids and treatment modifications—consult product literature for further information.

Infusion-related reactions Manufacturer advises that patients with mild or moderate infusion reactions may continue treatment with close monitoring and use of premedication according to local guidelines; discontinue treatment if severe infusion reactions occur.

**CONCEPTION AND CONTRACEPTION** Manufacturer advises effective contraception required during treatment and for at least 5 months after treatment in women of childbearing potential.

**PREGNANCY** Manufacturer advises avoid unless potential benefit outweighs risk—toxicity in animal studies.

**BREAST FEEDING** Manufacturer advises avoid—no information available.

**HEPATIC IMPAIRMENT** Manufacturer advises caution in moderate to severe impairment (limited information available).

**MONITORING REQUIREMENTS**

▶gMonitor for signs and symptoms of immune-related reactions, and cardiac and pulmonary reactions during treatment. Patients should be monitored for adverse reactions for at least 5 months after the last dose.

▶ Monitor for electrolyte disturbances before and periodically during treatment. M

**DIRECTIONS FOR ADMINISTRATION** Manufacturer advises for intermittent intravenous infusion, give undiluted or

dilute to a concentration of not less than 1 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 30 or 60 minutes (depending on dose—consult product literature) through an in-line filter (pore size 0.2–1.2 micron).

**PRESCRIBING AND DISPENSING INFORMATION** Nivolumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

**HANDLING AND STORAGE** Manufacturer advises store in a refrigerator (2–8 °C)—consult product literature for storage conditions after preparation of the infusion.

**PATIENT AND CARER ADVICE** Patients should be provided with a patient alert card with each prescription.

Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Nivolumab for treating advanced (unresectable or metastatic) melanoma (February 2016) NICE TA384 Recommended

▶ Nivolumab in combination with ipilimumab for treating advanced melanoma (July 2016) NICE TA400 Recommended with restrictions

▶ Nivolumab for adjuvant treatment of completely resected melanoma with lymph node involvement or metastatic disease (March 2021) NICE TA684 Recommended

▶ Nivolumab for previously treated advanced renal cell carcinoma (updated November 2017) NICE TA417 Recommended

▶ Nivolumab with ipilimumab for untreated advanced renal cell carcinoma (March 2022) NICE TA780 Recommended

▶ Nivolumab for treating relapsed or refractory classical Hodgkin lymphoma (updated November 2017) NICE TA462 Recommended with restrictions

▶ Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy (October 2020) NICE TA655 Recommended with restrictions

▶ Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy (July 2021) NICE TA713 Recommended with restrictions

▶ Nivolumab with ipilimumab and chemotherapy for untreated metastatic non-small-cell lung cancer (September 2021) NICE TA724 Not recommended

▶ Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (July 2018) NICE TA530 Not recommended

▶ Nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer (June 2021) NICE TA707 Recommended

▶ Nivolumab for adjuvant treatment of resected oesophageal or gastro-oesophageal junction cancer (November 2021) NICE TA746 Recommended

▶ Nivolumab with ipilimumab for previously treated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (July 2021) NICE TA716 Recommended

▶ Nivolumab for treating recurrent or metastatic squamous cell carcinoma of the head and neck after platinum-based chemotherapy (October 2021) NICE TA736 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Nivolumab (Opdivo ®) for the treatment of locally advanced or metastatic squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adults (July 2016) SMC No. 1144/16 Recommended

▶ Nivolumab (Opdivo ®) for the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adults (October 2016) SMC No. 1180/16 Recommended with restrictions

▶ Nivolumab (Opdivo ®) in combination with ipilimumab and 2 cycles of platinum-based doublet chemotherapy for the first-line treatment of metastatic non-small cell lung cancer in adults whose tumours have no sensitising epidermal growth factor receptor mutations or anaplastic lymphoma kinase translocations (January 2022) SMC No. SMC2397 Not recommended

▶ Nivolumab (Opdivo ®) for use as monotherapy for the

treatment of advanced (unresectable or metastatic) melanoma in adults (August 2016) SMC No. 1120/16 Recommended with restrictions
▶ Nivolumab (Opdivo ∘) in combination with ipilimumab for the treatment of advanced (unresectable or metastatic) melanoma in adults (November 2016) SMC No. 1187/16 Recommended with restrictions
▶ Nivolumab (Opdivo ∘) as monotherapy for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection (December 2018) SMC No. SMC2112 Recommended
▶ Nivolumab (Opdivo ∘) as monotherapy for the treatment of advanced renal cell carcinoma after prior therapy in adults (June 2017) SMC No. 1188/16 Recommended
▶ Nivolumab (Opdivo ∘) in combination with ipilimumab for the first-line treatment of adult patients with intermediate/poorrisk advanced renal cell carcinoma (June 2019) SMC No. SMC2153 Recommended
▶ Nivolumab (Opdivo ∘) for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) after autologous stem cell transplant (ASCT) and treatment with brentuximab vedotin (July 2017) SMC No. 1240/17 Recommended
▶ Nivolumab (Opdivo ∘) as monotherapy, for the treatment of squamous cell cancer of the head and neck (SCCHN) in adults progressing on or after platinum-based therapy (September 2017) SMC No. 1261/17 Recommended with restrictions
▶ Nivolumab (Opdivo ∘) as monotherapy for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy (January 2018) SMC No. 1285/18 Not recommended
▶ Nivolumab (Opdivo ∘) as monotherapy for the treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma after prior fluoropyrimidine and platinum-based combination chemotherapy (August 2021) SMC No. SMC2362 Recommended
▶ Nivolumab (Opdivo ∘) in combination with ipilimumab for the treatment of adults with mismatch repair deficient or microsatellite instability-high metastatic colorectal cancer who have been previously treated with fluoropyrimidinebased combination chemotherapy (December 2021) SMC No. SMC2394 Recommended
▶ Nivolumab (Opdivo ∘) in combination with ipilimumab for the first-line treatment of adult patients with unresectable malignant pleural mesothelioma (MPM) (February 2022) SMC No. SMC2385 Recommended
ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for infusion
EXCIPIENTS: May contain Polysorbates
ELECTROLYTES: May contain Sodium
▶ Nivolumab (Non-proprietary)
Nivolumab 10 mg per 1 ml Opdivo 120mg/12ml concentrate for solution for infusion vials | 1 vialP £1,317.00 (Hospital only)
▶ Opdivo (Bristol-Myers Squibb Pharmaceuticals Ltd)
Nivolumab 10 mg per 1 ml Opdivo 40mg/4ml concentrate for solution for infusion vials | 1 vialP £439.00 (Hospital only)
Opdivo 100mg/10ml concentrate for solution for infusion vials | 1 vialP £1,097.00 (Hospital only)
Opdivo 240mg/24ml concentrate for solution for infusion vials | 1 vialP £2,633.00 (Hospital only)



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## Obinutuzumab 11-Nov-2020

ı INDICATIONS AND DOSE
Treatment of previously untreated chronic lymphocytic leukaemia in patients for whom full-dose fludarabinebased therapy is unsuitable due to co-morbidities | Treatment of previously untreated advanced follicular lymphoma | Treatment of follicular lymphoma in patients who did not respond or who progressed during or up to six months after treatment with rituximab or a rituximab-containing regimen
▶ BY INTRAVENOUS INFUSION
▶ Adult: (consult product literature or local protocols)
ı CONTRA-INDICATIONS For obinutuzumab contraindications, consult product literature.
ı CAUTIONS For full details on the cautions of obinutuzumab, consult product literature.
▶ Hepatitis B infection and reactivation Hepatitis B infection and reactivation (including fatal cases) have been reported in patients taking obinutuzumab. Manufacturer advises

patients with positive hepatitis B serology should be referred to a liver specialist for monitoring and initiation of antiviral therapy before treatment initiation; treatment should not be initiated in patients with evidence of current hepatitis B infection until the infection has been adequately treated. Manufacturer also advises patients should be closely monitored for clinical and laboratory signs of active hepatitis B infection (consult product literature).

ı INTERACTIONS → Appendix 1: monoclonal antibodies

ı SIDE-EFFECTS

▶ Common or very common Arrhythmias . chest pain . dyspepsia . eye erythema . gastrointestinal disorders . heart failure . hypertension . hyperuricaemia . lymph node pain . nasal complaints . skin reactions . squamous cell carcinoma . tumour lysis syndrome . urinary disorders . weight increased

▶ Frequency not known Acute coronary syndrome . angina pectoris . chills . dizziness . dyspnoea . flushing . hypotension . nausea . viral infection reactivation

ı CONCEPTION AND CONTRACEPTION Use effective contraception during and for 18 months after treatment.

ı PREGNANCY Avoid unless potential benefit outweighs risk of B-lymphocyte depletion in fetus.

ı BREAST FEEDING Avoid breast-feeding during and for 18 months after treatment—present in milk in animal studies.

ı MONITORING REQUIREMENTS Patients should be closely monitored for clinical and laboratory signs of active hepatitis B infection during treatment and for up to a year following the last infusion (consult product literature).

ı PRESCRIBING AND DISPENSING INFORMATION Infusion related side-effects have been reported; Patients should receive premedication with paracetamol, an antihistamine, and a corticosteroid before each dose—consult product literature for details.

