SCHEDULING STATUS:
S3

1. NAME OF THE MEDICINE
BIO DICLOFENAC INJECTION, 25 mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 3 ml ampoule contains diclofenac sodium 25 mg/ml.
Excipients: Benzyl alcohol 4 % m/v as preservative, sodium metabisulphite 0,3 % m/v as anti-oxidant
Contains sugar: mannitol (6 mg/ml).
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Injection
A clear colourless to slightly yellow solution free from foreign particles.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
BIO DICLOFENAC INJECTION, when administered by intramuscular injection, is indicated for:
- Initial therapy for inflammatory and degenerative rheumatic disease.
- Treatment of mild to moderately painful conditions due to inflammation of non-rheumatic origin.

Intravenous infusion of BIO DICLOFENAC INJECTION is indicated for:
- Treatment or prevention of post-operative mild to moderate pain of inflammatory origin in the absence of infection.

4.2 Posology and method of administration
BIO DICLOFENAC INJECTION should not be mixed with other injection solutions.
BIO DICLOFENAC INJECTION should not be given for more than two days: If necessary the treatment can be continued with an oral preparation of diclofenac or with suppositories. Use the lowest effective dose for the shortest possible duration of treatment.
Intramuscular injection
NOTE: The directions for intramuscular injection must be followed in order to avoid damage to a nerve or other tissue at the injection site.
It should be administered as a deep intragluteal injection into the upper outer quadrant.
After inserting the needle the plunger should be pulled back to avoid inadvertent intravascular injection.
Adults:
75 mg once daily.
In severe cases, 75 mg twice daily (separated by an interval of a few hours, one injection into each buttock).
Alternatively, it is possible to combine 75 mg of BIO DICLOFENAC INJECTION intramuscularly with an oral dose of diclofenac up to a maximum daily dosage of 150 mg.
Intravenous Infusion
BIO DICLOFENAC INJECTION must not be given as an intravenous bolus injection. Do not use infusion other than those recommended.
For preparation of intravenous infusion, see section 6.6.
Two alternative dosage regimens of BIO DICLOFENAC INJECTION are recommended
Moderate to severe postoperative pain.
75 mg should be infused continuously over a period of 30 minutes to 2 hours. If necessary treatment may be repeated after 4 to 6 hours, but a total dosage of 150 mg within any period of 24 hours must not be exceeded.
Prevention of postoperative pain.
25 mg to 50 mg of BIO DICLOFENAC INJECTION infused after surgery over 15 minutes to 1 hour, followed by a continuous infusion of approximately 5 mg per hour up to a maximum daily dosage of 150 mg.

4.3 Contraindications
NB. The intravenous use of BIO DICLOFENAC INJECTION is absolutely contraindicated in patients with impaired renal function and/or any form of shock.
- Hypersensitivity to diclofenac or to any of the ingredients of BIO DICLOFENAC INJECTION, especially sodium metabisulphite.
- Hypersensitivity to other NSAIDs including aspirin.
- Gastric or intestinal ulcer.
- Bleeding disorders.
- History of gastrointestinal perforation, ulceration or bleeding (PUBs) related to previous NSAIDs, including BIO DICLOFENAC INJECTION.
- Active or history of recurrent ulcer/haemorrhage/perforations (two or more distinct episodes of proven ulceration or bleeding).
- Asthmatic patients in whom attacks or asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or by other medicines with prostaglandin-synthase inhibiting activity.
- The intravenous use of BIO DICLOFENAC INJECTION is contraindicated in children due to insufficient evidence.
- Porphyria.
- Pregnancy and lactation.
- Severe hepatic or heart failure.
- Moderate or severe renal impairment (serum creatinine > 160 µmol/l).
- Established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.
- Concomitant NSAID or anticoagulant use (including low doses of heparin).
- History of haemorrhagic diathesis, a history of confirmed or suspected cerebrovascular bleeding.
- Operations associated with a high risk of haemorrhage.
- Hypovolemia or dehydration from any cause.

