English Language

PACKAGE INSERT

SCHEDULING STATUS
S3

1. NAME OF MEDICINE:
INNOFLAM 100 (Hard Capsules)
INNOFLAM 200 (Hard Capsules)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each **INNOFLAM** 100 capsule contains 100 mg celecoxib.
Each **INNOFLAM** 200 capsule contains 200 mg celecoxib.
Excipient with known effect
Contains sugar: Lactose monohydrate
Each **INNOFLAM** 100 capsule contains 25 mg of lactose monohydrate
Each **INNOFLAM** 200 capsule contains 50 mg of lactose monohydrate

For the full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM
Hard gelatin capsules.
INNOFLAM 100 (Capsules):
Hard gelatin capsules size "3" having imprinting "135" on the opaque white body with blue ink and "A" on the opaque white cap with blue ink filled with white to off white colored granular powder.

INNOFLAM 200 (Capsules):
Hard gelatin capsules size "1" having imprinting "136" on the opaque white body with golden yellow ink and "A" on the opaque white cap with golden yellow ink filled with white to off white colored granular powder.

4.CLINICAL PARTICULARS
4.1 Therapeutic Indications
- Symptomatic treatment of inflammation and pain in osteoarthritis and rheumatoid arthritis.
- Treatment of pain after dental surgery.
- Treatment of mild to moderate post-operative pain.
- Treatment of mild to moderate musculoskeletal pain.
- Treatment of mild to moderate primary dysmenorrhoea.
- Relief of symptoms of ankylosing spondylitis.

4.2 Posology and method of administration
Posology
As the cardiovascular risks of **INNOFLAM** may increase with dose and duration of exposure, the lowest effective daily dose should be used, for the shortest possible duration of treatment.
Osteoarthritis
The recommended daily dose is 200 mg, taken as a single dose or as two divided doses. Doses up to 400 mg per day have been studied.
Rheumatoid arthritis
The recommended daily dose is 100 mg or 200 mg twice per day.
Pain post-dental surgery
The recommended dose is 100 mg to 200 mg, up to a maximum daily dose of 400 mg. Dosing intervals should not be less than 4 hours.
Mild to moderate post-operative pain
The recommended dose is 200 mg once daily. Some patients may benefit from an additional 200 mg dose.
Mild to moderate musculoskeletal pain
The recommended dose is 200 mg twice daily.
Mild to moderate primary dysmenorrhea
The recommended dose is 400 mg initially, followed by an additional 200 mg dose if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily.
Ankylosing spondylitis
The recommended daily dose is 200 mg, taken as a single dose or as 100 mg twice daily. Some patients may benefit from a total daily dose of 400 mg.
Special populations
Hepatic impairment
No dosage adjustment is necessary in patients with mild hepatic impairment. Introduce **INNOFLAM** at the lowest recommended dose in patients with moderate hepatic impairment. There is no clinical experience in patients with severe hepatic impairment (See sections 4.3 and 5.2).
Renal impairment
No dosage adjustment is necessary in patients with mild or moderate renal impairment. There is no clinical experience in patients with severe renal impairment. (See sections 4.3 and 5.2).
Elderly
No dosage adjustment is necessary. However, for elderly patients with a body mass of 50 kg or less it is advisable to initiate therapy at the lowest recommended dose.
Children
As no data are available, **INNOFLAM** is not recommended in persons under 18 years old.
Method of administration
Oral use. **INNOFLAM** should be taken whole with a glass of water, with or without food.

4.3 Contraindications:
- Hypersensitivity to celecoxib, or any other excipient of **INNOFLAM** (see section 6.1).
- Known hypersensitivity to sulphonamide.
- Severe hepatic impairment (serum albumin < 25 g/L or Child-Pugh score > 10).
- Severe renal impairment with estimated creatinine clearance < 30 mL/min.
- Asthma, urticaria, or allergic-type reactions precipitated by aspirin or non-steroidal anti-inflammatory drugs (NSAIDs), including other cyclooxygenase - 2 (COX-2) specific inhibitors.
- Established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.
- Peri-operative analgesia against the background of coronary artery bypass surgery (CABG).
- Active peptic ulceration or gastrointestinal (GI) bleeding.
- Inflammatory bowel disease.
- In pregnancy and in women of childbearing potential unless using an effective method of contraception (see section 4.6). The potential for human risk in pregnancy is unknown but cannot be excluded.
- Breastfeeding (see section 4.6).

4.4 Special warnings and precautions for use

INNOFLAM may predispose to cardiovascular incidents, cerebrovascular incidents, gastrointestinal events or cutaneous reactions that may be fatal.

Safety and efficacy of **INNOFLAM** have not been established for treatment exceeding 12 weeks in osteoarthritis and 24 weeks in rheumatoid arthritis.
Cardiovascular effects
Increased number of serious cardiovascular (CV) events, mainly myocardial infarction, has been reported in patients with sporadic adenomatous polyps treated with celecoxib (as in **INNOFLAM**) at doses of 200 mg twice daily and 400 mg twice daily, compared to placebo (see section 5.1).
As the cardiovascular risks of **INNOFLAM** may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. NSAIDs, including COX-2 selective inhibitors, have been associated with increased risk of cardiovascular and thrombotic adverse events when taken long term. The exact magnitude of the risk associated with a single dose has not been determined, nor has the exact duration of therapy associated with increased risk. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically, etspecially in patients with osteoarthritis (see sections 4.2, 4.3, 4.8 and 5.1).
Caution is advised when **INNOFLAM** is prescribed to patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).
INNOFLAM is not a substitute for aspirin for prophylaxis of cardiovascular thromboembolic diseases because of their lack of antiplatelet effects. Therefore, antiplatelet therapies should not be discontinued.
Anaphylactoid reactions
As with NSAIDs in general, anaphylactoid reactions occurred in patients exposed to **INNOFLAM** (see sections 4.3).
Gastrointestinal (GI) effects
Upper and lower gastrointestinal complications (perforations, ulcers or bleedings (PUBs)), some resulting in fatalities, have occurred in patients treated with celecoxib (as in **INNOFLAM**). Caution is advised with treatment of patients most at risk of developing a gastrointestinal complication with NSAIDs; the elderly, patients using any other NSAID or antiplatelet medicines (such as aspirin) or glucocorticoids concomitantly, patients using alcohol, or patients with a prior history of gastrointestinal disease, such as ulceration and GI bleeding.
When **INNOFLAM** is taken concomitantly with aspirin (even at low doses), there is further increase in the risk of gastrointestinal adverse effects for celecoxib (gastrointestinal ulceration or other gastrointestinal complications).
A significant difference in GI safety between selective COX-2 inhibitors plus aspirin vs NSAIDs plus aspirin has not been demonstrated in long-term clinical trials.
Concomitant NSAID use
The concomitant use of **INNOFLAM** and a non-aspirin NSAID should be avoided.
Fluid retention and oedema
Fluid retention and oedema have been observed in patients taking celecoxib (as in **INNOFLAM**). Therefore, **INNOFLAM** should be used with caution in patients with history of cardiac failure, left ventricular dysfunction or hypertension, and in patients with pre-existing oedema from any other reason, since prostaglandin inhibition may result in deterioration of renal function and fluid retention.
Caution is also required in patients taking diuretic treatment or otherwise at risk of hypovolaemia.
Patients with pre-existing congestive heart failure or hypertension should be closely monitored.
Hypertension
NSAIDs, including celecoxib (as in **INNOFLAM**) can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Therefore, blood pressure should be monitored closely during the initiation of therapy with **INNOFLAM** and throughout the course of therapy.
Hepatic and renal effects
Compromised renal or hepatic function and especially cardiac dysfunction are more likely in the elderly and therefore medically appropriate supervision should be maintained.
NSAIDs, including **INNOFLAM**, may cause renal toxicity. Celecoxib has shown renal effects similar to those observed with comparator NSAIDs. Patients at greatest risk for renal toxicity are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, angiotensin converting enzyme (ACE)-inhibitors, angiotensin II receptor antagonists, and the elderly (see section 4.5). Such patients should be carefully monitored while receiving treatment with **INNOFLAM**.
Some cases of severe hepatic reactions, including fulminant hepatitis (some with fatal outcome), liver necrosis and hepatic failure (some with fatal outcome or requiring liver transplant), have been reported with celecoxib (contained in **INNOFLAM**. Among the cases that reported time to onset, most of the severe adverse hepatic events developed within one month after initiation of celecoxib (contained in **INNOFLAM** treatment (see section 4.8).
If during treatment, patients deteriorate in any of the organ system functions described above, appropriate measures should be taken and discontinuation of **INNOFLAM** therapy should be considered.
Caution should be used when initiating treatment in patients with dehydration. It is advisable to first rehydrate patients and then commence with **INNOFLAM** therapy.
CYP2D6 inhibition
Celecoxib inhibits CYP2D6. Although it is not a strong inhibitor of this enzyme, a dose reduction of **INNOFLAM** may be necessary for individually dose-titrated medicines that are metabolised by CYP2D6 (see section 4.5).
CYP2C9 poor metabolisers
Patients known to be CYP2C9 poor metabolisers should be treated with caution.
Skin and systemic hypersensitivity reactions
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of celecoxib (as in **INNOFLAM**), see section 4.8.
Patients appear to be at highest risk for these events early in the course of therapy: the onset of the event occurring in the majority of cases within the first month of treatment. Serious hypersensitivity reactions (including anaphylaxis, angioedema and drug rash with eosinophilia and systemic symptoms (DRESS), or hypersensitivity syndrome), have been reported in patients receiving celecoxib (as in **INNOFLAM**), see section 4.8.
Patients with a history of sulphonamide allergy or any medicine allergy may be at greater risk of serious skin reactions or hypersensitivity reactions (see section 4.3). **INNOFLAM** should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as **INNOFLAM**. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophillia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue **INNOFLAM** and evaluate the patient immediately.
General
INNOFLAM may mask fever and other signs of inflammation.
Use with oral anticoagulants
In patients on concurrent therapy with warfarin, serious bleeding events, of which some were fatal, have been reported (see sections 4.8 and 4.5). Because increases in prothrombin time (INR) have been reported, anticoagulant activity should be closely monitored in patients receiving warfarin/coumarin-type oral anticoagulants, particularly when therapy with **INNOFLAM** is initiated, or its dose is changed (see section 4.5). Concomitant use of anticoagulants with NSAIDs may increase the risk of bleeding. Caution should be exercised when combining **INNOFLAM** with warfarin or other oral anticoagulants, including novel anticoagulants (e.g. apixaban, dabigatran, and rivaroxaban).
Excipients
INNOFLAM 100 mg and 200 mg capsules contain lactose monohydrate (see sections 2 and 6.1). Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose/galactose malabsorption should not take **INNOFLAM**.