ı NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia (June 2015) NICE TA343 Recommended with restrictions

▶ Obinutuzumab for untreated advanced follicular lymphoma (March 2018) NICE TA513 Recommended with restrictions

▶ Obinutuzumab with bendamustine for treating follicular lymphoma after rituximab (May 2020) NICE TA629 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Obinutuzumab (Gazyvaro ®) in combination with bendamustine followed by obinutuzumab maintenance is indicated for the treatment of patients with follicular lymphoma who did not respond or who progressed during or up to six months after treatment with rituximab or a rituximab-containing regimen (March 2017) SMC No. 1219/17 Recommended

▶ Obinutuzumab (Gazyvaro ®) in combination with chemotherapy, followed by maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma (FL) (September 2018) SMC No. SMC2015 Not recommended

ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

▶ Gazyvaro (Roche Products Ltd)

Obinutuzumab 25 mg per 1 ml Gazyvaro 1000mg/40ml concentrate for solution for infusion vials | 1 vialP £3,312.00 (Hospital only)

## Panitumumab 21-Jul-2020

ı DRUG ACTION Panitumumab is a monoclonal antibody that binds to the epidermal growth factor receptor (EGFR).

ı INDICATIONS AND DOSE

Treatment of non-mutated RAS metastatic colorectal cancer (combination therapy) | Treatment of nonmutated RAS metastatic colorectal cancer (monotherapy after failure of fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: SEVERE SKIN REACTIONS

Severe skin reactions have been reported very commonly in patients treated with panitumumab. Patients receiving panitumumab who have severe skin reactions or develop worsening skin reactions should be monitored for the development of inflammatory or

infectious sequelae (including cellulitis, sepsis, and necrotising fasciitis). Appropriate treatment should be promptly initiated and panitumumab withheld or discontinued.

MHRA/CHM ADVICE: EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) INHIBITORS: SERIOUS CASES OF KERATITIS AND ULCERATIVE KERATITIS (MAY 2012)

Keratitis and ulcerative keratitis have been reported following treatment with epidermal growth factor receptor (EGFR) inhibitors for cancer (cetuximab, erlotinib, gefitinib and panitumumab). In rare cases, this has resulted in corneal perforation and blindness. Patients undergoing treatment with EGFR inhibitors who present with acute or worsening signs and symptoms suggestive of keratitis should be referred promptly to an ophthalmology specialist. Treatment should be interrupted or discontinued if ulcerative keratitis is diagnosed.

**CONTRA-INDICATIONS** Interstitial pulmonary disease . the combination of panitumumab with oxaliplatin-containing chemotherapy is contra-indicated in patients with mutant RAS metastatic colorectal cancer or for whom RAS status is unknown

**CAUTIONS** History of keratitis . history of severe dry eye . history of ulcerative keratitis . pulmonary disease . risk factors for keratitis . risk factors for severe dry eye . risk factors for ulcerative keratitis (including contact lens use)

**INTERACTIONS** → Appendix 1: monoclonal antibodies



**SIDE-EFFECTS**

▶ Common or very common Alopecia . anaemia . anxiety . appetite decreased . asthenia . chest pain . chills . constipation . cough . dehydration . diarrhoea . dizziness . dry eye . dry mouth . dyspnoea . electrolyte imbalance . embolism and thrombosis . eye discomfort . eye disorders . eye inflammation . fever . flushing . gastrointestinal discomfort . gastrooesophageal reflux disease . haemorrhage . hair changes . headache . hyperglycaemia . hyperhidrosis . hypersensitivity (may be delayed) . hypertension . hypotension . increased risk of infection . insomnia . leucopenia . mucositis . nail disorders . nausea . oral disorders . pain . peripheral oedema . skin reactions . skin ulcer . tachycardia . vomiting . weight decreased

▶ Uncommon Angioedema . cyanosis . infusion related reaction . nasal dryness . onycholysis . respiratory disorders . severe cutaneous adverse reactions (SCARs)

▶ Rare or very rare Anaphylactic reaction

**CONCEPTION AND CONTRACEPTION** Manufacturer advises effective contraception during and for 6 months after treatment.

**PREGNANCY** Avoid (toxicity in animal studies). See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

**BREAST FEEDING** Manufacturer advises avoid breastfeeding during and for 2 months after treatment.

**PRE-TREATMENT SCREENING** Evidence of non-mutated RAS status (at exons 2, 3 and 4 of KRAS and NRAS) is required before panitumumab treatment is initiated, and should be determined by an experienced laboratory using a validated test method.

**MONITORING REQUIREMENTS**

▶ Monitor for hypomagnesaemia.

▶ Monitor for hypocalcaemia.

▶ Monitor for dermatological reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis (consult product literature).

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy (January 2012) NICE TA242 Not recommended

▶ Cetuximab and panitumumab for previously untreated metastatic colorectal cancer (updated September 2017) NICE TA439 Recommended with restrictions

**MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion
ELECTROLYTES: May contain Sodium
▶ Vectibix (Amgen Ltd)
Panitumumab 20 mg per 1 ml Vectibix 400mg/20ml concentrate for solution for infusion vials | 1 vialP £1,517.16 (Hospital only)
Vectibix 100mg/5ml concentrate for solution for infusion vials | 1 vialP £379.29 (Hospital only)

## Pembrolizumab 01-Mar-2022

I DRUG ACTION Pembrolizumab is a monoclonal antibody, which binds to the programmed death-1 (PD-1) receptor, thereby potentiating an immune response to tumour cells.
I INDICATIONS AND DOSE
Melanoma (specialist use only) | Non-small cell lung cancer (specialist use only) | Urothelial carcinoma (specialist use only) | Classical Hodgkin lymphoma (specialist use only) | Head and neck squamous cell carcinoma (specialist use only) | Renal cell carcinoma (specialist use only) | Colorectal cancer (specialist use only) | Oesophageal carcinoma (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: 200 mg every 3 weeks, for treatment interruption or discontinuation due to side-effects and infusion-related reactions—consult product literature, alternatively 400 mg every 6 weeks, for treatment interruption or discontinuation due to side-effects and infusion-related reactions—consult product literature
IMPORTANT SAFETY INFORMATION
MHRA/CHM ADVICE: PEMBROLIZUMAB (KEYTRUDA ▪): REPORTS OF ORGAN TRANSPLANT REJECTION (JULY 2017)
A European review of worldwide data concluded that pembrolizumab may increase the risk of rejection in organ transplant recipients. The MHRA recommends considering the benefit of treatment with pembrolizumab versus the risk of possible organ transplant rejection for each patient.
MHRA/CHM ADVICE: ATEZOLIZUMAB (TECENTRIQ ▪) AND OTHER IMMUNE-STIMULATORY ANTI-CANCER DRUGS: RISK OF SEVERE CUTANEOUS ADVERSE REACTIONS (SCARS) (JUNE 2021)
Severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients treated with immunostimulant antineoplastic drugs, such as pembrolizumab. Healthcare professionals are advised to monitor patients for suspected severe skin reactions and exclude other causes. Patients should be advised to seek urgent medical attention if severe skin reactions occur. If a SCAR is suspected, pembrolizumab therapy should be withheld and the patient referred to a specialist for diagnosis and treatment. Pembrolizumab should be permanently discontinued for any grade confirmed SJS or TEN, and for any grade 4 SCAR. Caution is recommended when considering the use of pembrolizumab in patients with a history of severe or life-threatening SCAR associated with other immunostimulant antineoplastic drugs.
I CAUTIONS May increase risk of severe graft-versus-host reaction in patients who have had prior haematopoietic stem cell transplant (particularly in those with a prior history) . patients may need pretreatment to minimise the development of adverse reactions (consult product literature)
I INTERACTIONS → Appendix 1: monoclonal antibodies
I SIDE-EFFECTS
▶ Common or very common Alopecia . anaemia . appetite decreased . arrhythmias . arthritis . asthenia . chills . connective tissue disorders . constipation . cough . cytokine release syndrome . decreased leucocytes . diarrhoea . dizziness . dry eye . dry mouth . dyspnoea . electrolyte imbalance . enterocolitis haemorrhagic . eye inflammation . eyelid hypopigmentation . fever . fluid imbalance . gastrointestinal discomfort . gastrointestinal disorders . genital abnormalities . headache . hepatic disorders . hypersensitivity . hypertension . hyperthyroidism . hypothyroidism . increased risk of infection . influenza like illness . infusion related reaction . insomnia . joint disorders . lethargy . lip swelling . musculoskeletal discomfort . myalgia . myopathy . myxoedema . nausea . nerve disorders . neutropenia .

oedema . pain . pressure ulcer . respiratory disorders . severe cutaneous adverse reactions (SCARs) . skin reactions . taste altered . thrombocytopenia . thyroid disorder . thyroiditis . torticollis . vomiting

▶ Uncommon Adrenal hypofunction . cardiac inflammation . diabetic ketoacidosis . eosinophilia . epilepsy . glomerulonephritis . hair colour changes . hypophysitis . hypopituitarism . nephritis . nephrotic syndrome . pancreatitis . pericardial effusion . renal impairment . sarcoidosis . tendon disorders . type 1 diabetes mellitus

▶ Rare or very rare Cholangitis sclerosing . cystitis . erythema nodosum . haemolytic anaemia . haemophagocytic lymphohistiocytosis . meningitis . meningitis non-infective . neuromuscular dysfunction . pure red cell aplasia . transverse myelitis . vasculitis

▶ Frequency not known Solid organ transplant rejection

SIDE-EFFECTS, FURTHER INFORMATION Immune-related reactions Most immune-related adverse reactions are reversible and managed by temporarily stopping treatment and administration of a corticosteroid—consult product literature for further information.

Infusion-related reactions Manufacturer advises to permanently discontinue treatment in patients with severe infusion reactions.

| CONCEPTION AND CONTRACEPTION Manufacturer recommends effective contraception during treatment and for at least 4 months after treatment in women of childbearing potential.

| PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—no information available

| BREAST FEEDING Manufacturer advises avoid—no information available.

| MONITORING REQUIREMENTS Manufacturer advises monitor for signs and symptoms of infusion- and immunerelated reactions.

| DIRECTIONS FOR ADMINISTRATION Manufacturer advises for intermittent intravenous infusion (Keytruda ®), dilute to a concentration of 1 mg/mL to 10 mg/mL with Glucose 5% or Sodium Chloride 0.9%; give over 30 minutes using a lowprotein binding 0.2–5 micron filter.

| PRESCRIBING AND DISPENSING INFORMATION Pembrolizumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

| HANDLING AND STORAGE Manufacturer advises store in a refrigerator at 2–8°C.

| PATIENT AND CARER ADVICE Patients should be provided with an alert card and advised to keep it with them at all times. A patient information brochure highlighting important safety information to minimise the risk of immune-related side-effects is also available.

Driving and skilled tasks Patients should be counselled on the effects on driving and performance of skilled tasks—increased risk of dizziness and fatigue.

| NATIONAL FUNDING/ACCESS DECISIONS For full details see funding body website

NICE decisions

▶ Pembrolizumab for treating advanced melanoma after disease progression with ipilimumab (updated September 2017) NICE TA357 Recommended with restrictions

▶ Pembrolizumab for advanced melanoma not previously treated with ipilimumab (updated September 2017) NICE TA366 Recommended with restrictions

▶ Pembrolizumab for adjuvant treatment of completely resected stage 3 melanoma (February 2022) NICE TA766 Recommended

▶ Pembrolizumab for treating PD-L1-positive non-small-cell lung cancer after chemotherapy (updated September 2017) NICE TA428 Recommended with restrictions

▶ Pembrolizumab for untreated PD-L1-positive metastatic nonsmall-cell lung cancer (July 2018) NICE TA531 Recommended with restrictions

▶ Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (March 2021) NICE TA683 Recommended with restrictions

▶ Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (February 2022) NICE TA770 Recommended with restrictions

▶ Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (April 2021) NICE TA692 Not recommended
▶ Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma [in adults who have had autologous stem cell transplant and brentuximab vedotin] (September 2018) NICE TA540 Not recommended
▶ Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma [in adults who have had brentuximab vedotin and cannot have autologous stem cell transplant] (September 2018) NICE TA540 Recommended with restrictions
▶ Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma after stem cell transplant or at least 2 previous therapies (February 2022) NICE TA772 Recommended with restrictions
▶ Pembrolizumab with axitinib for untreated advanced renal cell carcinoma (September 2020) NICE TA650 Not recommended
▶ Pembrolizumab for untreated metastatic or unresectable recurrent head and neck squamous cell carcinoma (November 2020) NICE TA661 Recommended with restrictions
▶ Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (June 2021) NICE TA709 Recommended with restrictions
▶ Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced oesophageal and gastro-oesophageal junction cancer (October 2021) NICE TA737 Recommended
Scottish Medicines Consortium (SMC) decisions
▶ Pembrolizumab (Keytruda •) as monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults previously untreated with ipilimumab (November 2015) SMC No. 1086/15 Recommended
▶ Pembrolizumab (Keytruda •) as monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults previously treated with ipilimumab (December 2016) SMC No. 1087/15 Not recommended
▶ Pembrolizumab (Keytruda •) as monotherapy for the adjuvant treatment of adults with stage III melanoma and lymph node involvement who have undergone complete resection (May 2019) SMC No. SMC2144 Recommended
▶ Pembrolizumab (Keytruda •) for the treatment of locally advanced or metastatic non-small cell lung carcinoma (NSCLC) in adults whose tumours express programmed death ligand 1 (PD-L1) and who have received at least one prior chemotherapy regimen (January 2017) SMC No. 1204/17 Recommended with restrictions
▶ Pembrolizumab (Keytruda •) as monotherapy for the first-line treatment of metastatic non-small cell lung carcinoma in adults whose tumours express programmed death ligand 1 with a 50% or more tumour proportion score with no epidermal growth factor receptor or anaplastic lymphoma kinase (ALK)-positive tumour mutations (July 2017) SMC No. 1239/17 Recommended with restrictions



▶ Pembrolizumab (Keytruda •) in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous non-small cell lung cancer in adults (September 2019) SMC No. SMC2187 Recommended with restrictions
▶ Pembrolizumab (Keytruda •) in combination with pemetrexed and platinum chemotherapy for the first-line treatment of metastatic non-squamous non-small cell lung carcinoma in adults whose tumours have no epidermal growth factor receptor or anaplastic lymphoma kinase (ALK)-positive mutations (October 2019) SMC No. SMC2207 Recommended with restrictions
▶ Pembrolizumab (Keytruda •) as monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinumcontaining chemotherapy (February 2018) SMC No. 1291/18 Recommended with restrictions
▶ Pembrolizumab (Keytruda •) as monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatincontaining chemotherapy (first line) (September 2018) SMC No. 1339/18 Not recommended
▶ Pembrolizumab (Keytruda •) as monotherapy for the treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem

cell transplant and brentuximab vedotin, or who are transplant-ineligible and have failed brentuximab vedotin (March 2018) SMC No. 1296/18 Recommended with restrictions

▶ Pembrolizumab (Keytruda ®) as monotherapy for the treatment of adult and paediatric patients aged 3 years and older with relapsed or refractory classical Hodgkin lymphoma who have failed autologous stem cell transplant (ASCT), or following at least two prior therapies when ASCT is not a treatment option (November 2021) SMC No. SMC2380 Recommended with restrictions

▶ Pembrolizumab (Keytruda ®) in combination with axitinib for the first-line treatment of advanced renal cell carcinoma (RCC) in adults (September 2020) SMC No. SMC2247 Recommended with restrictions

▶ Pembrolizumab (Keytruda ®) as monotherapy or in combination with platinum and 5-fluorouracil chemotherapy, for the first-line treatment of metastatic or unresectable recurrent head and neck squamous cell carcinoma in adults whose tumours express programmed death ligand 1 with a combined positive score of 1 or more (September 2020) SMC No. SMC2257 Recommended with restrictions

▶ Pembrolizumab (Keytruda ®) as monotherapy for the first-line treatment of metastatic microsatellite instability-high or mismatch repair deficient colorectal cancer in adults (September 2021) SMC No. SMC2375 Recommended with restrictions

ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Keytruda (Merck Sharp & Dohme (UK) Ltd)

Pembrolizumab 25 mg per 1 ml Keytruda 100mg/4ml concentrate for solution for infusion vials | 1 vialP £2,630.00 (Hospital only)

## Pertuzumab 17-May-2021

ı DRUG ACTION Pertuzumab is a recombinant humanised monoclonal antibody, and acts by inhibiting human epidermal growth factor receptor 2 protein (HER2) dimerisation.

ı INDICATIONS AND DOSE

HER2-positive early stage breast cancer (in combination with trastuzumab and chemotherapy) | HER2-positive metastatic or locally recurrent unresectable breast cancer (in combination with trastuzumab and docetaxel) (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature or local protocols)

ı CAUTIONS Conditions that could impair left ventricular function . history of congestive heart failure . impaired left ventricular function . prior anthracycline exposure . radiotherapy to the chest area . recent myocardial infarction . serious cardiac arrhythmia . uncontrolled hypertension

ı INTERACTIONS → Appendix 1: monoclonal antibodies

ı SIDE-EFFECTS

▶ Common or very common Alopecia . anaemia . appetite decreased . arthralgia . asthenia . chills . congestive heart failure . constipation . cough . cytokine release syndrome . diarrhoea . dizziness . dyspepsia . dyspnoea . excessive tearing . fever . headache . hypersensitivity . increased risk of infection . infusion related reaction . insomnia . left ventricular dysfunction . leucopenia . mucositis . myalgia . nail disorder . nausea . neutropenia . oedema . pain . peripheral neuropathy . respiratory disorders . skin reactions . stomatitis . taste altered . vomiting

SIDE-EFFECTS, FURTHER INFORMATION Side effects mostly described for pertuzumab in combination with trastuzumab and docetaxel.

ı CONCEPTION AND CONTRACEPTION Ensure effective contraception during and for six months after treatment in women of childbearing potential.

ı PREGNANCY Avoid (toxicity in animal studies). Most cytotoxic drugs are teratogenic and should not be administered during pregnancy, especially during the first trimester. Considerable caution is necessary if a pregnant woman presents with cancer requiring chemotherapy, and specialist advice should always be sought.

ı BREAST FEEDING Avoid—no information available.

ı HEPATIC IMPAIRMENT Manufacturer advises caution (no information available).