4.5 Interaction with other medicines and other forms of interaction
Pharmacodynamic interactions
Anticoagulants
In patients on concurrent therapy with warfarin, increases in prothrombin time (INR) have been reported (see section 4.4).)
Anticoagulant activity should be monitored particularly in the first few days after initiating or changing the dose of **INNOFLAM** in patients receiving warfarin or other anticoagulants since these patients have an increased risk of bleeding complications. Therefore, patients receiving oral anticoagulants should be closely monitored for their prothrombin time INR, particularly in the first few days when therapy with **INNOFLAM** is initiated or its dose is changed (see section 4.4). Bleeding events in association with increases in prothrombin time (INR) have been reported, predominantly in the elderly, in patients receiving celecoxib (as in **INNOFLAM**) concurrently with warfarin, some of them fatal.
Anti-hypertensives
NSAIDs, including **INNOFLAM**, may reduce the effect of antihypertensive medicines (including ACE inhibitors, angiotensin II receptor antagonists, diuretics and beta-blockers). This interaction should be given consideration in patients taking **INNOFLAM** concomitantly with antihypertensive medicines.
As for NSAIDs, the risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. dehydrated patients, patients on diuretics or elderly patients) when ACE inhibitors or angiotensin II receptor antagonists, and/or diuretics are combined with NSAIDs, including **INNOFLAM** (see section 4.4). Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to
monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.
Clinical studies, as well as post-marketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis.
Ciclosporin and tacrolimus
Co-administration of NSAIDs (including **INNOFLAM**) and ciclosporin or tacrolimus may increase the nephrotoxic effect of ciclosporin or tacrolimus, respectively. Renal function should be monitored when **INNOFLAM** and any of these medicines are combined.
Aspirin
INNOFLAM can be used with low-dose aspirin. However, concomitant administration of aspirin with **INNOFLAM** may result in an increased rate of GI ulceration or other complications, compared to use of **INNOFLAM** alone. Because of its lack of platelet effects, **INNOFLAM** is not a substitute for aspirin for cardiovascular prophylaxis.
There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thrombotic events associated with **INNOFLAM**.
An increased risk of gastrointestinal ulceration or other gastrointestinal complications compared to use of **INNOFLAM** alone was shown for concomitant administration of low-dose aspirin.
Pharmacokinetic interactions
*Effects of **INNOFLAM** on other medicines*
CYP2D6 inhibition
Celecoxib is an inhibitor of CYP2D6. The plasma concentrations of medicines that are substrates of this enzyme may be increased when **INNOFLAM** is used concomitantly. Examples of medicines which are metabolised by CYP2D6 are antidepressants (tricyclics and SSRIs), neuroleptics, antidysrhythmic medicines, etc. The dose of individually dose-titrated CYP2D6 substrates may need to be reduced when treatment with **INNOFLAM** is initiated or increased if treatment with **INNOFLAM** is terminated.
Concomitant administration of celecoxib 200 mg twice daily resulted in 2,6-fold and 1,5-fold increases in plasma concentrations of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to celecoxib CYP2D6 inhibition of the CYP2D6 substrate metabolism.
CYP2C19 inhibition
In vitro studies have shown some potential for celecoxib to inhibit CYP2C19 catalysed metabolism. The clinical significance of this in vitro finding is unknown. Examples of medicines which are metabolised by CYP2C19 are diazepam, citalopram and imipramine.
Methotrexate
In patients with rheumatoid arthritis celecoxib had no statistically significant effect on the pharmacokinetics (plasma or renal clearance) of methotrexate (in rheumatologic doses). However, adequate monitoring for methotrexate-related toxicity should be considered when combining these two medicines.
Lithium
In healthy persons, co-administration of celecoxib 200 mg twice daily with 450 mg twice daily of lithium resulted in a mean increase in C_{max} of 16 % and in area under the curve (AUC) of 18 % of lithium. Therefore, patients on lithium treatment should be closely monitored when **INNOFLAM** is introduced or withdrawn.
Oral contraceptives
In an interaction study, celecoxib had no clinically relevant effects on the pharmacokinetics of oral contraceptives (1 mg norethisterone/ 35 micrograms ethinylestradiol). Glibenclamide/tolbutamide Celecoxib does not affect the pharmacokinetics of tolbutamide (CYP2C9 substrate), or glibenclamide to a clinically relevant extent.
Phenytoin
In specific studies in healthy volunteers with other medicines metabolised by CYP2C9, celecoxib was found to produce no clinically significant pharmacokinetic interaction with phenytoin.
*Effects of other medicines on **INNOFLAM***
CYP2C9 poor metabolisers
In individuals who are CYP2C9 poor metabolisers and demonstrate increased systemic exposure to celecoxib, concomitant treatment with CYP2C9 inhibitors such as fluconazole could result in further increases in celecoxib exposure. Such combinations should be avoided in known CYP2C9 poor metabolisers (see section 4.4).
CYP2C9 inhibitors and inducers
Since celecoxib is predominantly metabolised by CYP2C9, **INNOFLAM** should be used at half the recommended dose in patients receiving fluconazole. Concomitant use of 200 mg single dose of celecoxib and 200 mg once daily of fluconazole, a potent CYP2C9 inhibitor, resulted in a mean increase in celecoxib Cmax of 60 % and in AUC of 130 %. Concomitant use of inducers of CYP2C9 such as rifampicin, carbamazepine and barbiturates may reduce plasma concentrations of celecoxib.
Ketoconazole and antacids
Ketoconazole or antacids have not been observed to affect the pharmacokinetics of celecoxib.
Paediatric populations
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation
Pregnancy
INNOFLAM is contraindicated in pregnancy (see section 4.3)
INNOFLAM may cause uterine inertia and premature closure of the ductus arteriosus and should be avoided during pregnancy.
Regular use of non-steroidal inflammatory drugs may result in:
First trimester
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies raise concern about an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1 %, up to approximately 1,5 %. In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-foetal lethality. In addition, increased incidences of various malformations including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.
Second and Third trimester.
During the third trimester of pregnancy, prostaglandin synthesis inhibitors, may expose the foetus to: cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension); renal dysfunction, which may progress to renal failure with oligo-hydroamniosis.
At the end of pregnancy, the mother and the neonate may be exposed to: possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses; inhibition of uterine contractions resulting in delayed or prolonged labour. The use of **INNOFLAM** should be limited to the lowest effective dose for the shortest duration, if deemed necessary by a healthcare professional. (see section 4.3 and 4.4)
Breastfeeding
Limited data indicate that **INNOFLAM** is excreted in breast milk and must therefore not be used during lactation.
Fertility
Based on the mechanism of action, the use of NSAIDs, including **INNOFLAM**, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women.

4.7 Effects on ability to drive and use machines
Patients who experience dizziness, vertigo or somnolence (see section 4.8) while taking **INNOFLAM** should refrain from driving or operating machinery.

4.8 Undesirable effects
Tabulated list of adverse reactions
Infections and infestations
Frequent: Sinusitis, upper respiratory tract infection, pharyngitis, urinary tract infection, bronchitis
Less frequent: Helicobacter infection, herpes zoster, erysipelas, bronchopneumonia, labyrinthitis, gingival infection
Blood and the lymphatic system disorders
Less frequent: Anaemia, leukopenia, thrombocytopenia, pancytopenia, agranulocytosis, ecchymosis
Immune system disorder
Frequent: Hypersensitivity, allergy aggravated
Less frequent: Anaphylactic shock, anaphylactic reaction, angioedema
Frequency unknown: Anaphylaxis
Metabolism and nutrition disorders
Frequent: Increased weight
Less frequent: Hyperkalaemia, increased blood sodium
Psychiatric disorders:
Frequent: Insomnia
Less frequent: Anxiety, depression, fatigue, confusional state, hallucinations
Nervous system disorders:
Frequent: Dizziness, hypertonia, headache
Frequency unknown: Cerebral infarction (stroke), paraesthesia, somnolence, ataxia, dysgeusia, intracranial haemorrhage (including fatal intracranial haemorrhage), aseptic meningitis, epilepsy (including aggravated epilepsy), ageusia, anosmia
Eye disorders:
Less frequent: Blurred vision, conjunctivitis, eye haemorrhage, retinal artery occlusion, retinal vein occlusion, vitreous floaters, conjunctival haemorrhage
Ear and labyrinth disorders:
Less frequent: Tinnitus, hypoacusis, dysphonia
Cardiac disorders:
Frequent: Myocardial infarction, angina pectoris
Less frequent: Cardiac failure, palpitations, tachycardia, dysrhythmia
Frequency unknown: Cardiovascular thrombotic incidents
Vascular disorder:
Frequent: Hypertension (including aggravated hypertension)
Less frequent: Pulmonary embolism, flushing, vasculitis, deep vein thrombosis
Respiratory, thoracic and mediastinal disorders:
Frequent: Rhinitis, cough, dyspnoea
Less frequent: Bronchospasm, pneumonitis
Gastrointestinal disorders:
Frequent: Nausea, abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dysphagia, irritable bowel syndrome, tooth disorder
Less frequent: Constipation, gastritis, stomatitis, gastrointestinal inflammation (including aggravation of gastrointestinal inflammation), eructation, gastrointestinal haemorrhage, duodenal ulcer, gastric ulcer, oesophageal ulcer, intestinal ulcer, large intestinal ulcer, intestinal perforation, oesophagitis, melaena, pancreatitis, colitis, haemorrhoidal haemorrhage, frequent bowel movements, mouth ulceration.
Hepatobiliary disorder
Less frequent: Abnormal hepatic function, increased hepatic enzymes (including increased AST and ALT), hepatitis, hepatic failure (sometimes fatal or requiring liver transplant), fulminant hepatitis (some with fatal outcome), hepatic necrosis, cholestasis, cholestatic jaundice
Skin and subcutaneous tissue disorder:
Frequent: Rash, pruritus (includes generalised pruritus)
Less frequent: Urticaria, ecchymosis, alopecia, photosensitivity, exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP), bullous dermatitis, lipoma, allergic dermatitis, ganglion
Musculoskeletal and connective tissue disorders:
Frequent: Arthralgia
Less frequent: Muscle spasms (leg cramps), myositis, lower limb fracture
Renal and urinary disorders:
Less frequent: Increased blood creatinine, increased blood urea, acute renal failure, hyponatraemia, tubulointerstitial nephritis, nephrotic syndrome, glomerulonephritis minimal lesion, nephrolithiasis, nocturia
Reproductive system and breast disorders:
Less frequent: Menstrual disorder
Frequency unknown: Female infertility (female fertility decreased), vaginal haemorrhage, breast tenderness
General disorders and administration site conditions:
Frequent: Influenza-like illness, peripheral oedema/fluid retention
Less frequent: Face oedema, chest pain
Injury, poisoning and procedural complications disorders:
Frequent Accidental injury
Description of selected adverse reactions:
In final data (adjudicated) from the APC and PreSAP trials in patients treated with celecoxib 400 mg daily for up to 3 years (pooled data from both trials), the excess rate over placebo for myocardial infarction was 7,6 events per 1 000 patients (less frequent) and there was no excess rate for stroke (types not differentiated) over placebo. Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) [see Section 4.4]
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
There is no clinical experience of overdose. Single doses up to 1 200 mg and multiple doses up to 1 200 mg twice daily have been administered to healthy persons without significant clinical adverse effects.
In the event of a suspected overdose, appropriate supportive medical care should be provided. Dialysis is not likely to be an efficient method of medicine removal.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Category A, class 3.1 Antirheumatics (anti-inflammatory agents)
Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic drugs, NSAIDs, Coxibs, ATC code: M01AH01.
Celecoxib is a specific cyclooxygenase-2 (COX-2) inhibitor (SCI)
Cyclooxygenase-2 is induced in response to inflammatory stimuli. This leads to the synthesis and accumulation of inflammatory prostanoids, particularly prostaglandin E2, causing inflammation, oedema and pain.
Celecoxib acts as an anti-inflammatory, analgesic and anti-pyretic medicine by blocking the production of inflammatory prostanoids via COX-2 inhibition. Celecoxib has a very low affinity for the constitutively expressed cyclooxygenase -1 enzyme (COX-1).

5.2 Pharmacokinetic properties
Absorption: When given under fasting conditions celecoxib reaches peak plasma concentrations after approximately 2-3 hours.
Celecoxib exhibits linear and dose proportional pharmacokinetics over the therapeutic dose range.
Plasma protein binding is concentration independent and is about 97 % at therapeutic plasma concentrations and the medicine is not preferentially bound to erythrocytes in the blood.
Taking a dose with food (a high fat meal) delays absorption, resulting in a Tmax of about 4 hours, and increases bioavailability by about 20 %.
Biotransformation: Celecoxib is metabolised in the liver by hydroxylation, oxidation and some glucuronidation. It was demonstrated that celecoxib is predominantly metabolised by cytochrome P450 CYP2C9. Pharmacological activity resides in the parent medicine. The main metabolites found in the circulation have no detectable COX-1 or COX-2 inhibitory activity.
Elimination: Celecoxib is mostly eliminated by hepatic metabolism with less than 1 % of the dose excreted unchanged in urine. After multiple dosing, the elimination half-life is 8-12 hours and the rate of clearance about 500 mL/min. With multiple dosing steady state plasma concentrations are reached before day 5.
Variability among patients on the main pharmacokinetic parameters (AUC, Cmax, elimination half-life) is about 30 %. The mean steady state volume of distribution is about 500 L/70 kg in young healthy adults after a single 200 mg dose, indicating wide distribution of celecoxib into the tissues. Pre-clinical studies indicate that celecoxib crosses the blood/brain barrier.
Special populations:
Hepatic impairment
Plasma concentrations of celecoxib in patients with mild hepatic impairment are not significantly different from those of age and sex matched controls. In patients with moderate hepatic impairment celecoxib plasma concentrations are about twice those of matched controls. Patients with severe hepatic impairment have not been studied but can be expected to show accumulation of parent substance, as the main route of metabolism is via the liver.
Renal impairment
In elderly volunteers with age-related reductions in glomerular filtration rate (GFR) (mean GFR > 65 mL/min per 1,73 m2) and in patients with chronic stable renal insufficiency (GFR 35 - 60 mL/min per 1,73 m2) celecoxib pharmacokinetics were comparable to those seen in patients with normal renal function. No significant relationship was found between serum creatinine (or creatinine clearance) and celecoxib clearance.
Renal effects
The relative roles of COX-1 and COX-2 in renal physiology are not clear. celecoxib reduces the urinary excretion of PGE2 and 6-keto-PGF1µ (a prostacyclin metabolite) but leaves serum thromboxane B2 (TXB2) and urinary excretion of 11-dehydro-TXB2, a thromboxane metabolite (both COX-1 products) unaffected. Specific studies have shown that celecoxib produces no decrease in GFR in the elderly or those with chronic renal insufficiency. These studies have also shown transient reductions in fractional excretion of sodium.
Elderly patients 65 years and older
In the population > 65 years there is a two-fold increase in mean Cmax and AUC for celecoxib. This is a predominantly weight-related rather than age-related change. Celecoxib levels are higher in lower weight individuals and therefore in the elderly population who are generally of lower mean weight than the younger population. Elderly females therefore tend to have slightly higher celecoxib plasma concentrations than elderly males.
Children
Celecoxib has not been studied in patients under 18 years old.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
INNOFLAM 100 and 200
Croscarmellose sodium, FD & C blue # 2 aluminum lake, gelatin, lactose monohydrate, magnesium stearate, povidone, purified water, shellac, sodium lauryl sulfate, titanium dioxide E 171, yellow iron oxide

6.2 Incompatibilities
None

6.3 Shelf life
36 months from manufacturing date

6.4 Special Precautions for storage
Store at or below 30 °C in original container to protect from moisture.

6.5 Nature and contents of container
INNOFLAM 100 and 200 is available in
- (10's, 20, 30's & 60's) blisters of aluminum foil & CFB foil in one carton. In pack sizes of multiples of 10 capsules per blister.
- (10's, 20's, 30's & 60's) blisters of aluminum foil & transparent PVC/PE/PVDC film in one carton. In pack sizes of multiples of 10 capsules per blister.