ı RENAL IMPAIRMENT gUse with caution in severe

impairment (no information available). M
MONITORING REQUIREMENTS
▶ Assess for signs and symptoms of congestive heart failure (including left ventricular ejection fraction) before and during treatment—consult product literature, and withhold treatment if necessary.
▶ Monitor for febrile neutropenia.
DIRECTIONS FOR ADMINISTRATION Manufacturer advises resuscitation facilities should be available.
NATIONAL FUNDING/ACCESS DECISIONS
For full details see funding body website
NICE decisions
▶ Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer (December 2016) NICE TA424 Recommended with restrictions
▶ Pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer (March 2018) NICE TA509 Recommended with restrictions



▶ Pertuzumab for adjuvant treatment of HER2-positive early stage breast cancer (March 2019) NICE TA569 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Pertuzumab (Perjeta ®) for use in combination with trastuzumab and chemotherapy for the neoadjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive, locally advanced, inflammatory, or early stage breast cancer at high risk of recurrence (December 2018) SMC No. SMC2119 Recommended
▶ Pertuzumab (Perjeta ®) for use in combination with trastuzumab and docetaxel in adult patients with HER2-positive metastatic or locally recurrent unresectable breast cancer, who have not received previous anti-HER2 therapy or chemotherapy for their metastatic disease (January 2019) SMC No. SMC2120 Recommended
▶ Pertuzumab (Perjeta ®) for use in combination with trastuzumab and chemotherapy for the adjuvant treatment of adult patients with human epidermal growth factor receptor 2 (HER2)-positive early breast cancer (eBC) at high risk of recurrence (September 2020) SMC No. SMC2284 Recommended with restrictions
MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for infusion
▶ Perjeta (Roche Products Ltd)
Pertuzumab 30 mg per 1 ml Perjeta 420mg/14ml concentrate for solution for infusion vials | 1 vialP £2,395.00 (Hospital only)

## Pertuzumab with trastuzumab 06-Aug-2021

The properties listed below are those particular to the combination only. For the properties of the components please consider, pertuzumab p. 952, trastuzumab p. 958.
INDICATIONS AND DOSE
HER2-positive early stage breast cancer (in combination with chemotherapy) (specialist use only) | HER2-positive metastatic or locally recurrent unresectable breast cancer (in combination with docetaxel) (specialist use only)
▶ BY SUBCUTANEOUS INJECTION
▶ Adult: (consult product literature or local protocols)
INTERACTIONS → Appendix 1: monoclonal antibodies
CONCEPTION AND CONTRACEPTION gEnsure effective contraception during and for 7 months after treatment in females of childbearing potential. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
BREAST FEEDING gAvoid breast-feeding during treatment and for at least 7 months afterwards—no information available. M
PRESCRIBING AND DISPENSING INFORMATION Pertuzumab with trastuzumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1;grecord the brand name and batch number after each administration. M
HANDLING AND STORAGE gStore in a refrigerator (2–8ºC); consult product literature for storage conditions after preparation of the injection. M
PATIENT AND CARER ADVICE
Driving and skilled tasks gPatients and carers should be counselled on the effects on driving and other skilled tasks—increased risk of injection-related reactions and dizziness. M
NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website
Scottish Medicines Consortium (SMC) decisions
▶ Pertuzumab/trastuzumab (Phesgo ®) used in combination with chemotherapy for the treatment of adults with HER2-positive early stage breast cancer or in combination with docetaxel for the treatment of adults with HER2-positive metastatic or locally recurrent unresectable breast cancer (July 2021) SMC No. SMC2364 Recommended with restrictions
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for injection
EXCIPIENTS: May contain Polysorbates, sucrose
▶ Phesgo (Roche Products Ltd) A
Pertuzumab 60 mg per 1 ml, Trastuzumab 60 mg per 1 ml Phesgo 600mg/600mg/10ml solution for injection vials | 1 vialP £3,617.00 (Hospital only)
Trastuzumab 40 mg per 1 ml, Pertuzumab 80 mg per 1 ml Phesgo 1200mg/600mg/15ml solution for injection vials | 1 vialP £6,012.00 (Hospital only)

## Polatuzumab vedotin 12-Nov-2020

I DRUG ACTION Polatuzumab vedotin is an antibody-drug conjugate that contains polatuzumab covalently linked to MMAE, a cytotoxic microtubule disrupting agent.
I INDICATIONS AND DOSE
Relapsed or refractory diffuse large B-cell lymphoma (in combination with bendamustine and rituximab) (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: (consult product literature)
I CONTRA-INDICATIONS Active severe infection
I CAUTIONS High tumour burden—risk of tumour lysis syndrome . patients may need pre-medication to mimimise infusion-related reactions . peripheral neuropathy . rapidly proliferating tumours—risk of tumour lysis syndrome
CAUTIONS, FURTHER INFORMATION
▶ Pre-medication Manufacturer advises pre-medication with an antihistamine and antipyretic to minimise the development of infusion-related reactions—consult product literature.
I INTERACTIONS → Appendix 1: monoclonal antibodies
I SIDE-EFFECTS
▶ Common or very common Anaemia . appetite decreased . arthralgia . asthenia . bone marrow disorders . chills . constipation . cough . decreased leucocytes . diarrhoea . dizziness . electrolyte imbalance . fever . gait abnormal . gastrointestinal discomfort . hypoalbuminaemia . increased risk of infection . infusion related reaction . nausea . neutropenia . peripheral neuropathy . pneumonitis . pruritus . sensation abnormal . sepsis . thrombocytopenia . vision blurred . vomiting . weight decreased
▶ Frequency not known Gastrointestinal toxicity . hepatic disorders . progressive multifocal leukoencephalopathy (PML) . reactivation of infection
I CONCEPTION AND CONTRACEPTION Manufacturer advises females of childbearing potential should confirm pregnancy status before treatment and use effective contraception during treatment and for 9 months after last treatment; male patients should use effective contraception during treatment and for 6 months after last treatment if their partner is pregnant or of childbearing potential. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962
I PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—toxicity in animal studies. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962



I BREAST FEEDING Manufacturer advises avoid breast feeding during treatment and for at least 2 months after treatment.
I HEPATIC IMPAIRMENT Manufacturer advises avoid in moderate to severe hepatic impairment. Manufacturer advises monitor liver enzymes and bilirubin levels (risk of hepatic toxicity)—consult product literature.
I RENAL IMPAIRMENT
Dose adjustments Manufacturer advises no dose adjustment required if creatinine clearance is more than

30 mL/minute; no established dose if creatinine clearance less than 30 mL/minute—no information available. See p. 21.

I MONITORING REQUIREMENTS Manufacturer advises monitor complete blood counts prior to each dose; more frequent monitoring may be required—consult product literature for treatment adjustment.

I PRESCRIBING AND DISPENSING INFORMATION Polatuzumab vedotin is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; manufacturer advises to record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in a refrigerator (2-8°C) and protect from light—consult product literature for further information regarding storage conditions after reconstitution and dilution.

I PATIENT AND CARER ADVICE

Driving and skilled tasks Manufacturer advises patients and carers should be counselled on the effects on driving and other skilled tasks—increased risk of infusion-related reactions, peripheral neuropathy, fatigue, and dizziness.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Polatuzumab vedotin with rituximab and bendamustine for treating relapsed or refractory diffuse large B-cell lymphoma (September 2020) NICE TA649 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Polatuzumab vedotin (Polivy ®) in combination with bendamustine and rituximab for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant (September 2020) SMC No. SMC2282 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

EXCIPIENTS: May contain Polysorbates, sucrose

▶ Polivy (Roche Products Ltd) A

Polatuzumab vedotin 30 mg Polivy 30mg powder for concentrate for solution for infusion vials | 1 vialP £2,370.00 (Hospital only)

Polatuzumab vedotin 140 mg Polivy 140mg powder for concentrate for solution for infusion vials | 1 vialP £11,060.00 (Hospital only)

## Ramucirumab 20-Aug-2020

I DRUG ACTION Ramucirumab is a human monoclonal antibody that binds to the vascular endothelial growth factor receptor-2 (VEGFR-2), inhibiting VEGF-induced angiogenesis.

I INDICATIONS AND DOSE

Treatment of advanced gastric cancer or gastrooesophageal junction adenocarcinoma, in combination with paclitaxel, in patients with disease progression after prior platinum and fluoropyrimidine chemotherapy

▶ BY INTRAVENOUS INFUSION

▶ Adult: 8 mg/kg on days 1 and 15 of a 28 day cycle, dose to be administered prior to paclitaxel infusion, consult product literature for dose adjustments due to sideeffects and infusion-related reactions

Treatment of advanced gastric cancer or gastrooesophageal junction adenocarcinoma, as monotherapy, in patients with disease progression after prior platinum or fluoropyrimidine chemotherapy, and for whom treatment in combination with paclitaxel is not appropriate

▶ BY INTRAVENOUS INFUSION

▶ Adult: 8 mg/kg every 2 weeks, consult product literature for dose adjustments due to side-effects and infusion-related reactions

Treatment of metastatic colorectal cancer, in combination with FOLFIRI (irinotecan, fluorouracil and folinic acid), in patients with disease progression on, or after, prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine

▶ BY INTRAVENOUS INFUSION

▶ Adult: 8 mg/kg every 2 weeks, dose to be administered prior to FOLFIRI administration, consult product literature for dose adjustments due to side-effects and infusion-related reactions

Treatment of locally advanced or metastatic non-small cell lung cancer, in combination with docetaxel, in patients with disease progression after platinum-based chemotherapy

▶ BY INTRAVENOUS INFUSION

▶ Adult: 10 mg/kg on day 1 of a 21 day cycle, dose to be

administered prior to docetaxel infusion, consult product literature for dose adjustments due to sideeffects and infusion-related reactions

IMPORTANT SAFETY INFORMATION

MHRA/CHM ADVICE: SYSTEMICALLY ADMINISTERED VEGF PATHWAY INHIBITORS: RISK OF ANEURYSM AND ARTERY DISSECTION (JULY 2020)

A European review of worldwide data concluded that systemically administered VEGF pathway inhibitors may lead to aneurysm and artery dissection in patients with or without hypertension. Some fatal cases have been reported, mainly in relation to aortic aneurysm rupture and aortic dissection. The MHRA advises healthcare professionals to carefully consider the risk of aneurysm and artery dissection in patients with risk factors before initiating treatment with ramucirumab; any modifiable risk factors (such as smoking and hypertension) should be reduced as much as possible. Patients should be monitored and treated for hypertension as required.