6.6 Special precautions for disposal and other handling
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Innovata Pharmaceuticals (Pty) Ltd
Crownwood Office Park, Block D,
100 Northern Parkway
Ormonde, Johannesburg, 2091,
South Africa

MANUFACTURER:
Alembic Pharmaceuticals Limited
(Formulation Division)
Village Panelav, P.O. Tajpura,
Near Baska, Taluka-Halol, District-Panchmahal,
Gujarat- 389350, India

8. REGISTRATION NUMBERS
South Africa:
INNOFLAM 100: A 51/3.1/0722
INNOFLAM 200: A 51/3.1/0723
Zimbabwe: PP
INNOFLAM 100: 2021/3.1/6167
INNOFLAM 200: 2021/3.1/6168
Botswana: S2
INNOFLAM 100: BOT1803546
INNOFLAM 200: BOT1803547

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
28 September 2021

10. DATE OF REVISION OF THE TEXT

PI/INNOF/000

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS
S3

INNOFLAM 100 mg capsules, hard
INNOFLAM 200 mg capsules, hard
Celecoxib
Contains sugar: Lactose monohydrate.
Each **INNOFLAM** 100 capsule contains 25 mg of lactose monohydrate.
Each **INNOFLAM** 200 capsule contains 50 mg of lactose monohydrate.

Read all of this leaflet carefully before you start taking INNOFLAM
- Keep this leaflet. You may need to read it again
- If you have further questions, please ask your doctor, pharmacist, nurse, or other health care provider.
- **INNOFLAM** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet
1. What **INNOFLAM** is and what it is used for
2. What you need to know before you take **INNOFLAM**
3. How to take **INNOFLAM**
4. Possible side effects
5 How to store **INNOFLAM**
6. Contents of the pack and other information

1. What INNOFLAM is and what it is used for
INNOFLAM belongs to a group of medicines called nonsteroidal anti-inflammatory drugs (NSAIDs), and specifically a sub-group known as cyclooxygenase-2 (COX-2) inhibitors. Your body makes substances called prostaglandins. Some prostaglandins may cause pain and inflammation. In conditions such as rheumatoid arthritis and osteoarthritis your body makes more of these. **INNOFLAM** acts by reducing the production of prostaglandins, thereby reducing the pain and inflammation.
INNOFLAM is used in adults for the relief of signs and symptoms of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis (progressive stiffening of the spine).
INNOFLAM is also used in the treatment of pain following an operation, including dental surgery, musculoskeletal pain, primary dysmenorrhoea (painful menstrual periods).

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE INNOFLAM
Do not take INNOFLAM:
- if you are hypersensitive (allergic) to celecoxib or any of the ingredients of **INNOFLAM** (see section 6);
- if you have had an allergic reaction to a group of medicines called "sulphonamides" (medicines that prevent the growth of bacteria)
- if you have severe liver disease;
- if you have severe kidney disease;
- if you have had allergic reactions such as asthma, nose polyps, severe nasal congestion, or an itchy skin rash, swelling of the face, lips, tongue or throat, breathing difficulties or wheezing from aspirin or other NSAIDs (anti-inflammatory and pain-relieving medicines, such as diclofenac, ibuprofen).
- Established ischaemic heart disease, or cerebrovascular disease, e.g. you have been diagnosed with a heart attack, stroke, or blockages of blood vessels to the heart or brain;
- if you are about to have coronary artery bypass graft surgery;
- if you currently have an ulcer in your stomach or intestines, or if you are bleeding in your stomach or intestines (you may notice that you have black sticky stools or bloody diarrhoea);
- if you have an inflammatory disease of the intestines such as ulcerative colitis or Crohn's disease
- if you are pregnant or it is possible that you could become pregnant;
- if you are breastfeeding. Talk to your doctor or pharmacist before taking **INNOFLAM**: Take special care with **INNOFLAM**:
- if you smoke, have diabetes, high blood pressure or high blood cholesterol;
- if you have had a serious allergic reaction or a serious skin reaction to any medicines;
- if you have previously had an ulcer or bleeding in your stomach or intestines. (Do not take **INNOFLAM** if you currently have an ulcer or bleeding in your stomach or intestine);
- if you are taking corticosteroid medicines (for example prednisone);
- if you are taking aspirin (even at low dose for heart protective purposes);
- if you use medicines to reduce blood clotting (e.g. warfarin/warfarin like anticoagulants or novel oral anti-clotting medicines, e.g. apixaban).
- if you are taking **INNOFLAM** at the same time as other non-aspirin NSAIDs such as ibuprofen or diclofenac. The use of these medicines together should be avoided;
- if you have fluid retention (such as swollen ankles and feet);
- if you have heart failure or other heart problems;
- if you have high blood pressure;
- if your liver or kidneys are not working well, as your doctor may want to keep a regular check on you;
- if you are dehydrated, for instance due to sickness, diarrhoea or the use of diuretics (medicines used to get rid of excess fluid in the body);
- if you feel ill due to an infection, or think you have an infection, as **INNOFLAM** may mask a fever or other signs of infection and inflammation.
- If you are above 65 years of age your doctor will want to monitor you regularly. The consumption of alcohol and NSAIDs may increase the risk of gastrointestinal problems.

INNOFLAM may lead to an increase in blood pressure. Your doctor may want to monitor your blood pressure on a regular basis.
Some cases of severe liver reactions, including severe liver inflammation, liver damage, liver failure (some with fatal outcome or requiring liver transplant), have been reported with celecoxib. Of the cases that reported time to onset, most severe liver reactions occurred within one month of start of treatment.

Other medicines and INNOFLAM:
Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)
Before you take **INNOFLAM**, make sure your doctor knows if you are taking the following medicines:
- Warfarin (used to prevent blood from clotting)
- ACE inhibitors, angiotensin II receptor antagonists, beta blockers (used for high blood pressure and heart failure)
- Diuretics (used to treat fluid retention)
- Ciclosporin and tacrolimus (used for immune system suppression e.g. after transplants).
- Aspirin (used for pain and fever). **INNOFLAM** can be taken with low dose aspirin (75 mg or less daily). Ask your doctor for advice before taking both medicines together **INNOFLAM** has no antiplatelet effect and is therefore not a substitute for aspirin for prevention of thrombosis
- Neuroleptics (used to treat some mental disorders)
- Medicines for anxiety (diazepam) or to treat depression (citalopram, imipramine)
- Medicines to treat an irregular heartbeat (amiodarone, quinidine)
- Dextromethorphan (used to treat coughs)
- Methotrexate (used to treat rheumatoid arthritis, psoriasis and leukaemia)
- Lithium (used to treat some types of depression)
- Oral contraceptives
- Glibenclamide, tolbutamide (medicines used in the management of type 2 diabetes)
- Phenytoin, a medicine used in epilepsy (seizure disorder)
- Fluconazole (used to treat fungal infection)
- Rifampicin (used to treat bacterial infections)
- Carbamazepine (used to treat epilepsy/seizures and some forms of pain or depression)
- Barbiturates (used to treat epilepsy/seizures and some sleep disorders)
- Ketoconazole (an antifungal medicine)
- Antacids (used for heartburn).

Pregnancy and breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking **INNOFLAM**.
Pregnancy
INNOFLAM must not be used by women who are pregnant or can become pregnant (i.e. women of childbearing potential who are not using adequate contraception) during ongoing treatment. If you become pregnant during treatment with **INNOFLAM** you should discontinue the treatment and contact your doctor for alternative treatment.
Breastfeeding
INNOFLAM must not be used during breastfeeding.
Fertility
NSAIDs, including **INNOFLAM**, may make it more difficult to become pregnant. You should tell your doctor if you are planning to become pregnant or if you have problems becoming pregnant.

Driving and using machines:
You should be aware of how you react to **INNOFLAM** before you drive or operate machinery. If you feel dizzy or drowsy after taking **INNOFLAM**, do not drive or operate machinery until these effects wear off.

INNOFLAM contains sucrose:
INNOFLAM contains lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking **INNOFLAM**.

3. HOW TO TAKE INNOFLAM
Do not share medicines prescribed for you with any other person. Always take **INNOFLAM** exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
If you think or feel that the effect of **INNOFLAM** is too strong or too weak, talk to your doctor or pharmacist.
Use the lowest effective dose for the shortest possible time.
Your doctor will tell you what dose you should take.
The recommended dose for osteoarthritis is 200 mg taken as a single dose, or as two divided doses.
The recommended dose for rheumatoid arthritis is 100 mg or 200 mg twice daily.
The recommended dose for pain following dental surgery is 100 mg or 200 mg twice daily.
The recommended dose for pain following an operation is 200 mg once daily.
The recommended dose for musculoskeletal pain is 200 mg twice daily.
The recommended dose for primary dysmenorrhoea is 400 mg initially, followed by an additional 200 mg on the first day if needed. On subsequent days, the recommended dose is 200 mg twice daily.
The recommended dose for ankylosing spondylitis is 200 mg daily, taken as a single dose or as 100 mg twice daily.
If you have liver problems, or if you weigh less than 50 kg, your doctor will recommend the lowest recommended dose.
Children:
No information is available on the use of **INNOFLAM** in children and it is therefore not recommended for use in children.
Method of administration:
INNOFLAM is for oral use. Swallow the capsules whole with a glass of water at any time of the day, with or without food. However, try to take each dose of **INNOFLAM** at the same time each day. Do not chew or crush the granules.
Contact your doctor within two weeks of starting treatment if you do not experience any benefit.
If you take more INNOFLAM than you should
You should not take more capsules than your doctor tells you to.
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.
If you forget to take INNOFLAM
If you forget to take a capsule, take it as soon as you remember.
Do not take a double dose to make up for forgotten individual doses.
If you stop taking INNOFLAM
Suddenly stopping your treatment with **INNOFLAM** may lead to your symptoms getting worse. Do not stop taking **INNOFLAM** unless your doctor tells you to. Your doctor may tell you to reduce the dose over a few days before stopping completely.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS
INNOFLAM can have side effects.
Not all side effects reported for **INNOFLAM** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **INNOFLAM**, please consult your doctor, pharmacist or other healthcare provider for advice.

If any of the following happens, stop taking INNOFLAM and tell your doctor immediately or go to the casualty department at your nearest hospital:
- swelling of the hands, feet ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing.
- a serious skin reaction with rash, blistering or peeling of the skin.

These are all very serious side effects. If you have them, you may have had a serious reaction to **INNOFLAM**. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital
if you notice any of the following
- weakness or clumsiness of a hand, arm or leg, difficulties with speech and swallowing, vision problems and headache. These may be signs of a stroke or bleeding in the brain, which may be fatal
- shortness of breath or difficulty breathing, sudden chest pain, cramping or tingling sensation up the left arm (heart attack)
- problems breathing, shortness of breath, chest pain. You may have a blood clot in the lung (pulmonary embolism) and will need urgent medical attention
- throbbing or cramping pain in a leg, swelling in a leg, warm skin around painful area (deep vein thrombosis)
- severe stomach pain or any sign of bleeding in the stomach or intestines, such as passing black or bloodstained stools, or vomiting blood
- liver failure (symptoms may include nausea (feeling sick), diarrhoea, jaundice (your skin or the whites of your eyes look yellow))
- bladder or kidney infections. Some signs may be fever, chills, blood in the urine or frequent urination • acute renal failure/nephrotic syndrome (decreased urine output, swelling of legs, fatigue, foamy urine, loss of appetite)
- painful blisters, sensitive to touch (shingles)
- red, swollen, painful skin with fever (a bacterial skin infection, known as erysipelas)
- ache or burning pain in your abdomen (Helicobacter infection).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- infections of the airways such as sinusitis (swelling and redness of the nasal sinuses) or bronchitis (inflammation of the mucous membranes of the airways)
- worsening of existing allergies
- weight gain
- trouble sleeping
- dizziness, abnormal muscle tension
- headache
- high blood pressure, worsening of existing high blood pressure. you may not know that you have high blood pressure unless you have your blood pressure tested.
- runny nose, sore throat, shortness of breath.
- nausea (feeling sick), vomiting (being sick)
- indigestion, windiness, pain on stomach
- problem swallowing
- sore teeth
- skin rash, itching skin.
- accidental injury.
- flu-like illness
- keeping fluid back in the body tissues, with swollen ankles, legs and/or hands.

Less frequent side effects
- inflammation or infection of the inner ear (dizziness or feeling that everything is spinning around you)
- infection of the gums
- blood disorders, such as anaemia (too few red blood cells or their haemoglobin content is too low), leukopenia (a lowered white blood cell count) or thrombocytopenia (deficiency of platelets in the blood)* * You will only know that you have these disorders if your doctor orders blood tests. See your doctor if you are pale and tired, get more infections than usual or have problems to stop bleeding, or if you have unexpected bruising
- increased sodium in blood, increased potassium in blood (determined by blood tests)
- feeling tired, confused
- feeling anxious or depressed
- seeing or hearing things that do not exist (hallucinations)
- blurred vision, eye inflammation and bloodshot eyes, vitreous floaters (seeing spots or strings that move when you move your eyes), bleeding in an eye, painful eyes
- ringing in the ears, above normal hearing sense, voice disorder
- irregular heart rhythm, increased heart rate
- flushing
- inflammation of a blood vessel (you may feel unwell with fever, sweats and tiredness)
- tightness in the chest with coughing and wheezing (bronchospasm)
- shortness of breath, cough, fatigue (inflammation of the lung tissues - pneumonitis)
- abdominal pain, cramping, bloating, constipation
- mouth ulcers, numbness, burning sensation in the mouth (stomatitis)
- hair loss
- muscle spasms (leg cramps), muscle pain
- lower limb fracture
- kidney function disorders (shown by laboratory tests)
- frequent urination during the night (nocturia)
- menstrual disorders
- swollen face
- chest pain.