ı CAUTIONS Elective surgery—discontinue treatment for at least 4 weeks prior to surgery . hypertension . impaired wound healing—discontinue treatment until wound fully healed . pretreatment is recommended to minimise the development of adverse reactions (consult product literature) . risk factors for aneurysm or artery dissection . risk of bleeding



CAUTIONS, FURTHER INFORMATION

▶ Monitoring of blood pressure The MHRA advises to monitor blood pressure regularly—consult product literature if hypertension occurs during treatment.

ı INTERACTIONS → Appendix 1: monoclonal antibodies

ı SIDE-EFFECTS

▶ Common or very common Arterial thromboembolism . diarrhoea . electrolyte imbalance . epistaxis . gastrointestinal discomfort . gastrointestinal disorders . headache . hepatic coma . hepatic encephalopathy . hepatic pain . hypertension . hypoalbuminaemia . infusion related reaction . nephrotic syndrome . neutropenia . peripheral oedema . proteinuria . rash . thrombocytopenia

▶ Frequency not known Aneurysm . artery dissection . cardiac arrest . cerebrovascular insufficiency . haemangioma . myocardial infarction . thrombotic microangiopathy

SIDE-EFFECTS, FURTHER INFORMATION Infusion-related hypersensitivity reactions have been reported with ramucirumab, particularly during or following the first or second infusion; if the patient experiences a grade 1 or 2 infusion-related reaction, the manufacturer advises to reduce rate of infusion by 50% and give premedication for all subsequent infusions—consult product literature. Manufacturer advises to permanently discontinue treatment in the event of a grade 3 or 4 infusion-related reaction.

ı CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception during treatment and for up to 3 months after treatment in women of childbearing potential.

ı PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk—no information available.

ı BREAST FEEDING Manufacturer advises discontinue breast-feeding during treatment and for at least 3 months after treatment—no information available.

ı HEPATIC IMPAIRMENT Manufacturer advises caution in severe cirrhosis, cirrhosis with hepatic encephalopathy, cirrhosis with clinically significant ascites, or hepatorenal syndrome (risk of progressive hepatic failure, no information available).

ı MONITORING REQUIREMENTS Manufacturer advises monitor for signs of infusion-related hypersensitivity reactions; monitor for development or worsening of proteinuria during treatment—consult product literature; monitor blood counts and coagulation parameters in patients at risk of bleeding.

ı DIRECTIONS FOR ADMINISTRATION For intravenous infusion (Cyramza ®), manufacturer advises give intermittently in Sodium chloride 0.9%; dilute requisite dose with infusion fluid to final volume of 250mL and invert gently to mix. Do not exceed a rate of 25 mg/minute, and give over approximately 60 minutes via an infusion pump using a separate infusion line with a protein sparing 0.22 micron

filter.

ı PRESCRIBING AND DISPENSING INFORMATION For Cyramza ⁎, each 10mL vial contains sodium 17mg (equivalent to $Na^+$ 0.74 mmol).

ı NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Ramucirumab for treating advanced gastric cancer or gastrooesophageal junction adenocarcinoma previously treated with chemotherapy (January 2016) NICE TA378 Not recommended

▶ Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer (August 2016) NICE TA403 Not recommended

ı MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for infusion

ELECTROLYTES: May contain Sodium

▶ Cyramza (Eli Lilly and Company Ltd)

Ramucirumab 10 mg per 1 ml Cyramza 100mg/10ml concentrate for solution for infusion vials | 1 vialᴘ £500.00 (Hospital only)

Cyramza 500mg/50ml concentrate for solution for infusion vials | 1 vialᴘ £2,500.00 (Hospital only)

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## Rituximab 16-Nov-2020

ı INDICATIONS AND DOSE

Rheumatoid arthritis (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 1 g, then 1 g after 2 weeks, consult product literature for information on retreatment

Non-Hodgkin's lymphoma (specialist use only) | Chronic lymphocytic leukaemia (specialist use only) | Granulomatosis with polyangiitis and microscopic polyangiitis (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature)

Non-Hodgkin's lymphoma (specialist use only)

▶ BY SUBCUTANEOUS INJECTION

▶ Adult: (consult product literature)

Pemphigus vulgaris (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: 1 g, then 1 g after 2 weeks; maintenance 0.5 g, at months 12 and 18, and then every 6 months thereafter if needed, consult product literature for the treatment of relapse

ı CONTRA-INDICATIONS

GENERAL CONTRA-INDICATIONS Severe infection

SPECIFIC CONTRA-INDICATIONS

▶ When used for granulomatosis with polyangiitis and microscopic polyangiitis Severe heart failure . severe, uncontrolled heart disease

▶ When used for pemphigus vulgaris Severe heart failure . severe, uncontrolled heart disease

▶ When used for rheumatoid arthritis Severe heart failure . severe, uncontrolled heart disease

CONTRA-INDICATIONS, FURTHER INFORMATION

For full details on contra-indications, consult product literature.

ı CAUTIONS

GENERAL CAUTIONS History of cardiovascular disease (exacerbation of angina, arrhythmia, and heart failure have been reported) . patients receiving cardiotoxic chemotherapy (exacerbation of angina, arrhythmia, and heart failure have been reported) . pre-medication recommended to minimise adverse reactions (consult product literature) . predisposition to infection . transient hypotension occurs frequently during infusion (antihypertensives may need to be withheld for 12 hours before infusion)

SPECIFIC CAUTIONS

▶ When used for granulomatosis with polyangiitis and microscopic polyangiitis Pneumocystis jirovecii pneumonia—consult product literature for prophylaxis requirements

▶ When used for pemphigus vulgaris Pneumocystis jirovecii pneumonia—consult product literature for prophylaxis requirements

CAUTIONS, FURTHER INFORMATION For full details on cautions, consult product literature or local treatment protocol.

▶ Hepatitis B infection and reactivation Hepatitis B infection and reactivation (including fatal cases) have been reported in patients taking rituximab. Manufacturer advises patients

with positive hepatitis B serology should be referred to a liver specialist for monitoring and initiation of antiviral therapy before treatment initiation; treatment should not be initiated in patients with evidence of current hepatitis B infection until the infection has been adequately treated. Manufacturer also advises patients should be closely monitored for clinical and laboratory signs of active hepatitis B infection (consult product literature).

**INTERACTIONS** → Appendix 1: monoclonal antibodies

**SIDE-EFFECTS**

▶ Common or very common Angioedema . anxiety . appetite decreased . arrhythmias . bone marrow disorders . bursitis . cancer pain . cardiac disorder . chest pain . chills . dizziness . dysphagia . dyspnoea . ear pain . electrolyte imbalance . gastrointestinal discomfort . gastrointestinal disorders . hepatitis B . hypercholesterolaemia . hyperglycaemia . hyperhidrosis . hypertension . hypotension . insomnia . lacrimation disorder . malaise . migraine . multi organ failure . muscle complaints . muscle tone increased . nausea . nerve disorders . oedema . oral disorders . osteoarthritis . respiratory disorders . sensation abnormal . sepsis . skin reactions . throat irritation . tinnitus . vasodilation . weight decreased

▶ Uncommon Asthma . coagulation disorder . heart failure . hypoxia . ischaemic heart disease . lymphadenopathy . taste altered

▶ Rare or very rare Cytokine release syndrome . facial paralysis . renal failure . Stevens-Johnson syndrome (discontinue) . toxic epidermal necrolysis . tumour lysis syndrome . vasculitis . vision disorders

▶ Frequency not known Epistaxis . hearing loss . hypogammaglobulinaemia . infective thrombosis . influenza like illness . irritability . muscle weakness . nasal congestion . posterior reversible encephalopathy syndrome (PRES) . psychiatric disorder . seizure . skin papilloma . tremor

**SIDE-EFFECTS, FURTHER INFORMATION** Associated with infections, sometimes severe, including tuberculosis, septicaemia, and hepatitis B reactivation. Progressive multifocal leucoencephalopathy has been reported in association with rituximab; patients should be monitored for cognitive, neurological, or psychiatric signs and symptoms. If progressive multifocal leucoencephalopathy is suspected, suspend treatment until it has been excluded.

**CONCEPTION AND CONTRACEPTION** Effective contraception in females of childbearing potential required during and for 12 months after treatment.

**PREGNANCY** Avoid unless potential benefit to mother outweighs risk of B-lymphocyte depletion in fetus.

**BREAST FEEDING** Avoid breast-feeding during and for 12 months after treatment.

**MONITORING REQUIREMENTS** For full details on monitoring requirements consult product literature.

**DIRECTIONS FOR ADMINISTRATION** For intravenous infusion, give intermittently in Glucose 5% or Sodium chloride 0.9%; dilute to 1–4 mg/mL and gently invert bag to avoid foaming; for further information, consult product literature.

**PRESCRIBING AND DISPENSING INFORMATION** Rituximab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1.

**PATIENT AND CARER ADVICE**

Alert card

▶ When used for Granulomatosis with polyangiitis and microscopic polyangiitis or Rheumatoid arthritis or Pemphigus vulgaris Patients should be provided with a patient alert card with each infusion.

**NATIONAL FUNDING/ACCESS DECISIONS**

For full details see funding body website

NICE decisions

▶ Rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis (March 2014) NICE TA308 Recommended with restrictions

▶ Adalimumab, etanercept, infliximab, rituximab, and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor (August 2010) NICE TA195 Recommended with restrictions
▶ Rituximab for the first-line treatment of stage III-IV follicular lymphoma (January 2012) NICE TA243 Recommended
▶ Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (February 2008) NICE TA137 Recommended with restrictions
▶ Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia (July 2010) NICE TA193 Recommended with restrictions
▶ Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma (June 2011) NICE TA226 Recommended
▶ Rituximab for the first-line treatment of chronic lymphocytic leukaemia (July 2009) NICE TA174 Recommended
▶ Idelalisib for treating chronic lymphocytic leukaemia [in combination with rituximab] (October 2015) NICE TA359 Recommended
▶ Venetoclax with rituximab for previously treated chronic lymphocytic leukaemia (February 2019) NICE TA561 Recommended with restrictions
Scottish Medicines Consortium (SMC) decisions
▶ Rituximab (MabThera ®) for use in combination with glucocorticoids for the induction of remission in adult patients with severe, active granulomatosis with polyangiitis (Wegener' s) and microscopic polyangiitis (September 2013) SMC No. 894/13 Recommended with restrictions
▶ Rituximab (MabThera ®) subcutaneous injection for the treatment of non-Hodgkin' s lymphoma in adults (July 2014) SMC No. 975/14 Recommended with restrictions
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Solution for injection
▶ MabThera (Roche Products Ltd)
Rituximab 119.66 mg per 1 ml MabThera 1400mg/11.7ml solution for injection vials | 1 vialP £1,344.65 (Hospital only)
Solution for infusion
EXCIPIENTS: May contain Polysorbates
ELECTROLYTES: May contain Sodium
▶ MabThera (Roche Products Ltd)
Rituximab 10 mg per 1 ml MabThera 100mg/10ml concentrate for solution for infusion vials | 2 vialP £349.25 (Hospital only)
MabThera 500mg/50ml concentrate for solution for infusion vials | 1 vialP £873.15 (Hospital only)
▶ Rixathon (Sandoz Ltd) A
Rituximab 10 mg per 1 ml Rixathon 100mg/10ml concentrate for solution for infusion vials | 2 vialP £314.33 (Hospital only)
Rixathon 500mg/50ml concentrate for solution for infusion vials | 1 vialP £785.84 (Hospital only) | 2 vialP £1,571.67 (Hospital only)
▶ Ruxience (Pfizer Ltd) A
Rituximab 10 mg per 1 ml Ruxience 100mg/10ml concentrate for solution for infusion vials | 1 vialP £157.17 (Hospital only)
Ruxience 500mg/50ml concentrate for solution for infusion vials | 1 vialP £785.84 (Hospital only)
▶ Truxima (Napp Pharmaceuticals Ltd) A
Rituximab 10 mg per 1 ml Truxima 100mg/10ml concentrate for solution for infusion vials | 2 vialP £314.33 (Hospital only)
Truxima 500mg/50ml concentrate for solution for infusion vials | 1 vialP £785.84 (Hospital only)



## Sacituzumab govitecan 01-Apr-2022

I DRUG ACTION Sacituzumab govitecan is an antibody-drug conjugate. The monoclonal antibody component, sacituzumab binds to tumor-associated calcium signal transducer 2 (Trop-2) expressing cancer cells to deliver the linked topoisomerase I inhibitor component into the cells, leading to apoptosis and cell death.
I INDICATIONS AND DOSE
Breast cancer (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: 10 mg/kg on days 1 and 8 of a 21-day cycle, for dose adjustments or discontinuation due to sideeffects and infusion-related reactions—consult product literature
I CAUTIONS Patients with reduced uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1) activity (increased risk of adverse reactions) . pre-medication recommended to minimise the development of adverse reactions and infusion-related reactions—consult product literature
I INTERACTIONS → Appendix 1: sacituzumab govitecan

I SIDE-EFFECTS

▶ Common or very common Allergic rhinitis . alopecia . anaemia . appetite decreased . arthralgia . asthma . back pain . chest discomfort . choking . constipation . cough . decreased leucocytes . dehydration . diarrhoea . dizziness . dyspnoea . electrolyte imbalance . epistaxis . eye inflammation . eye pruritus . facial swelling . fatigue . fever . flushing . gastrointestinal discomfort . headache . hyperglycaemia . hypersensitivity . hypotension . increased risk of infection . insomnia . nausea . neutropenia . oedema . oral disorders . respiratory disorders . scrotal oedema . seasonal allergy . skin reactions . swelling . taste altered . throat tightness . vomiting . weight decreased

I ALLERGY AND CROSS-SENSITIVITY gContra-indicated in patients with hypersensitivity to previous irinotecan therapy. M

I CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception during treatment and for 6 months after last treatment; male patients should use effective contraception during treatment and for 3 months after last treatment if their partner is of childbearing potential. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.g Female fertility may be impaired—impairment of fertility has been observed in animal studies. M

I PREGNANCY gAvoid—theoretically teratogenic (topoisomerase I inhibitor). MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING gAvoid during treatment and for 1 month after last treatment—no information available. M

I HEPATIC IMPAIRMENT gAvoid in moderate or severe impairment (no information available). M

I MONITORING REQUIREMENTS

▶gMonitor complete blood count before each dose and as clinically indicated.

▶ Monitor patients for signs and symptoms of infusionrelated reactions during and for at least 30 minutes after completion of each infusion. M

I DIRECTIONS FOR ADMINISTRATION Resuscitation facilities should be available during administration of sacituzumab govitecan.

I PRESCRIBING AND DISPENSING INFORMATION Sacituzumab govitecan is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in refrigerator (2–8°C)—consult product literature for storage conditions after preparation of the infusion.

I PATIENT AND CARER ADVICE Patients and their carers should be advised to seek immediate medical attention if they have black stools, rectal bleeding, dehydration or are unable to tolerate oral fluids.

Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of dizziness.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

Scottish Medicines Consortium (SMC) decisions

▶ Sacituzumab govitecan (Trodelvy ®) for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior lines of systemic therapies, at least one of them given for unresectable locally advanced or metastatic disease (March 2022) SMC No. SMC2446 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Trodelvy (Gilead Sciences Ltd) A

Sacituzumab govitecan 180 mg Trodelvy 180mg powder for concentrate for solution for infusion vials | 1 vialP £793.00 (Hospital only)

## Siltuximab 30-Jul-2020

I DRUG ACTION Siltuximab is a monoclonal antibody that inhibits interleukin-6 receptor binding.

I INDICATIONS AND DOSE

Treatment of multicentric Castleman's disease (MCD) in patients who are human immunodeficiency virus (HIV) negative and human herpesvirus-8 (HHV-8) negative

▶ BY INTRAVENOUS INFUSION

▶ Adult: 11 mg/kg every 3 weeks

I CAUTIONS Patients at increased risk of gastrointestinal perforation—promptly investigate those presenting with symptoms suggestive of gastrointestinal perforation . severe infection—withhold treatment until resolved . treat infection prior to treatment

CAUTIONS, FURTHER INFORMATION

▶ Hypersensitivity reactions Infusion-related side-effects are reported commonly with siltuximab; resuscitation facilities should be available during treatment. Consult product literature for further information about siltuximab cautions.

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Abdominal pain . arthralgia . constipation . diarrhoea . dizziness . dyslipidaemia . gastrooesophageal reflux disease . headache . hypersensitivity . hypertension . hyperuricaemia . increased risk of infection . infusion related reaction . localised oedema . nausea . neutropenia . oral ulceration . oropharyngeal pain . pain in extremity . renal impairment . skin reactions . thrombocytopenia . vomiting . weight increased

SIDE-EFFECTS, FURTHER INFORMATION Siltuximab therapy should be discontinued permanently in the event of a severe infusion-related reaction, anaphylaxis, a severe allergic reaction, or the occurrence of cytokine-release syndrome. Mild to moderate infusion-related reactions may improve by temporarily reducing the rate or stopping the infusion. When restarting treatment, a reduced infusion rate and the administration of antihistamines,



paracetamol, and corticosteroids may be considered. Consider discontinuation of siltuximab if more than 2 doses are delayed due to treatment-related toxicities during the first 48 weeks—for full details consult product literature.