Frequency unknown
- sleepiness
- abnormal skin sensations (tingling or tickling or itching or burning)
- problems with coordination and speech (ataxia)
- no sense of smell or taste, or taste affected
- worsening of existing epilepsy (seizure disorder)
- female fertility decreased
- vaginal bleeding
- tender breasts.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.
Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/-Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **INNOFLAM**

5. HOW TO STORE INNOFLAM
- Keep out of reach and sight of children.
- Store at or below 30 °C in the original carton until removed for use.
- Protect from moisture.
- Do not use this medicine after the expiry date shown on the pack.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or the sewerage system (e.g. toilets).

6. CONTENTS OF THE PACK AND OTHER INFORMATION
What INNOFLAM contains:
The active substance is celecoxib.
1 capsule contains 100 mg or 200 mg celecoxib.
The other ingredients are: croscarmellose sodium, FD & C blue # 2 aluminium lake, gelatin, lactose monohydrate, magnesium stearate, povidone, purified water, shellac, sodium lauryl sulfate, titanium dioxide E 171, yellow iron oxide.

What INNOFLAM looks like and contents of the pack
INNOFLAM 100: Hard gelatin capsules size "3" having imprinting "135" on the opaque white body with blue ink and "A" on the opaque white cap with blue ink filled with white to off white colored granular powder.
INNOFLAM 200: Hard gelatin capsules size "1" having imprinting "136" on the opaque white body with golden yellow ink and "A" on the opaque white cap with golden yellow ink filled with white to off white colored granular powder.
INNOFLAM 100 & 200 are available in:
- (10's, 20, 30's & 60's) blisters of aluminum foil & CFB foil in one carton. In pack sizes of multiples of 10 capsules per blister.
- (10's, 20's, 30's & 60's) blisters of aluminum foil & transparent PVC/PE/PVDC film in one carton. In pack sizes of multiples of 10 capsules per blister.

Holder of Certificate of Registration
Innovata Pharmaceuticals (Pty) Ltd
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Ormonde, Johannesburg, 2091,
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Manufacturer:
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INNOFLAM 100: BOT1803546
INNOFLAM 200: BOT1803547

03-03-2022

PIL/INNOF/000

Pharmacode
Pharmacode
Pharmacode
520 mm
400 mm
Front Side

Type: Pack Insert
Size: 400 x 520 mm

Afrikaans Language

PASIËNTINLIGTINGSBILJET

SKEDULERINGSTATUS
S3

INNOFLAM 100 (Kapsules, hard)
INNOFLAM 200 (Kapsules, hard)
Selekoksib
Bevat suiker: Laktose monohidraat
Elke **INNOFLAM** 100 kapsule bevat 25 mg van laktose monohidraat.
Elke **INNOFLAM** 200 kapsule bevat 50 mg van laktose monohidraat.

Lees die volledige biljet noukeurig deur voordat u begin om INNOFLAM te neem
- Hou hierdie biljet. U mag dit moontlik weer wil lees.
- Indien u verdere vrae het, raadpleeg asseblief u dokter, apteker, verpleegster of ander gesondheidsorgvoorsiener.
- **INNOFLAM** is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander persone deel nie. Dit kan hulle kwaad aandoen, selfs indien hulle dieselfde simptome as u het.

Wat is in hierdie biljet
1. Wat **INNOFLAM** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **INNOFLAM** neem
3. Hoe om **INNOFLAM** te neem
4. Moontlike newe-effekte
5. Hoe om **INNOFLAM** te berg
6. Inhoud van die pakkie en ander inligting

1. WAT INNOFLAM IS EN WAARVOOR DIT GEBRUIK WORD:
INNOFLAM behoort aan 'n groep van medisynes wat genoem word nie-steroïede anti-inflammatoriese medisynes (NSAIMs) en spesifiek 'n sub-groep bekend as siklo-okigenase-2 (COX-2) inhibeerders.
U liggaam maak substanse wat genoem word prostaglandiene. Sommige prostaglandiene kan pyn en inflammasie veroorsaak. By toestande soos rumatoïede artritis en osteoartritis maak u liggaam meer daarvan. **INNOFLAM** werk deur vermindering van die produksie van prostaglandiene, wat daardeur die pyn en inflammasie verminder.
INNOFLAM word gebruik by volwassenes vir die verligting van tekens en simptome van rumatoïede artritis, osteoartritis en ankiloserende spondilitis (progressiewe verstywing van die rugstring).
INNOFLAM word ook gebruik by die behandeling van pyn na 'n operasie, insluitende tandsjirurgie, muskuloskeletale pyn, primêre dismenoree (pynlike menstruele periodes).

2. WAT U BEHOORT TE WEET VOORDAT U DUELOKS NEEM
Moenie **INNOFLAM** neem:
- indien u hipersensitief (allergies) is vir selekoksib of enige van die bestanddele van **INNOFLAM** nie (sien afdeling 6);
- u 'n allergiese reaksie gehad het met 'n groep van medisynes wat genoem word "sulfonamiede" (medisynes wat die groei van bakterieë verhoed);
- u ernstige lewersiekte het;
- u ernstige niersiekte het;
- indien u allergiese reaksies gehad het soos asma, neuspoliepe, ernstige neusverstopping, of 'n jeukerige veluitslag, opswel van die gesig, lippe, tong of keel, probleme met asemhaling of asemfluit van aspirien of ander NSAIMs (anti-inflammatoriese en pynverligtende medisynes, soos diklofenak, ibuprofeen).
- Bewese isgemiese hartsiekte, of serebrovaskulêre siekte, bv. u was gediagnoseer met 'n hartaanval, beroerte, of blokkasie van bloedvate na die hart of brein;
- indien u koronêre arteriële omweg-weefselsjirurgie moet ondergaan;
- indien u tans 'n ulkus in u maag of ingewande het, of indien u bloeding in u maag of ingewande het (u mag opmerk dat u swart klewerige stoelgang of bloederige diarree het);
- indien u 'n inflammatoriese ingewand-siekte het, soos ulseratiewe kolitis of Crohn se siekte;
- indien u swanger is of indien dit moontlik is dat u swanger kan word;
- indien u borsvoed. Raadpleeg u dokter of apteker voordat u **INNOFLAM** neem: Neem spesiale sorg met **INNOFLAM**:
- indien u rook, diabetes, hoë bloeddruk of hoë cholesterol het;
- indien u voorheen 'n ulkus of bloeding in u maag of ingewande gehad het. (Moenie **INNOFLAM** neem nie indien u tans 'n ulkus het of bloeding in u maag of ingewande);
- indien u kortikosteroïede medisynes neem (byvoorbeeld prednisoon);
- indien u aspirien neem (selfs teen 'n lae dosering vir hartbeskermingsdoeleindes);
- indien u medisynes gebruik vir vermindering van bloedklonte (bv. warfarien/warfarien soos antikoagulante of onbekende orale antistollingsmedisynes, bv. apiksaban).
- indien u **INNOFLAM** neem dieselfde tyd as ander nie-aspirien NSAIMs soos ibuprofeen of diklofenak. Die gesamentlike gebruik van hierdie medisynes moet vermy word;
- indien u vloeistofretensie het (soos opgeswelde enkels en voete);
- indien u hartversaking het of ander hartprobleme;
- indien u hoë bloeddruk het;
- indien lewer of niere nie goed werk nie, omdat u dokter u moontlik gereëld wil opvolg;
- indien u gedehidreer is, byvoorbeeld weens siekte, diarree of die gebruik van diuretika (medisynes wat gebruik word om ontslae te raak van oormatige vloeistof in die liggaam;
- indien u siek voel weens 'n infeksie, of dink dat u 'n infeksie het, omdat **INNOFLAM** koors of ander tekens van infeksie en inflammasie kan maskeer.
- Indien u ouer is as 65 jaar, sal u dokter u gereëld wil moniteer. Die gebruik van alkohol en NSAIMs kan die risiko van gastroïntestinale probleme laat toeneem.

INNOFLAM kan 'n toename in bloeddruk tot gevolg hê. U dokter mag moontlik u bloeddruk op 'n gereëlde basis wil moniteer. Sommige gevalle van ernstige lewer-reaksies, insluitende ernstige lewerinflammasie, lewerskade, leweversaking (sommige noodlottig, of waar daar leweroorplanting benodig was), is gerapporteer met selekoksib. Van die gevalle gerapporteer vanaf aanvangstyd, het die meeste lewer-reaksies voorgekom binne een maand na die begin van behandeling.

Ander medisynes en INNOFLAM
Vertel altyd u gesondheidsorgvoorsiener indien u enige ander medisyne neem. (Dit sluit in komplementere of tradisionele medisynes.) Voordat u **INNOFLAM** neem, maak seker dat u dokter bewus is indien u enige van die volgende medisynes neem:
- Warfarien (word gebruik vir voorkoming van bloedklonte)
- AOE-inhibeerders, angiotensien II reseptor-antagoniste, beta-blokkeermiddels (word gebruik vir hoë bloeddruk en hartversaking)
- Diuretika (word gebruik vir behandeling van vloeistofretensie)
- Siklosporien en takrolimus (word gebruik vir immuunstelselonderdrukking, bv. na oorplantings)
- Aspirien (word gebruik vir pyn en koors). **INNOFLAM** kan geneem word met lae dosis aspirien (75 mg of minder per dag). Raadpleeg u dokter vir advies voordat u hierdie medisynes saam gebruik. **INNOFLAM** het geen antiplaatjie effek nie en is dus nie geskik as 'n vervanging vir aspirien vir voorkoming van trombose nie
- Neuroleptika (word gebruik by behandeling van sommige geestesafwykings)
- Medisynes vir angs (diasepam) of vir behandeling van depressie (sitalopram, imipramien)
- Medisynes vir behandeling van ongereëlde hartklop (amiodaroon, kinidien)
- Dekstrometorfaan (word gebruik vir behandeling van hoes)
- Metotreksaat (word gebruik vir behandeling van rumatoïede artritis, psoriase en leukemie)
- Litium (word gebruik vir behandeling van sekere tipes van depressie)
- Orale voorbehoedmiddels
- Glibenklamied, tolbutamied (medisynes wat gebruik word by die behandeling van tipe 2 diabetes)
- Fenitoïen, 'n medisyne wat gebruik word vir epilepsie (siekte-afwyking)
- Flukonasool (word gebruik vir behandeling van fungus-infeksie)
- Rifampisien (word gebruik vir behandeling van bakteriële infeksies)
- Karbamasepien word gebruik vir behandeling van epilepsie/siekte-aanvalle en sommige vorms van pyn of depressie)
- Barbiturate (word gebruik vir behandeling van epilepsie/siekte-aanvalle en sommige slaapafwykings)
- Ketokonasool ('n antifungus medisyne)
- Teensuurmiddels (word gebruik vir sooibrand)

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is of borsvoed, dink dat u swanger is of 'n baba beplan, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgvoorsiener vir advies voordat u **INNOFLAM** neem.
Swangerskap
INNOFLAM moet nie gebruik word deur vrouens wat swanger is of swanger kan word nie (d.w.s. vrouens van kinderbarende potensiaal wat nie voldoende kontrasepsie gebruik nie), gedurende volgehoue terapie. Indien u swanger word gedurende behandeling met **INNOFLAM** moet u die behandeling staak en u dokter kontak vir alternatiewe behandeling.
Borsvoeding
INNOFLAM moet nie gebruik word gedurende swangerskap nie.
Fertiliteit
NSAIMs, insluitend **INNOFLAM** , kan dit moeiliker maak om swanger te word. U moet u dokter raadpleeg indien u swangerskap beplan of indien u probleme het om swanger te word.

Bestuur en gebruik van masjinerie
U moet bewus wees van hoe u voel na die neem van **INNOFLAM** voordat u bestuur of masjinerie hanteer. Indien u duiselig of lomerig voel nadat u **INNOFLAM** geneem het, moenie bestuur of masjinerie hanteer nie, totdat hierdie effekte verby is.

INNOFLAM bevat laktose
INNOFLAM bevat laktose ('n tipe suiker). Indien u deur u dokter ingelig is dat u 'n intoleransie het vir sommige suiker, kontak u dokter voordat u **INNOFLAM** gebruik.

3. HOE OM DUELOKS TE NEEM
Moenie medisynes wat vir u voorgeskryf is met enige ander persoon deel nie.
Neem altyd **INNOFLAM** presies soos u dokter of apteker aanbeveel het. Raadpleeg u dokter of apteker indien u nie seker is nie.
Indien u dink, of die gevoel het, dat die effek van **INNOFLAM** te sterk of te swak is, raadpleeg u dokter of apteker.

Gebruik die laagste effektiewe dosis vir die kortste moontlike tyd.
U dokter sal u inlig omtrent die dosis wat u moet neem.
Die aanbevole dosering vir osteoartritis is 200 mg geneem as 'n enkel dosis, of as twee verdeelde doserings.
Die aanbevole dosering vir rumatoïede artritis is 100 mg of 200 mg twee keer per dag.
Die aanbevole dosering vir pyn na dentale (tande) sjirurgie is 100 mg of 200 mg twee keer per dag.
Die aanbevole dosering vir pyn na 'n operasie is 200 mg een keer per dag.
Die aanbevole dosering vir muskuloskeletale pyn is 200 mg twee per dag.
Die aanbevole dosering vir primêre dismenorree is 400 mg aanvanklik, gevolg deur 'n addisionele 200 mg op die eerste dag, indien nodig. Op daaropvolgende dae, is die aanbevole dosering 200 mg twee keer per dag.
Die aanbevole dosering vir ankiloserende spondilitis is 200 mg per dag, geneem as 'n enkel dosis, of as 100 mg twee keer per dag
Indien u lewerprobleme het, of indien u gewig minder is as 50 kg, sal u dokter die laagste moontlike dosis aanbeveel.
Kinders:
Geen inligting is beskikbaar omtrent die gebruik van **INNOFLAM** by kinders nie en dit word gevolglik nie aanbeveel vir gebruik by kinders nie.
Metode van toediening:
INNOFLAM is vir orale gebruik. Sluk die kapsules heel in met 'n glas water enige tyd van die dag, met of sonder voedsel. Probeer egter om elke dosis **INNOFLAM** dieselfde tyd elke dag te neem. Moenie die granules kou of fyn druk nie.
Kontak u dokter binne twee weke na begin van behandeling of indien u nie enige voordele ondervind nie.
Indien u meer INNOFLAM geneem het as wat u moes
U behoort nie meer kapsules te neem as wat u dokter aanbeveel het nie. Ingeval van oordosering, raadpleeg u dokter of apteker. Indien albei nie beskikbaar is nie, kontak die naaste hospitaal of vergiftingsentrum.
Indien u vergeet het om INNOFLAM te neem
Indien u vergeet het om 'n kapsule te neem, neem dit so gou as wat u onthou. Moenie 'n dubbel dosis neem om op te maak vir die individuele doserings wat u vergeet het om te neem nie.
Indien u die gebruik van INNOFLAM staak
Die skielike staak van u **INNOFLAM** behandeling kan tot gevolg hê dat u simptome erger word. Moenie die gebruik van **INNOFLAM** staak nie, tensy u dokter dit aanbeveel. U dokter kan u aanraai om die dosis te verminder oor 'n paar dae voordat u dit heeltemal staak.
Indien u enige verdere vrae het omtrent die gebruik van hierdie medisyne, raadpleeg u dokter of apteker.

4. MOONTLIKE NEWE-EFFEKTE
INNOFLAM kan newe-effekte hê.
Nie alle newe-effekte gerapporteer vir **INNOFLAM** is ingesluit in hierdie biljet nie. Indien u algemene gesondheid agteruitgaan of indien u enige ongewenste effekte ondervind terwyl u **INNOFLAM** neem, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgvoorsiener vir advies.

Indien enige van die volgende gebeur, staak die gebruik van INNOFLAM en vertel u dokter onmiddellik of gaan na die ongevalle departement by u naaste hospitaal:
- opswel van die hande, voete, enkels, gesig, lippe en mond of keel, wat probleme kan veroorsaak met sluk of asemhaling.
- 'n ernstige velreaksie met uitslag, blasievorming of afdop van vel. Hierdie is alles baie ernstige newe-effekte. Indien u dit ontwikkel, het u 'n baie ernstige reaksie gehad met **INNOFLAM**. U kan dringende mediese aandag benodig of hospitalisering.

Vertel u dokter onmiddellik of gaan na die ongevalle afdeling by u naaste hospitaal indien u enige van die volgende opmerk:
- swakheid of lompheid van 'n hand, arm of been, probleme met spraak en sluk, visie probleme en hoofpyn. Hierdie kan tekens wees van beroerte of bloeding op die brein, wat noodlottig kan wees
- asemtekort of probleme met asemhaling, skielike borspyn, krampe of prikkelgevoel van die linkerarm (hartaanval)
- asemhalingsprobleme, asemtekort, borspyn. U kan 'n bloedklont hê in die longe (pulmonêre embolisme) en kan dringende mediese aandag benodig
- geklop of krampende pyn in 'n been, opswel van 'n been, vel is warm rondom pynlike area (diep veneuse trombose)
- ernstige maagpyn of enige teken van bloeding in die maag of ingewande, soos die passeer van swart of bloederige stoelgange, of die opbring van bloed
- lewerversaking (simptome kan insluit naarheid (siek gevoel), diarree, geelsug (u vel of die wit van u oë lyk geel))
- blaas- of nierinfeksies. Sommige tekens kan insluit koors, koue rillings, bloed in die uriene of dikwelse urinering
- akute nierversaking/nefrotiese sindroom (verminderde uriene uitsetting, opswel van bene, uitputting, skuimerige uriene, verlies van aptyt)
- pynlike blasies, sensitiwiteit by aanraking (gordelroos)
- rooi, geswelde, pynlike vel met koors ('n bakteriële vel-infeksie, bekend as erisipelas
- pyn of brandpyn in u ingewande (Helicobacter infeksie). Hierdie is alles ernstige newe-effekte. U kan dringende mediese sorg benodig.

Vertel u dokter indien u enige van die volgende agterkom:
Dikwelse newe-effekte:
- infeksies van die lugweë soos sinusitis (opswel en rooiheid van die nasale sinus) of brongitis (inflammasie van die slym-membrane van die lugweë)
- agteruitgang van bestaande allergieë
- massatoename
- slaap-probleme
- duiseligheid, abnormale spierspanning
- hoofpyn
- hoë bloeddruk, agteruitgang van bestaande hoë bloeddruk. U mag nie weet dat u hoë bloeddruk het nie, tensy u u bloeddruk laat toets het
- loopneus, seerkeel, asemtekort
- naarheid (siek gevoel), braking (siek wees)
- slegte spysvertering, winderigheid, maagpyn
- probleme met sluk
- seer tande
- veluitslag, jeuk van vel
- toevallige besering
- griepagtige siekte
- terughou van vloeistof in die liggaamweefsels, met geswelde enkels, bene en/of hande.

Minder dikwelse newe-effekte:
- inflammasie of infeksie van die binne-oor (duiseligheid of gevoel dat alles om u draai)
- infeksie van die tandvleis
- bloedafwykings, soos anemie (te min rooibloedselle of die hemoglobien inhoud is te laag), leukopenie ('n verlaagde witbloedseltelling) of trombositopenie (tekort van plaatjies in die bloed)* * U sal slegs weet dat u hierdie afwykings het indien u dokter bloedtoetse laat doen. Sien u dokter indien u bleek en moeg voel, meer infeksies kry as gewoonlik of probleme het om bloeding te stop, of indien u onverwagte kneusplekke het
- verhoogde natrium in bloed, verhoogde kalium in bloed (word bepaal deur bloedtoetse)
- gevoel van moeg wees, verwarring
- gevoel van angstigheid of depressie
- dinge sien of hoor wat nie bestaan nie (hallusinasies)
- dowwe visie, ooginflammasie en bloedbelope oë, glasige drywers (sien van spikkels of lyne wanneer u u oë beweeg), bloeding in 'n oog, pynlike oë
- gelui in die ore, bo normale gehoor, stemafwyking
- ongereëlde hartritme, verhoogde hart-tempo
- blosing
- inflammasie van 'n bloedvaat (u kan ongesond voel met koors, sweet en moegheid)
- engheid in die bors met hoes en asemfluit (brongospasma)
- asemtekort, hoes, uitputting (inflammasie van die longweefsels - pneumonitis)
- abdominale pyn, krampe, opgeblasenheid, hardlywigheid
- ulkusse, gevoelloosheid, brandsensasie in die mond (stomatitis)
- haarverlies
- spierspasma (beenkrampe), spierpyn
- onderste ledemaat fraktuur
- nierfunksie afwykings (bewys deur laboratoriumtoetse)
- dikwelse urinering gedurende die nag (nokturie)
- menstruele afwykings
- opgeswelde gesig
- borspyn.

Frekwensie onbekend:
- slaperigheid
- abnormale velsensasies (tinteling of prikkel of jeuk of brand)
- probleme met koördinasie en spraak (ataksie)
- geen reuk of smaak, of smaak word beïnvloed
- agteruitgang van bestaande epilepsie (stuipe-aanval)
- vroulike fertiliteit agteruitgang
- vaginale bloeding
- gevoelige borste.

Indien u enige newe-effekte agterkom wat nie gemeld word in hierdie biljet nie, stel asseblief u dokter of apteker in kennis daarvan.
Rapporteer van newe-effekte
Indien u newe-effekte ontwikkel, raadpleeg u dokter, apteker of verpleegster. U kan dit ook rapporteer aan SAHPRA via die "**6.04 Adverse Drug Reaction Reporting Form**", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte te rapporteer, kan u help om meer inligting te voorsien omtrent die veiligheid van INNOFLAM.

5. HOE OM DUELOKS TE BERG
- Hou buite die bereik en sig van kinders.
- Berg by of benede 30 °C in die oorspronklike karton totdat dit uitgehaal word vir gebruik.
- Beskerm teen vog.
- Moenie hierdie medisyne gebruik na die vervaldatum wat op die pakkie verskyn nie.
- Neem alle ongebruikte medisyne terug na u apteker.
- Moenie ontslae raak van ongebruikte medisyne deur dit in afvoerpype of die riolsisteem te gooi nie (bv. toilette).

6. INHOUD VAN DIE PAK EN ANDER INLIGTING
Wat INNOFLAM bevat:
Die aktiewe substans is selekoksib.
1 kapsule bevat 100 mg of 200 mg selekoksib.
Die ander bestanddele is: kroskarmellose natrium, FD & C blou # 2 aluminium lake, gelatien, laktose monohidraat, magnesiumstearaat, povidoon, gesuiwerde water, shellac, natriumlourielsulfaat, titaniumdioksied E 171, geel ysteroksied.

Hoe INNOFLAM lyk en inhoud van die pakkie
INNOFLAM 100: Harde gelatien kapsules grootte "3" gedruk met "135" op die ondeursigtige wit romp met blou ink en "A" op die ondeursigtige wit doppie met blou ink gevul met wit tot naaswit gekleurde granulêre poeier.
INNOFLAM 200: Harde gelatien kapsules grootte "1" gedruk met "136" op die ondeursigtige wit romp met goud-geel ink en "A" op die ondeursigtige wit doppie met goud-geel ink gevul met wit tot naaswit gekleurde granulêre poeier.
INNOFLAM 100 & 200 is beskikbaar in:
- (10's, 20's, 30's & 60's) stolpe van aluminumfoelie & CFB foelie in een karton. In pakgroottes van meervoude van 10 kapsules per stolp.
- (10's, 20's, 30's & 60's) stolpe van aluminumfoelie & deursigtige PVC/PE/PVDC film in een karton. In pakgroottes in veelvoude van 10 kapsules per stolp.

Houer van Sertifikaat van Registrasie
Innovata Pharmaceuticals (EDMS) Bpk
Crownwood Kantoorpark, Blok D
Northern Parkway 100
Ormonde, Johannesburg, 2091,
Suid-Afrka

Vervaardiger
Alembic Pharmaceuticals Limited
(Formulation Division)
Village Panelav, P.O. Tajpura,
Near Baska, Taluka-Halol, District-Panchmahal,
Gujarat- 389350, India

Hierdie biljet was verander in
28 September 2021

Registrasienommers
South Africa:
INNOFLAM 100: A 51/3.1/0722
INNOFLAM 200: A 51/3.1/0723
Zimbabwe: PP
INNOFLAM 100: 2021/3.1/6167
INNOFLAM 200: 2021/3.1/6168
Botswana: S2
INNOFLAM 100: BOT1803546
INNOFLAM 200: BOT1803547

VOUBILJET

SKEDULERINGSTATUS
S3

1. NAAM VAN MEDISYNE:
INNOFLAM 100 (harde kapsules)
INNOFLAM 200 (harde kapsules)

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING:
Elke **INNOFLAM** 100 kapsule bevat 100 mg selekoksib.
Elke **INNOFLAM** 200 kapsule bevat 200 mg selekoksib.
Eksipiënt met bekende effek
Bevat suiker: Laktose monohidraat
Elke **INNOFLAM** 100 kapsule bevat 25 mg laktose monohidraat
Elke **INNOFLAM** 200 kapsule bevat 50 mg laktose monohidraat
Vir die volledige lys van eksipiënte, sien afdeling 6.1

3. FARMASEUTIESE VORM
Harde gelatien kapsules.
INNOFLAM 100: Harde gelatien kapsules grootte "3" gedruk met "135" op die ondeursigtige wit romp met blou ink en "A" op die ondeursigtige wit doppie met blou ink, gevul met wit tot naaswit gekleurde granulêre poeier.
INNOFLAM 200: Harde gelatien kapsules grootte "1" gedruk met "136" op die ondeursigtige wit romp met goud-geel ink en "A" gedruk op die ondeursigtige wit doppie met goud-geel ink, gevul met wit tot naaswit gekleurde granulêre poeier.

4. KLINIESE BESONDERHEDE
4.1 Indikasies
- Simptomatiese behandeling van inflammasie en pyn in osteoartritis en rumatoïede artritis.
- Behandeling van pyn na dentale sjirurgie.
- Behandeling van ligte tot matige post-operatiewe pyn.
- Behandeling van ligte tot matige muskuloskeletale pyn.
- Behandeling van ligte tot matige primêre dismenoree.
- Verligting van simptome van ankilose spondilitis.