I CONCEPTION AND CONTRACEPTION Women of childbearing potential should use effective contraception during and for 3 months after treatment.

I PREGNANCY Manufacturer advises avoid unless potential benefit outweighs risk.

I BREAST FEEDING Manufacturer advises avoid—no information available.

I HEPATIC IMPAIRMENT Manufacturer advises caution (no information).

I MONITORING REQUIREMENTS

▶ Monitor neutrophil and platelet count, and haemoglobin levels prior to each dose of siltuximab treatment for the first 12 months and thereafter prior to every third dosing cycle. Consider delaying treatment if required neutrophil, platelet, and haemoglobin levels not achieved—consult product literature for details.

▶ Monitor for infection during treatment.

I DIRECTIONS FOR ADMINISTRATION For intravenous infusion (Sylvant ▪), manufacturer advises give intermittently in Glucose 5%. Allow vials to reach room temperature over approximately 30 minutes, then reconstitute each 100mg vial with 5.2mL of water for injection, and each 400mg vial with 20mL of water for injection, to produce a 20 mg/mL solution. Gently swirl without shaking to dissolve. Further dilute to 250mL with glucose 5% and gently mix. Use within 6 hours of dilution and give over 60 minutes using an administration set lined with polyvinyl chloride or polyurethane, through a low-protein binding in-line 0.2 micron filter.

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

▶ Sylvant (EUSA Pharma (UK) Ltd) A

Siltuximab 100 mg Sylvant 100mg powder for concentrate for solution for infusion vials | 1 vialP £502.00 (Hospital only)

Siltuximab 400 mg Sylvant 400mg powder for concentrate for solution for infusion vials | 1 vialP £2,009.00 (Hospital only)

## Tafasitamab 02-Mar-2022

I DRUG ACTION Tafasitamab is a monoclonal antibody that binds to CD19, a cell-surface antigen, resulting in lysis of B lymphocytes by immune-mediated actions and apoptosis.

I INDICATIONS AND DOSE
Diffuse large B-cell lymphoma (specialist use only)
▶ BY INTRAVENOUS INFUSION
▶ Adult: (consult product literature)
I CAUTIONS Active infection (should be treated and well controlled) . high tumour burden (risk of tumour lysis syndrome) . history of recurring or chronic infections . patients may need premedication to minimise infusionrelated reactions . rapidly proliferating tumours (risk of tumour lysis syndrome)
CAUTIONS, FURTHER INFORMATION
▶ Premedication gPremedication with an antihistamine, antipyretic, or corticosteroid is recommended—consult product literature. M
I INTERACTIONS → Appendix 1: monoclonal antibodies
I SIDE-EFFECTS
▶ Common or very common Abdominal pain . alopecia . anaemia . appetite decreased . arthralgia . asthenia . basal cell carcinoma . constipation . COPD exacerbated . cough . decreased leucocytes . diarrhoea . dyspnoea . electrolyte imbalance . fever . headache . hyperbilirubinaemia . hyperhidrosis . hypogammaglobulinaemia . increased risk of infection . infusion related reaction . malaise . mucositis . muscle spasms . nasal congestion . nausea . neutropenia . pain . paraesthesia . peripheral oedema . sepsis . skin reactions . taste altered . thrombocytopenia . vomiting . weight decreased
▶ Frequency not known Bone marrow depression . tumour lysis syndrome
I CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception during treatment and for at least 3 months after last treatment. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
I PREGNANCY gAvoid—no information available; if exposed during pregnancy, monitor infant for B-cell depletion. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.
I BREAST FEEDING gAvoid during treatment and for at least 3 months after last treatment—no information available. M
I MONITORING REQUIREMENTS gMonitor complete blood counts before each treatment cycle and throughout treatment. M
I PRESCRIBING AND DISPENSING INFORMATION Tafasitamab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.
I HANDLING AND STORAGE Store in a refrigerator (2–8°C) and protect from light—consult product literature for storage conditions after preparation of the infusion.
I PATIENT AND CARER ADVICE
Driving and skilled tasks Patients and carers should be counselled on the effects on driving and performance of skilled tasks—increased risk of fatigue.
I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Powder for solution for infusion
EXCIPIENTS: May contain Polysorbates
▶ Tafasitamab (non-proprietary) A
Tafasitamab 200 mg Minjuvi 200mg powder for concentrate for solution for infusion vials | 1 vialPs (Hospital only)

## Trastuzumab 20-Apr-2021

I INDICATIONS AND DOSE
Treatment of early breast cancer which overexpresses human epidermal growth factor receptor-2 (HER2) (initiated by a specialist) | Treatment of metastatic breast cancer in patients with HER2-positive tumours who have not received chemotherapy for metastatic breast cancer and in whom anthracycline treatment is inappropriate (in combination with paclitaxel or docetaxel) (initiated by a specialist) | Treatment of metastatic breast cancer in postmenopausal patients with hormone-receptor positive HER2-positive tumours not previously treated with trastuzumab (in combination with an aromatase inhibitor) (initiated by a specialist)
▶ BY INTRAVENOUS INFUSION, OR BY SUBCUTANEOUS INJECTION
▶ Adult: (consult product literature or local protocols)

Monotherapy for metastatic breast cancer in patients with tumours that overexpress HER2 who have received at least 2 chemotherapy regimens including, where appropriate, an anthracycline and a taxane (initiated by a specialist)

▶ BY INTRAVENOUS INFUSION, OR BY SUBCUTANEOUS INJECTION

▶ Adult: Women with oestrogen-receptor-positive breast cancer should also have received hormonal therapy (consult product literature or local protocols)

Treatment of metastatic gastric cancer in patients with HER2-positive tumours who have not received treatment for metastatic gastric cancer (in combination with capecitabine or fluorouracil and cisplatin) (initiated by a specialist)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature or local protocols)

I CONTRA-INDICATIONS Severe dyspnoea at rest

I CAUTIONS Coronary artery disease . elderly . history of hypertension . impaired left ventricular function . symptomatic heart failure . uncontrolled arrhythmias

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Alopecia . anaemia . angioedema . anxiety . appetite decreased . arrhythmias . arthralgia . arthritis . asthenia . asthma . breast abnormalities . cardiomyopathy . chest pain . chills . constipation . cough . cystitis . depression . diarrhoea . dizziness . drowsiness . dry eye . dry mouth . dyspnoea . excessive tearing . eye inflammation . fever . gastrointestinal discomfort . haemorrhage . haemorrhoids . headache . heart failure . hepatic disorders . hyperhidrosis . hypersensitivity . hypotension . increased risk of infection . influenza like illness . infusion related reaction (may be delayed) . insomnia . leucopenia . malaise . mucositis . muscle complaints . muscle tone increased . nail disorders . nausea . neutropenia . neutropenic sepsis . oedema . oral disorders . pain . palpitations . paraesthesia . peripheral neuropathy . renal disorder . respiratory disorders . rhinorrhoea . skin reactions . taste altered . thrombocytopenia . tremor . vasodilation . vomiting . weight decreased

▶ Uncommon Deafness . pericardial effusion

▶ Frequency not known Cancer progression . cardiogenic shock . glomerulonephritis . hyperkalaemia . hypoprothrombinaemia . hypoxia . pulmonary fibrosis (may be delayed) . pulmonary oedema (may be delayed) . renal failure

I CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception in women of childbearing potential during and for 7 months after treatment. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY Manufacturer advises avoid—oligohydramnios reported. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING Avoid breast-feeding during treatment and for 7 months afterwards.

I MONITORING REQUIREMENTS

▶ Cardiotoxicity Monitor cardiac function before and during treatment—for details of monitoring and managing cardiotoxicity, consult product literature.

I DIRECTIONS FOR ADMINISTRATION Resuscitation facilities should be available during administration of trastuzumab.

I PRESCRIBING AND DISPENSING INFORMATION When prescribing, dispensing, or administering, check that this is the correct preparation—trastuzumab is not interchangeable with trastuzumab emtansine or trastuzumab deruxtecan.