4.2 Posologie en metode van behandeling
Posologie
Omdat die kardiovaskulêre risikos van **INNOFLAM** kan toeneem met dosering en tydperk van blootstelling, moet die laagste effektiewe daaglikse dosering gebruik word, vir die kortste tydperk van behandeling.
Osteoartrose
Die aanbevole daaglikse dosering is 200 mg, geneem as 'n enkel dosering of as twee verdeelde doserings. Doserings van tot 400 mg per dag is bestudeer.
Rumatoïede artritis
Die aanbevole daaglikse dosering is 100 mg of 200 mg twee keer per dag.
Pyn na dentale sjirurgie
Die aanbevole dosering is 100 mg tot 200 mg, tot 'n maksimum daaglikse dosering van 400 mg. Doseringsintervalle moet nie minder wees as 4 uur nie.
Ligte tot matige post-operatiewe pyn
Die aanbevole dosering is 200 mg een keer per dag. Sommige pasiënte kan voordeel trek met 'n addisionele 200 mg dosering.
Ligte tot matige muskuloskeletale pyn
Die aanbevole dosering is 200 mg twee keer per dag.
Ligte tot matige primêre dismenorree
Die aanbevole dosering is 400 mg aanvanklik, gevolg deur 'n addisionele 200 mg dosering indien nodig op die eerste dag. Op die daaropvolgende dae is die aanbevole dosering 200 mg twee keer per dag.
Ankiloserende spondilitis
Die aanbevole daaglike dosering is 200 mg, geneem as 'n enkel dosis of as 100 mg twee keer per dag. Sommige pasiënte kan voordeel trek uit 'n totale daaglikse dosering van 400 mg.
Spesiale bevolkings
Hepatiese inkorting
Geen doseringsaanpassing is nodig by pasiënte met ligte hepatiese inkorting nie. Begin met **INNOFLAM** teen die laagste aanbevole dosering by pasiënte met matige hepatiese inkorting. Daar is geen kliniese ondervinding by pasiënte met ernstige hepatiese inkorting nie. (Sien afdelings 4.3 en 5.2).
Renale inkorting
Geen doseringsaanpassing is nodig by pasiënte met ligte of matige nierinkorting nie. Daar is geen kliniese ondervinding by pasiënte met ernstige nierinkorting nie. (Sien afdelings 4.3 en 5.2).
Bejaardes
Geen doseringsaanpassing is nodig nie. By bejaarde pasiënte met 'n liggaamsmassa van 50 kg of minder, word dit egter aanbeveel om terapie te begin teen die laagste aanbevole dosering.
Kinders
Omdat geen data beskikbaar is nie, word **INNOFLAM** nie aanbeveel by persone van jonger as 18 jaar nie.
Metode van toediening
Orale gebruik. **INNOFLAM** moet heel ingesluk word met 'n glas water, met of sonder voedsel.

4.3 Kontra-indikasies:
- Hipersensitiwiteit vir selekoksib, of enige ander eksipiënte van **INNOFLAM** (sien afdeling 6.1).
- Bekende hipersensitiwiteit tot sulfonamiede.
- Ernstige hepatiese inkorting (serum-albumien < 25 g/L van Child-Pugh telling > 10).
- Ernstig renale inkorting met beraamde kreatinienopruiming < 30 mL/min.
- Asma, urtikarie, of allergiese-tipe reaksies gepresipiteer deur aspirien of nie-steroïed anti-inflammatoriese middels (NSAIMs), insluitend ander siklo-oksigenase-2 (COX-2) spesifieke inhibeerders.
- Vasgestelde isgemiese hartsiekte en/of serebrovaskulêre siekte (beroerte) en perifêre ateriële siekte.
- Peri-operatiewe analgesie teen die agtergrond van koronêre arteriële deurgang sjirurgie (CABG).
- Aktiewe peptiese ulserasie of gastroïntestinale (GI) bloeding.
- Inflammatoriese ingewandsiekte.
- Gedurende swangerskap en by vrouens van kinderbarende potensiaal, tensy 'n effektiewe metode van kontrasepsie gebruik word (sien afdeling 4.6). Die potensiaal vir menslike risiko gedurende swangerskap is onbekend maar kan nie uitgesluit word nie.
- Borsvoeding (sien afdeling 4.6).

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

INNOFLAM kan neig tot kardiovaskulêre voorvalle, serebrovaskulêre voorvalle, gastroïntestinale voorvalle of kutaneuse reaksies wat noodlottig kan wees.

Veiligheid en effektiwiteit van **INNOFLAM** is nog nie vasgestel vir behandeling van meer as 12 weke in osteoartritis en 24 weke in rumatoïede artritis nie.
Kardiovaskulêre effekte
Verhoogde hoeveelheid van ernstige kardiovaskulêre (KV) voorvalle, hoofsaaklik miokardiale infarksie, is gerapporteer by pasiënte met sporadiese adenomateuse poliepe wat behandel was met selekoksib (soos in **INNOFLAM**) teen doserings van 200 mg twee keer per dag en 400 mg twee keer per dag, wanneer vergelyk met plasebo (sien afdeling 5.1).
Omdat die kardiovaskulêre risikos van **INNOFLAM**kan toeneem met dosering en tydperk van blootstelling, moet die kortste tydperk moontlik en die laagste effektiewe daaglikse dosis gebruik word. NSAIMs, insluitend COX-2 selektiewe inhibeerders, word geassosieer met verhoogde risiko van kardiovaskulêre en trombotiese ongunstige voorvalle wanneer langtermyn geneem word. Die presiese omvang van die risiko geassosieer met 'n enkel dosis is nog nie bepaal nie, sowel as die presiese tydperk van terapie geassosieer met verhoogde risiko. Die pasiënt se behoefte vir simptomatiese verligting en respons tot terapie moet weer periodiek ge-evalueer word, veral by pasiënte met osteoartritis (sien afdelings 4.2, 4.3, 4.8 en 5.1).
Versigtigheid word aanbeveel wanneer **INNOFLAM** voorgeskryf word by pasiënte met risiko faktore vir kardiovaskulêre voorvalle (bv. hipertensie, hiperlipidemie, diabetes mellitus, rook).
INNOFLAM is nie 'n substituut vir aspirien vir profilakse van kardiovaskulêre tromboëmboliese siekte nie, weens hul gebrek aan antiplaatjie effekte. Dus behoort antiplaatjie-terapie nie gestaak te word nie.
Anafilaktoïede reaksies
Soos gewoonlik met NSAIMs, het anafilaktoïede reaksies voorgekom by pasiënte wat blootgestel was aan **INNOFLAM** (sien afdeling 4.3).
Gastroïntestinale (GI) effekte
Boonste en onderste gastroïntestinale komplikasies (perforasies, ulkusse of bloedings (PUBs)), sommige wat noodlottig was, het voorgekom by pasiënte wat behandel was met selekoksib (soos in **INNOFLAM**). Versigtigheid word aanbeveel met behandeling van pasiënte wat die grootste risiko het om 'n gastroïntestinale komplikasie te ontwikkel met NSAIMs; by bejaardes, pasiënte wat enige ander NSAIM of antiplaatjie medisynes saam gebruik (soos aspirien) of glukukortikoïede, pasiënte wat alkohol gebruik, of pasiënte met 'n vorige geskiedenis van gastroïntestinale siekte, soos ulserasie en GI bloeding.
Wanneer **INNOFLAM** geneem word saam met aspirien (selfs teen laer doserings), is daar 'n verdere verhoging in die risiko van gastroïntestinale ongunstige effekte vir selekoksib (gastroïntestinale ulserasie of ander gastroïntestinale komplikasies). 'n Beduidende verskil in GI veiligheid tussen selektiewe COX-2 inhibeerders plus aspirien vs NSAIMs plus aspirien is nog nie gedemonstreer in langtermyn kliniese studies nie.
Meegaande gebruik met NSAIM
Die meegaande gebruik van **INNOFLAM** en 'n nie-aspirien NSAIM moet vermy word.
Vloeistofretensie en edeem
Vloeistofretensie en edeem is waargeneem by pasiënte wat selekoksib neem (soos in **INNOFLAM**). Dus behoort **INNOFLAM** versigtig gebruik te word by pasiënte met 'n geskiedenis van hartversaking, linker ventrikulêre disfunksie of hipertensie en by pasiënte met voorafbestaande edeem vir enige ander rede, omdat prostaglandien inhibisie tot gevolg kan hê in agteruitgang van nierfunksie en vloeistofretensie. Omsigtigheid is ook nodig by pasiënte op diuretiese behandeling of wat andersins 'n risiko het vir hipovolemie. Pasiënte met voorafbestaande kongestiewe hartversaking of hipertensie moet gemonitor word.
Hipertensie
NSAIMs, insluitend selekoksib (soos in **INNOFLAM** kan tot gevolg hê die begin van nuwe hipertensie of agteruitgang van bestaande hipertensie, beide wat kan bydra tot die verhoogde insidensie van kardiovaskulêre voorvalle. Dus behoort bloeddruk versigtig gemonitor te word gedurende die begin van terapie met **INNOFLAM** en regdeur behandeling.
Hepatiese en renale effekte
Gekompromitteerde renale of hepatiese funksie en veral kardiale disfunksie is meer algemeen by bejaardes en dus moet toepaslike mediese toesig volgehou word. NSAIMs, insluitend **INNOFLAM**, kan niertoksisiteit veroorsaak. Selekoksib het gewys om soortgelyke renale effekte te hê as die wat waargeneem word met vergelykende NSAIMs. Pasiënte met die grootste risiko vir renale toksisiteit is die met ingekorte renale funksie, hartversaking, lewerdisfunksie, die wat diuretika neem, angiotensien-omskakelings-ensiem (AOE)-inhibeerders, angiotensien II reseptor antagoniste, en by bejaardes (sien afdeling 4.5). Sulke pasiënte moet versigtig gemonitor word terwyl hulle behandeling ontvang met **INNOFLAM**.
Sommige gevalle van ernstige hepatiese reaksies, insluitende fulminante hepatitis (sommige met noodlottige gevolge), lewernekrose en lewerversaking (sommige met noodlotting gevolge of wat leweroorplanting benodig het), is gerapporteer met selekoksib (bevat in **INNOFLAM**). Tussen die gevalle wat tyd tot aanvang gerapporteer het, het die meeste van die ernstige ongunstige hepatiese voorvalle ontwikkel binne een maand na begin van selekoksib (bevat in **INNOFLAM**-behandeling) (sien afdeling 4.8). Indien gedurende behandeling 'n pasiënte agteruitgaan in enige van die orgaansisteemfunksies hierbo beskryf, moet toepaslike maatreëls geneem word en onttrekking van **INNOFLAM**-terapie moet oorweeg word. Omsigtigheid is nodig wanneer behandeling begin word by pasiënte wat gehidreer is. Dit word aanbeveel om eers die pasiënte te rehidreer en dan te begin met **INNOFLAM**-terapie
CYP2D6 inhibisie
Selekoksib inhibeer CYP2D6. Alhoewel dit nie 'n sterk inhibeer van hierdie ensiem is nie, kan 'n doseringsafname van **INNOFLAM** nodig wees vir individuele dosis-getitreerde medisynes wat gemetaboliseer word deur CYP2D6 (sien afdeling 4.5).
CYP2C9 swak metaboliseerders
Pasiënte wat geneig is om swak metaboliseerders te wees van CYP2C9 moet versigtig behandel word.
Vel- en sistemiese hipersensitiwiteitsreaksies
Ernstige velreaksies, sommige wat noodlottig was, insluitende eksfoliatiewe dermatitis, Stevens-Johnson sindroom en toksiese epidermale nekrolise, is baie selde gerapporteer in assosiasie met die gebruik van selekoksib (soos in **INNOFLAM**), sien afdeling 4.8.
Die grootste risiko vir pasiënte blyk om vroeg na begin van terapie te wees: die begin van die voorval kom voor in die meeste gevalle binne die eerste maand van behandeling.
Ernstige hipersensitiwiteitsreaksies (insluitend anafilakse, angio-edeem en medisyne-uitslag met esinofilie en sistemiese simptome (DRESS), of hipersensitiwiteit-sindroom), is gerapporteer by pasiënte wat selekoksib ontvang het (soos in **INNOFLAM**), sien afdeling 4.8.
Pasiënte met 'n geskiedenis van sulfonamiede allergie of enige medisyne allergie kan 'n groter risiko hê van ernstige velreaksies of hipersensitiwiteit (sien afdeling 4.3). **INNOFLAM** moet onttrek word by die eerste voorkoms van veluitslag, mukosale letsels, of enige ander teken van hipersensitiwiteit.
Medisyne Reaksie met Esinofilie en Sistemiese Simptome (DRESS) is gerapporteer by pasiënte wat NSAIMs geneem het, soos in **INNOFLAM**. Sommige van hierdie voorvalle was noodlottig of lewensgevaarlik. DRESS tipies, alhoewel nie eksklusief nie, presenteer met koors, uitslag, limfadenopatie, en/of opswel van gesig. Ander kliniese manifestasies kan insluit hepatitis, nefritis, hematologiese abnormaliteite, miokarditis, of miositis. Soms kan simptome van DRESS ooreenstem met akute virale infeksie. Esinofilie is dikwels teenwoordig. Omdat hierdie afwyking veranderlik kan wees in sy voordoening, kan orgaan-sisteme nie opgemerk word om betrokke te wees nie. Dit is belangrik om op te merk dat vroeë manifestasies van hipersensitiwiteit, soos koors of limfadenopatie, teenwoordig kan wees, selfs al was uitslag nie duidelik nie. Indien sulke tekens of simptome teenwoordig is, staak **INNOFLAM** en evalueer die pasiënt onmiddellik.
Algemeen
INNOFLAM kan koors en ander tekens van inflammasie maskeer.
Gebruik met orale antikoagulante
By pasiënte op meegaande terapie met warfarien, is ernstige bloedingvoorvalle, waarvan sommige noodlottig was, gerapporteer (sien afdelings 4.8 en 4.5). Omdat toenames in protrombientyd (INR) gerapporteer is, moet antikoagulant aktiwiteit versigtig gemonitor word by pasiënte wat warfarien/kumarien-tipe orale antikoagulante ontv terapie met **INNOFLAM** begin word, of sy dosering verander word (sien 4.5). Meegaande gebruik van antikoagulante met NSAIMs kan die risiko van bloeding laat toeneem. Omsigtigheid is nodig wanneer **INNOFLAM** met warfarien gekombineer word of ander orale antikoagulante, insluitend nuwe antikoagulante (bv. apiksaban, dabigatran, en rivaroksaban).
Eksipiënte
INNOFLAM100 mg en 200 mg kapsules bevat laktose monohidraat (sien afdelings 2 en 6.1). Pasiënte met rare oorerflike probleme van galaktose intoleransie, totale laktase tekort of glukose/galaktose wanabsorpsie moet nie **INNOFLAM** gebruik nie.

4.5 Interaksie met ander medisynes en ander vorms van interaksie
Farmakodinamiese interaksies
Antikoagulante
By pasiënte op meegaande terapie met warfarien, was verhogings in protrombientyd (INR) gerapporteer (sien afdeling 4.4).
Antikoagulant aktiwiteit moet gemonitor word, veral na die eerste paar dae van begin of verandering van die dosering van **INNOFLAM** in pasiënte wat warfarien ontvang of ander antikoagulate, omdat hierdie pasiënte 'n verhoogde risiko het van bloedingskomplikasies. Dus moet pasiënte wat orale antikoagulante ontvang versigtig gemonitor word vir hulle protrombientyd INR, veral aan die begin vir die eerste paar dae wanneer terapie met **INNOFLAM** begin word of die dosering verander word (sien afdeling 4.4). Bloedingsvoorvalle in assosiasie met verhogings in protrombientyd (INR) is gerapporteer, hoofsaaklik by bejaardes, by pasiënte wat selekoksib (soos in **INNOFLAM**) ontvang het saam met warfarien, waarvan sommige noodlottig.
NSAIMs, insluitend **INNOFLAM**, kan die effek van antihipertensiewe medisynes verminder (insluitend AOE-inhibeerders, angiotensien II reseptor antagoniste, diuretika en beta-blokkers). Hierdie interaksie behoort oorweeg te word by pasiënte wat **INNOFLAM** gebruik saam met antihipertensiewe medisynes.
Soos met NSAIMs, kan die risiko van akute nierontoereikendheid, wat gewoonlik omkeerbaar is, toeneem by sommige pasiënte met gekompromitteerde nierfunksie (bv. gehidreerde pasiënte, pasiënte op diuretiese middels of bejaarde pasiënte) wanneer AOE-inhibeerders of angiotensien II reseptor antagoniste, en/of diuretiese middels gekombineer word met NSAIMs, insluitend **INNOFLAM** (sien afdeling 4.4). Dus moet die kombinasie versigtig toegedien word, veral by bejaardes. Pasiënte moet voldoende gehidreer word en oorweging moet geskenk word aan monitering van renale funksie na begin van meegaande terapie, en periodiek daarna.
In kliniese tiasied studies, sowel as na bemarking waarnemings, het gewys dat NSAIMs die natriuretiese effek kan laat afneem van furosemied en tiasied by sommige pasiënte. Hierdie respons was toegeskryf aan inhibisie van renale prostaglandien sintese.
Siklosporien en takrolimus
Meegaande toediening van NSAIMs (insluitende **INNOFLAM**) en siklosporien of takrolimus kan die nefrotoksiese effek van siklosporien of takrolimus kan toeneem, respektiewelik. Nierfunksie moet gemonitor word wanneer **INNOFLAM** en enige van hierdie medisynes gekombineer word.
Aspirien
INNOFLAM kan gebruik word met lae-dosis aspirien. Nogtans kan meegaande toediening van aspirien **INNOFLAM** kan tot gevolg hê in 'n verhoogde ratio van GI ulserasie of ander komplikasies, wanneer vergelyk word met gebruik van **INNOFLAM** alleen. Weens sy gebrek van plaatjie effekte, is **INNOFLAM** nie 'n substituut vir aspirien vir kardiovaskulêre profilakse nie.
Daar is geen konsekwente bewys dat meegaande gebruik van aspirien die verhoogde risiko van ernstige kardiovaskulêre trombotiese voorvalle geassosieer met **INNOFLAM** verlig. 'n Verhoogde risiko van gastroïntestinale ulserasie of ander gastroïntestinale komplikasies wanneer vergelyk met gebruik van **INNOFLAM** alleen, word gewys met meegaande toediening van lae-dosis aspirien.
Farmakokinetiese interaksies
*Effekte van **INNOFLAM** op ander medisynes*
CYP2D6 inhibisie
Selekoksib is 'n inhibeerder van CYP2D6. Die plasma-konsentrasies van medisynes wat substrate is van hierdie ensiem kan toeneem wanneer **INNOFLAM** saam gebruik word. Voorbeelde van medisynes wat gemetaboliseer word deur CYP2D6 is antidepressante (trisiklies en SSRIs), neuroleptika, antidisritmiese medisynes, ens. Die dosering van individuele dosis-getitreerde CYP2D6 substrate kan verlaging benodig wanneer behandeling met **INNOFLAM** begin of verhoog word, indien behandeling met **INNOFLAM** gestaak word.
Meegaande toediening van selekoksib van 200 mg twee keer per dag het tot gevolg gehad in 2,6-voudige en 1,5-voudige toenames in plasmakonsentrasies van dekstrometorfan en metoprolol (CYP2D6 substrate), respektewielik CYP2D6 inhibisie van die CYP2D6 substrate metabolisme.
CYP2C19 inhibisie
In vitro studies het sekere potensiaal gewys vir selekoksib om CYP2C10 gekataliseerde metabolisme te inhibeer. Die kliniese betekenis van hierdie in vitro bevinding is nie bekend nie. Voorbeelde van medisynes wat gemetaboliseer word deur CYP2C19 is diasepam, sitalopram en imipramien.
Metotreksaat
By pasiënte met rumatoïede artritis het selekoksib geen statisties beduidende effek gehad op die farmakokinetika nie (plasma of renale opruiming) van metotreksaat (in rumatologiese doserings). Nogtans behoort voldoende monitering vir metotreksaat-verwante toksisiteit oorweeg te word wanneer hierdie twee medisynes gekombineer word.
Litium
By gesonde persone, het die meegaande toediening van selekoksib 200 mg twee keer per dag met 450 mg twee dag van litium tot gevolg gehad in 'n gemiddelde toename in Cmaks van 16 % en in area onder die kurwe (AOK) van 18 % of litium. Dus behoort pasiënte op litium-behandeling omsigtig gemonitor te word wanneer **INNOFLAM** begin of onttrek word.
Orale kontraseptiewe middels
In 'n interaksie studie, het selekoksib geen klinies relevante effekte op die farmakokinetika gehad van orale kontraseptiewe middels nie (1 mg noretisteroon/ 35 mikrogram etinielestradiol).
Glibenklamied/tolbutamied
Selekoksib beïnvloed nie die farmakokinetika van tolbutamied (CYP2C9 substrate), of glibenklamied tot 'n klinies relevante omvang nie.
Fenitoïen
In spesifieke studies in gesonde vrywilligers met ander medisynes gemetaboliseer deur CYP2C9, was gevind dat selekoksib geen klinies beduidende farmakokinetiese interaksie met fenitoïen het nie.
*Effekte van ander medisynes op **INNOFLAM***
CYP2C9 swak metaboliseerders
In individue wat swak metaboliseerders is van CYP2C9 en verhoogde sistemiese blootstelling wys vir selekoksib, kan meegaande toediening met CYP2C9 inhibeerders soos flukonasool tot gevolg hê in verdere verhogings in selekoksib blootstelling. Sulke kombinasies moet vermy word in bekende swak metaboliseerders van CYP2C9 (sien afdeling 4.4).
CYP2C9 inhibeerders en induseerders
Omdat selekoksib hoofsaaklik gemetaboliseer word deur CYP2C9, moet INNOFLAM gebruik word teen die helfte van die aanbevole dosering by pasiënte wat flukonasool ontvang. Meegaande gebruik van 200 mg enkel dosis selekoksib en 200 mg een keer per dag flukonasool, 'n potente CYP2C9 inhibeerder, het tot gevolg gehad in 'n gemiddelde toename in selekoksib Cmaks van 60 % en in AOK van 130 %. Meegaande gebruik van induseerders van CYP2C9 soos rifampisien, karbamasepien en barbiturate kan insluit afname in plasma-konsentrasies van selekoksib.
Ketokonasool en teensuurmiddels
Daar is nie enige effekte waargeneem dat ketokonasool of teensuurmiddels die farmakokinetika van selekoksib beïnvloed nie.
Pediatriese bevolking
Interaksie studies is slegs gedoen by volwassenes.

4.6 Fertiliteit, swangerskap en laktasie
Swangerskap
INNOFLAM word teenaangedui gedurende swangerskap (sien afdeling 4.3)
INNOFLAM kan uteriene inertia en premature sluiting veroorsaak van die ductus arteriosus en moet vermy word gedurende swangerskap.
Gereëlde gebruik van nie-steroïede inflammatoriese medisynes kan tot gevolg hê in:
Eerste trimester
Inhibisie van prostaglandien sintese kan swangerskap en/of die embrio/fetale ontwikkeling ongunstig beïnvloed. Data van epidemiologiese studies gee kommer omtrent 'n verhoogde risiko en/of kardiale misvorming en gastroschisis na gebruik van 'n prostaglandien sintese inhibeerder gedurende vroeë swangerskap. Die absolute risiko vir kardiovaskulêre, tot ongeveer 1,5 %. In diere, was daar gewys dat toediening van 'n prostaglandien sintese inhibeerder tot gevolg gehad het in pre- en postinplanting verlies en embrio-fetale dood. Addisioneel is verhoogde insidente van verskillende misvormings insluitend kardiovaskulêre, is gerapporteer by diere na die toedien van 'n prostaglandien sintese inhibeerder gedurende die organogenetiese periode.
Tweede en Derde trimester.
Gedurende die derde trimester van swangerskap, kan prostaglandien sintese inhibeerders die fetus blootstel aan: kardiopulmonêre toksisiteit (met premature sluiting van die ductus arteriosus en pulmonêre hipertensie); renale disfunksie, wat kan voortgaan tot nierversaking met oligo-hidro-amniose.
Aan die einde van swangerskap, kan die moeder en die neonaat blootgestel word aan: moontlike verlenging van bloedingstyd, kan 'n anti-aggregasie effek voorkom teen baie lae doserings; inhibisie van uteriene kontraksies wat tot gevolg het in vertraagde of verlengde baring.
Die gebruik van **INNOFLAM** moet beperk word tot die laagste effektiewe dosis vir die kortste tydperk, indien nodig gevind word deur 'n gesondheidsorgpersoon. (Sien afdelings 4.3 en 4.4)
Borsvoeding
Beperkte data dui daarop dat **INNOFLAM** uitgeskei word in borsmelk en moet dus nie gebruik word gedurende laktasie nie.
Fertiliteit
Gebaseer op die werkingsmeganisme kan die gebruik van NSAIMs, insluitend **INNOFLAM**, die ruptuur verhoed van ovarium follikels vertraag of voorkom, wat geassosieer was met omkeerbare infertiliteit in sommige vrouens.

4.7 Effekte op vermoë om te bestuur en gebruik van masjiene
Pasiënte wat duiseligheid, vertigo of lomerigheid ondervind (sien afdeling 4.8) terwyl **INNOFLAM** gebruik word, moet nie bestuur of masjinerie hanteer nie.