Trastuzumab is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in a refrigerator (2-8°C); consult product literature for storage conditions after preparation of the infusion.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Guidance on the use of trastuzumab for the treatment of advanced breast cancer (March 2002) NICE TA34 Recommended with restrictions

▶ Lapatinib or trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormonereceptor-positive breast cancer that overexpresses HER2 (June 2012) NICE TA257 Not recommended

▶ Pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer (March 2018) NICE TA509 Recommended with restrictions

▶ Trastuzumab for the treatment of HER2-positive metastatic gastric cancer (November 2010) NICE TA208 Recommended with restrictions

Scottish Medicines Consortium (SMC) decisions

▶ Trastuzumab (Herceptin ®) for the treatment of adult patients with HER2 positive metastatic breast cancer and early breast cancer (January 2014) SMC No. 928/13 Recommended with restrictions

▶ Trastuzumab (Herceptin ®) in combination with capecitabine or fluorouracil and cisplatin for the treatment of patients with HER2 positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction who have not received prior anticancer treatment for their metastatic disease (October 2015) SMC No. 623/10 Recommended with restrictions

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Solution for injection

▶ Herceptin (Roche Products Ltd)

Trastuzumab 120 mg per 1 ml Herceptin 600mg/5ml solution for injection vials | 1 vialP £1,222.20 (Hospital only)

Powder for solution for infusion

▶ Herceptin (Roche Products Ltd)

Trastuzumab 150 mg Herceptin 150mg powder for concentrate for solution for infusion vials | 1 vialP £407.40 (Hospital only)

▶ Herzuma (Napp Pharmaceuticals Ltd) A

Trastuzumab 150 mg Herzuma 150mg powder for concentrate for solution for infusion vials | 1 vialP £366.66 (Hospital only)

Trastuzumab 420 mg Herzuma 420mg powder for concentrate for solution for infusion vials | 1 vialP £1,026.65 (Hospital only)

▶ Kanjinti (Amgen Ltd) A

Trastuzumab 150 mg Kanjinti 150mg powder for concentrate for solution for infusion vials | 1 vialP £366.66 (Hospital only)

Trastuzumab 420 mg Kanjinti 420mg powder for concentrate for solution for infusion vials | 1 vialP £1,026.65 (Hospital only)

▶ Ontruzant (Organon Pharma (UK) Ltd) A

Trastuzumab 150 mg Ontruzant 150mg powder for concentrate for solution for infusion vials | 1 vialP £366.66 (Hospital only)

▶ Trazimera (Pfizer Ltd) A

Trastuzumab 150 mg Trazimera 150mg powder for concentrate for solution for infusion vials | 1 vialP £366.66 (Hospital only)

Trastuzumab 420 mg Trazimera 420mg powder for concentrate for solution for infusion vials | 1 vialP £1,026.65 (Hospital only)

▶ Zercepac (Accord Healthcare Ltd) A

Trastuzumab 150 mg Zercepac 150mg powder for concentrate for solution for infusion vials | 1 vialP £366.65 (Hospital only)



## Trastuzumab deruxtecan 11-Feb-2022

I DRUG ACTION Trastuzumab deruxtecan is an antibodydrug conjugate that contains trastuzumab covalently linked to deruxtecan, a topoisomerase I inhibitor.

I INDICATIONS AND DOSE

HER2-positive unresectable or metastatic breast cancer (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature or local protocols)

I CAUTIONS History of interstitial lung disease or pneumonitis . impaired left ventricular function . patients aged 75 years and over (limited information available)

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Alopecia . anaemia . appetite decreased . asthenia . constipation . cough . decreased leucocytes . diarrhoea . dizziness . dry eye . dyspnoea . epistaxis . flushing . gastrointestinal discomfort . headaches . heart failure . hypersensitivity . hypokalaemia .

increased risk of infection . influenza like illness . infusion related reaction . lymphangitis . nausea . neutropenia . oral disorders . respiratory disorders . skin reactions . thrombocytopenia . vomiting

I CONCEPTION AND CONTRACEPTION gFemales of childbearing potential should use effective contraception during treatment and for at least 7 months after last treatment; male patients should use effective contraception during treatment and for at least 4 months after last treatment if their partner is of childbearing potential. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I PREGNANCY gAvoid—oligohydramnios reported with trastuzumab. MSee also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

I BREAST FEEDING gAvoid breast-feeding during and for 7 months after treatment. M

I HEPATIC IMPAIRMENT gCaution in moderate or severe impairment (primarily biliary excretion). M

I MONITORING REQUIREMENTS

▶gMeasure complete blood counts prior to initiation, before each dose, and as clinically indicated.

▶ Test cardiac function before treatment and regularly during treatment—delay or discontinue treatment in cases of left ventricular dysfunction; discontinue treatment in symptomatic heart failure.

▶ Monitor for signs and symptoms of interstitial lung disease or pneumonitis—discontinue if confirmed (fatal cases reported). M

I PRESCRIBING AND DISPENSING INFORMATION When prescribing, dispensing, or administering, check that this is the correct preparation—trastuzumab deruxtecan is not interchangeable with trastuzumab or trastuzumab emtansine.

Trastuzumab deruxtecan is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

I HANDLING AND STORAGE Store in a refrigerator (2-8°C); consult product literature for storage conditions after preparation of the infusion.

I NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 2 or more anti-HER2 therapies (May 2021) NICE TA704 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Trastuzumab deruxtecan (Enhertu ®) as monotherapy for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens (January 2022) SMC No. SMC2388 Recommended

I MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Powder for solution for infusion

EXCIPIENTS: May contain Polysorbates

▶ Enhertu (Daiichi Sankyo UK Ltd) A

Trastuzumab deruxtecan 100 mg Enhertu 100mg powder for concentrate for solution for infusion vials | 1 vialP £1,455.00 (Hospital only)

## Trastuzumab emtansine 17-May-2021

I DRUG ACTION Trastuzumab emtansine is an antibodydrug conjugate that contains trastuzumab covalently linked to DM1, a cytotoxic microtubule inhibitor.

I INDICATIONS AND DOSE

HER2-positive metastatic breast cancer (specialist use only) | HER2-positive early breast cancer (specialist use only)

▶ BY INTRAVENOUS INFUSION

▶ Adult: (consult product literature or local protocols)

I CAUTIONS Dyspnoea at rest—increased risk of pulmonary events . history of congestive heart failure . patients over 75 years . peripheral neuropathy (temporarily discontinue treatment—consult product literature) . recent history of myocardial infarction . recent history of unstable angina . risk of left ventricular dysfunction—consult product literature for specific risks with trastuzumab treatment . serious arrhythmias

I INTERACTIONS → Appendix 1: monoclonal antibodies

I SIDE-EFFECTS

▶ Common or very common Alopecia . anaemia . arthralgia . asthenia . chills . conjunctivitis . constipation . cough . diarrhoea . dizziness . dry eye . dry mouth . dyspnoea . excessive tearing . fever . gastrointestinal discomfort . haemorrhage . headache . hypersensitivity . hypertension . hypokalaemia . infusion related reaction . insomnia . left ventricular dysfunction . leucopenia . memory loss . musculoskeletal pain . myalgia . nail disorder . nausea . neutropenia . peripheral neuropathy . peripheral oedema . skin reactions . stomatitis . taste altered . thrombocytopenia . urinary tract infection . vision blurred . vomiting

▶ Uncommon Hepatic disorders . nodular regenerative hyperplasia . pneumonitis

ı CONCEPTION AND CONTRACEPTION Manufacturer advises effective contraception must be used during and for 7 months after stopping treatment in women and men. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

ı PREGNANCY Manufacturer advises avoid—oligohydramnios reported with trastuzumab. See also Pregnancy and reproductive function in Cytotoxic drugs p. 962.

ı BREAST FEEDING Manufacturer advises avoid breastfeeding during and for 7 months after treatment.

ı HEPATIC IMPAIRMENT Manufacturer advises caution—consult product literature.

Dose adjustments Manufacturer advises dose reduction according to liver function tests—consult product literature.

ı RENAL IMPAIRMENT gCaution in severe impairment (no information available). M

## 960 Antibody responsive malignancy BNF 84

Immune system and malignant disease

ı MONITORING REQUIREMENTS

▶ Monitor hepatic function before each dose.

▶ Monitor for signs and symptoms of neurotoxicity.

▶ Monitor closely for infusion-related and hypersensitivity reactions.

▶ Monitor platelet count before each dose and as clinically indicated (consult product literature for treatment modification in thrombocytopenia).

▶ Test cardiac function before treatment and regularly during treatment—delay or discontinue treatment in cases of left ventricular dysfunction.

▶ Monitor for dyspnoea, cough, fatigue and pulmonary infiltrates—discontinue if interstitial lung disease or pneumonitis confirmed (fatal cases reported).

ı DIRECTIONS FOR ADMINISTRATION Resuscitation facilities should be available during administration of trastuzumab emtansine.

ı PRESCRIBING AND DISPENSING INFORMATION When prescribing, dispensing, or administering, check that this is the correct preparation—trastuzumab emtansine is not interchangeable with trastuzumab or trastuzumab deruxtecan.

Trastuzumab emtansine is a biological medicine. Biological medicines must be prescribed and dispensed by brand name, see Biological medicines and Biosimilar medicines, under Guidance on prescribing p. 1; record the brand name and batch number after each administration.

ı HANDLING AND STORAGE Store in a refrigerator (2-8°C); consult product literature for storage conditions after preparation of the infusion.

ı NATIONAL FUNDING/ACCESS DECISIONS

For full details see funding body website

NICE decisions

▶ Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane (updated November 2017) NICE TA458 Recommended with restrictions

▶ Trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer (June 2020) NICE TA632 Recommended

Scottish Medicines Consortium (SMC) decisions

▶ Trastuzumab emtansine (Kadcyla ®) for HER2-positive, unresectable locally advanced or metastatic breast cancer after trastuzumab and a taxane (April 2017) SMC No. 990/14 Recommended

▶ Trastuzumab emtansine (Kadcyla ®) as a single agent, for the

adjuvant treatment of adult patients with HER2-positive early breast cancer who have residual invasive disease, in the breast and/or lymph nodes, after neoadjuvant taxane-based and HER2-targeted therapy (November 2020)
SMC No. SMC2298 Recommended
MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.
Powder for solution for infusion
► Kadcyla (Roche Products Ltd)
Trastuzumab emtansine 100 mg Kadcyla 100mg powder for concentrate for solution for infusion vials | 1 vial P £1,641.01
Trastuzumab emtansine 160 mg Kadcyla 160mg powder for concentrate for solution for infusion vials | 1 vial P £2,625.62