4.8 Ongewenste effekte
Tabel van ongunstige reaksies
Infeksies en infestasies:
Dikwels: Sinusitis, boonste lugweginfeksie, faringitis, urienweginfeksie, brongitis
Minder dikwels: Helicobacter infeksie, herpes zoster, erisipelas, brongopneumonie, labirintitis, tandvleis-infeksie
Bloed- en die limfatiese stelselafwykings
Minder dikwels: Anemie, leukopenie, trombositopenie, pansitopenie, agranulositose, eggimose
Immuunstelselafwyking:
Dikwels: Hipersensitiwiteit, allergie agteruitgang
Minder dikwels: Anafilaktiese skok, anafilaktiese reaksie, angio-edeem
Frekwensie onbekend: Anafilakse
Metabolisme en voedingsafwykings:
Dikwels: Massatoename
Minder dikwels: Hiperkalemie, toename in bloed-natrium
Psigiatriese afwykings:
Dikwels: Insomnie
Minder dikwels: Angstigheid, depressie, uitputting, verwarring, hallusinasies
Senuweestelselafwykings:
Dikwels: Duiseligheid, hipertonie, hoofpyn
Frekwensie onbekend: Serebrale infark (beroerte), parestesie, lomerigheid, ataksie, disgeusie, intrakraniale hemoragie (insluitend noodlottige aseptiese meningitis, epilepsie (insluitend verergering van epilepsie), ageusie, anosmie
Oogafwykings:
Minder dikwels: Dowwe visie, konjunktivis, oog-hemoragie, retinale arteriële okklusie, retinale aar-okklusie, vitreuse drywers, hemoragie, konjunktivale hemoragie
Oor- en labirintafwykings
Minder dikwels: Tinnitus, hipo-akusis, disfoni
Kardiale afwykings:
Dikwels: Miokardiale infarksie, angina pectoris
Minder dikwels: Hartversaking, hartklopping, tagikardie, disritmie Frekwensie onbekend: Kardiovaskulêre trombotiese voorvalle
Vaskulêre afwykings:
Dikwels: Hipertensie (insluitend agteruitgang van hipertensie)
Minder dikwels: Pulmonêre embolisme, blosing, vaskulitis, diep-aar trombose
Respiratoriese, torakale en mediastinale afwykings
Dikwels: Rinitis, hoes, dispnee
Minder dikwels: Brongospasma, pneumonitis
Gastroïntestinale siektes:
Dikwels: Naarheid, abdominale pyn, diarree, dispepsie, winderigheid, braking, disfagie, prikkelbare dermsindroom, tandafwyking
Minder dikwels: Hardlywigheid, gastritis, stomatitis, gastroïntestinale inflammasie (insluitend agteruitgang van gastroïntestinale inflammasie), eruktasie, gastroïntestinale hemoragie, duodenale ulkus, gastriese ulkus, esofageale ulkus, intestinale ulkus, groot intestinale ulkus, intestinale perforasie, esofagitis, melena, pankreatitis, kolitis, hemoroïede hemoragie, dikwelse ontlasting, mond-ulserasi
Hepatobiliêre afwykings:
Minder dikwels: Abnormale hepatiese funksie, verhoogde hepatiese ensieme (insluitend verhoogde AST en ALT), hepatitis, hepatiese versaking (soms noodlottig of wat leweroorplanting benodig), fulminante hepatitis (soms noodlottig), hepatiese nekrose, chlosetase, chlostatiese geelsug
Vel- en subkutaneuse weefselafwykings
Dikwels: Uitslag, pruritus (insluitend algemene pruritus)
Minder dikwels: Urtikarie, eggimose, alopesie, fotosensitiwiteit, eksfoliatiewe dermatitis, erythema multiforme, Stevens-Johnson sindroom, toksiese epidermale nekrolise, medisyne uitslag met esinofilie en sistemiese simptome (DRESS), akute algemene eksantematease pustulose (AGEP), bulleuse dermatitis, lipoma, allergiese dermatitis, ganglion
Muskuloskeletale en bindweefselafwykings:
Dikwels: Artralgie
Minder dikwels: Spierspasma (beenkrampe), miositis, onderste ledemaat fraktuur
Renale en urienwegafwykings:
Minder dikwels: Verhoogde bloedkreatinien, verhoogde bloedureum, akute nierversaking, hiponatremie, tubuloïnterstisiele nefritis, nefrotiese sindroom, glomerulonefritis minimale letsel, nefrolitiase, nokturie
Reproduktiewe sisteem en borsafwykings:
Minder dikwels: Menstruele afwyking
Frekwensie onbekend: Vroulike infertiliteit (vroulike fertiliteit afname), vaginale hemoragie, borsteerheid
Algemene afwykings en toediening situs toestande:
Dikwels: Griepagtige siekte, perifêre edeem/vloeistof retensie
Minder dikwels: Gesigsedeem, borspyn
Besering, vergifting en prosedure komplikasies afwykings
Dikwels: Toevallige besering
Beskrywing van geselekteerde ongunstige reaksies:
In finale data (beoordeel) van die APC en PreSAP studies in pasiënte wat behandel was met selekoksib 400 mg per dag vir tot 3 jaar (gepoelde data van beide studies), was die oormaat ratio oor plasebo vir miokardiale infarksie 7,6 voorvalle per 1 000 pasiënte (minder dikwels) en daar was geen oormaat ratio for beroerte (tipes nie onderskei) oor plasebo nie.
Medisyne Reaksie met Esinofillie en Sistemiese Simptome (DRESS) [sien afdeling 4.4].
Rapporteer van vermoedelike ongunstige reaksies
Rapporteer van vermoedelike ongunstige reaksies na goedkeuring van die medisyne is belangrik. Dit laat toe vir volgehoue monitering van die voordeel/risiko balans van die medisyne. Gesondheidsvoorsieners word gevra om enige vermoedelike ongunstige reaksies te rapporteer aan SAHPRA via die "**6.04 Adverse Drug Reactions Reporting Form**", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

4.9 Oordosering
Daar is geen kliniese ondervinding van oordosering nie. Enkel dosisse van tot 1 200 mg en veelvuldige doserings van tot 1 200 mg twee keer per dag was toegedien aan gesonde persone sonder beduidende klinies ongunstige effekte. Ingeval van 'n vermoedelike oordosering moet toepaslike ondersteunende mediese sorge voorsien word. Dialise is onwaarskynlik om 'n effektiewe metode te wees vir medisyne verwydering.

5.FARMAKOLOGIESE EIENSKAPPE
5.1 Farmakodinamiese eienskappe
Kategorie A, klas 3.1 Antirumatiek (anti-inflammatoriese middels)
Farmakoterapeutiese groep: Nie-steroïed anti-inflammatoriese en antirumatiek medisynes, NSAIMs, Coxibs, ATC kode: M01AH01.
Selekoksib is 'n spesifieke siklo-oksigenase-2 (COX-2) inhibeerder (SCI)
Siklo-oksigenase-2 word geïnduseer in respons tot inflammatoriese prikkeling. Dit het tot gevolg dat die sintese en akkumulasie van inflammatoriese prostanoïede, veral prostaglandien E2, inflammasie, edeem en pyn veroorsaak.
Selekoksib werk as 'n anti-inflammatoriese, analgetiese en antipiretiese medisyne deur blokkeer van die produksie van inflammatoriese prostanoïede via COX-2 inhibisie. Selekoksib het 'n baie lae affiniteit vir die samestellende uitgedrukte siklo-oksigenase -1 ensiem (COX-1).

5.2 Farmakokinetiese eienskappe
Absorpsie
Wanneer toegedien word onder vastende toestande bereik selekoksib piek plasmakonsentrasie toestande na ongeveer 2-3 uur. Selekoksib wys lineêr en dosis-proporsionele farmakokinetika oor die terapeutiese doseringsvorm.
Plasmaproteïen-binding is konsentrasie onafhanklik en is ongeveer 97 % by terapeutiese plasmakonsentrasies en die medisyne is nie hoofsaaklik gebonde tot eritrosiete in die bloed nie.
Neem van 'n dosis met voedsel ('n hoë vet maaltyd) vertraag absorpsie, wat tot gevolg het in 'n T_{maks} van ongeveer 4 uur en verhoog biobeskikbaarheid met ongeveer 20 %.
Biotransformasie
Selekoksib word gemetaboliseer in die lewer deur hidroksilasie, oksidasie en sekere glukuronidasie. Dit was gedemonstreer dat selekoksib hoofsaaklik gemetaboliseer word deur sitochroom P450 CYP2C9. Farmakologiese aktiwiteit is in die moedersamestelling. Die hoof metaboliete wat gevind word in die sirkulasie het geen waarneembare COX-1 of COX-2 inhiberende aktiwiteit nie.
Eliminasie
Selekoksib word meestal uitgeskei deur hepatiese metabolisme met minder as 1 % van die dosis onveranderd uitgeskei in uriene.
Na veelvuldige dosering is die eliminasie halfleeftyd 8-12 uur en die tempo van opruiming ongeveer 500 mL/min. Met veelvuldige dosering word vaste vlak plasma-konsentrasies bereik voor dag 5.
Veranderlikheid tussen pasiënte op die hoof farmakokinetiese parameters (AOK, Cmaks, eliminasie halfleef) is ongeveer 30 %. Die gemiddelde vaste vlak volume van distribusie is ongeveer 500 L/70 kg in jong gesonde volwassenes na 'n enkel 200 mg dosis, wat dui op wye verspreiding van selekoksib in die weefsels. Voorkliniese studies dui daarop dat selekoksib die bloed/breinskans kruis.
Spesiale bevolkings
Hepatiese inkorting
Plasma-konsentrasies van selekoksib by pasiënte met ligte hepatiese inkorting is nie beduidend verskillend van die met ouderdom- en geslagsvergelykende kontrole nie. By pasiënte met matige hepatiese selekoksib plasma-konsentrasies is ongeveer twee keer die van vergelykende kontrole. Pasiënte met ernstige hepatiese inkorting is nog nie bestudeer nie, maar dit kan verwag word om akkumulasie te wys van die moedersubstans, want die hoof roete van metabolisme is via die lewer.
Renale inkorting
In bejaarde vrywilligers met ouderdom-verwante afnames in glomerulêre filtrasie tempo (GFR) (gemiddelde GFR > 65 mL/min per 1,73 m2) en by pasiënte met chronies stabiele renale ontoereikendheid (GFR 35 - 60 mL/min per 1,73 m2) was selekoksib farmakokinetika vergelykbaar aan die wat gesien was by pasiënte met normale nierfunksie. Geen beduidende verwantskap was gevind tussen serum-kreatinien (of kreatinien-opruiming) en selekoksib-opruiming nie.
Renale effekte
Die relatiewe rolle van COX-1 en COX-2 in renale fisiologie is nie duidelik nie. **I**selekoksib verminder die urinêre ekskresie van PGE2 en 6-keto-PGF1µ ('n prostasiklien metaboliet) maar laat serum-tromboksaan B2 (TXB2) en urinêre ekskresie van 11-dehidro-TXB2, 'n tromboksaan metaboliet (beide COX-1 produkte) ongeaffekteer. Spesifieke studies het gewys dat selekoksib geen afname veroorsaak in GFR by bejaardes of die met chroniese nierontoereikendheid nie. Hierdie studies het ook kortstondige afnames in fraksionele ekskresie van natrium gewys.
Bejaarde pasiënte van 65 jaar en ouer
In die bevolking > 65 jaar is daar 'n tweevoudige toename in gemiddelde Cmaks en AOK vir selekoksib. Dit is 'n gewigsverwante eerder as ouderdomsverwante verandering. Selekoksib-vlakke is hoër in laer massa individue en dus in die bejaarde bevolking, wat gewoonlik 'n laer gemiddelde massa het as die jonger bevolking. Bejaarde vrouens neig dus om effense hoër selekoksib plasmakonsentrasies te hê as mans.
Kinders
Selekoksib is nog nie bestudeer by pasiënte van jonder as 18 jaar oud nie.

6. FARMASEUTIESE BESONDERHEDE
6.1 Lys van eksipiënte
INNOFLAM 100 EN 200 Kroskarmellose natrium, FD & C blou # 2 aluminum lake, gelatien, laktose monohidraat, magnesiumstearaat, povidoon, gesuiwerde water, shellac, natriumlourielsulfaat, titaniumdioksied E 171, geel ysteroksied

6.2 Onverenigbaarhede
Geen

6.3 Rakleeftyd
36 maande vanaf datum van vervaardiging.

6.4 Spesiale Voorsorgmaatreëls vir berging
Berg by of benede 30 °C in oorspronklike houer om te beskerm teen vog.

6.5 Aard en inhoud van houer
INNOFLAM 100 en 200 is beskikbaar in
- (10's, 20's, 30's & 60's) stolpe van aluminumfoelie & CFB foelie in een karton. In pakgroottes van meervoude van 10 kapsules per stolp.
- (10's, 20's, 30's & 60's) stolpe van aluminumfoelie & deursigtige PVC/PE/PVDC film in een karton. In pakgroottes in veelvoude van 10 kapsules per stolp.

6.6 Spesiale voorsorgmaatreëls vir weggooi en ander hantering
Enige medisyne of afvalmateriaal moet weggegooi word volgens plaaslike vereistes.

7. HOUER VAN SERTIFIKAAT VAN REGISTRASIE
Innovata Pharmaceuticals (EDMS) Bpk
Crownwood Kantoorpark, Blok D
Northern Parkway 100
Ormonde, Johannesburg, 2091,
Suid-Afrka

VERVAARDIGER:
Alembic Pharmaceuticals Limited
(Formulation Division)
Village Panelav, P.O. Tajpura,
Near Baska, Taluka-Halol, District-Panchmahal,
Gujarat- 389350, India

8. REGISTRASIENOMMERS
South Africa:
INNOFLAM 100: A 51/3.1/0722
INNOFLAM 200: A 51/3.1/0723
Zimbabwe: PP
INNOFLAM 100: 2021/3.1/6167
INNOFLAM 200: 2021/3.1/6168
Botswana: S2
INNOFLAM 100: BOT1803546
INNOFLAM 200: BOT1803547

9. DATUM VAN EERSTE GOEDKEURING/HERNUWING VAN DIE GOEDKEURING
28 September 2021

10. DATUM VAN REVISIE VAN DIE TEKS

03-03-2022

520 mm

400 mm
Back Side

Type: Pack Insert
Size: 400 x 520 mm