4.4 Special warnings and precautions for use
General:
As with other non-steroidal anti-inflammatory medicines including BIO DICLOFENAC INJECTION, allergic reactions, including anaphylactic reactions can also occur without earlier exposure to the medicine (see section 4.8).
Side effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.
Close medical surveillance and strict accuracy of diagnosis are imperative in patients with:
- Symptoms indicative of gastrointestinal disease.
- Ulcerative colitis.
- Crohn's disease.
- A case history suggestive of gastrointestinal disease.
- Impaired hepatic function.
- Pre-existing dyshematopoiesis or disorders of blood coagulation.

Concomitant use of BIO DICLOFENAC INJECTION and methotrexate could result in serious interactions (see section 4.5).
The concomitant use of BIO DICLOFENAC INJECTION with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive side effects (see section 4.5).
BIO DICLOFENAC INJECTION may mask signs and symptoms of infection.
The presence of sodium metabisulphite may lead to hypersensitivity reactions, especially in patients with bronchial asthma and this may result in an acute asthma attack, clouding consciousness or shock.
Gastrointestinal (GI) effects:
Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs including BIO DICLOFENAC INJECTION, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.
A reduction in dosage may be required in the elderly, especially the very frail or those with a low body mass.
The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of BIO DICLOFENAC INJECTION, in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation, and the elderly.
When gastrointestinal bleeding or ulceration occurs in patients receiving BIO DICLOFENAC INJECTION, treatment with BIO DICLOFENAC INJECTION should be stopped.
BIO DICLOFENAC INJECTION should be given with caution to patients with a history of gastrointestinal disease (e.g. ulcerative colitis, Crohn's disease, hiatus hernia, gastro-oesophageal reflux disease, angiodysplasia) as the condition may be exacerbated.
To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose.
Combination therapy with protective medicines (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant use of medicines containing low dose acetylsalicylic acid (ASA/aspirin or medicines likely to increase gastrointestinal risk (see section 4.5)).
Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding).
Caution is recommended in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors (SSRIs) or antiplatelet medicines such as acetylsalicylic acid (see section 4.5).
Skin effects:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. BIO DICLOFENAC INJECTION should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.
Patients appear to be at the highest risk of these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. BIO DICLOFENAC INJECTION should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.
Hepatic effects:
Close medical surveillance is required when prescribing BIO DICLOFENAC INJECTION to patients with impairment of hepatic function as their condition may be exacerbated.
As with other NSAIDs, including BIO DICLOFENAC INJECTION, values of one or more liver enzymes may increase.
During prolonged treatment with BIO DICLOFENAC INJECTION, full blood counts and monitoring of hepatic and renal function are indicated. If abnormal liver function tests persist and symptoms of hepatic disease develop, discontinue BIO DICLOFENAC INJECTION.
Hepatitis may occur with BIO DICLOFENAC INJECTION without prodromal symptoms.
Renal effects:
As fluid retention and oedema have been reported in association with NSAIDs therapy, including BIO DICLOFENAC INJECTION, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, the elderly, patients receiving concomitant treatment with diuretics or medicinal products that can significantly impact renal function, and those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery (see section 4.3).
Monitoring of renal function is recommended as a precautionary measure when using BIO DICLOFENAC INJECTION in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.
Systemic lupus erythematosus (SLE) and mixed connective tissue disease:
In patients with SLE and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).
Cardiovascular and cerebrovascular effects:
Caution is required in patients with a history of hypertension and/or heart failure, as fluid retention and oedema have been reported in association with BIO DICLOFENAC INJECTION therapy. In view of the BIO DICLOFENAC INJECTION's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients. Appropriate monitoring and advice are required for these patients.
Caution is required in patients with significant risk factors for cardiovascular events (e.g. uncontrolled hypertension, hyperlipidaemia, diabetes mellitus, smoking, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease) and should only be treated with BIO DICLOFENAC INJECTION after careful consideration.
The cardiovascular risks of BIO DICLOFENAC INJECTION may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used.
The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.
Clinical trial and epidemiological data consistently point towards increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of BIO DICLOFENAC INJECTION, particularly at high dose (150 mg daily) and in long term treatment.
Haematological effects:
During prolonged treatment with BIO DICLOFENAC INJECTION, as with other NSAIDs, monitoring of the blood count is recommended.
BIO DICLOFENAC INJECTION may reversibly inhibit platelet aggregation (see section 4.5). Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.
Pre-existing asthma:
In patients with asthma, seasonal allergic rhinitis, swelling of the nasal mucosa (i.e. nasal polyps), chronic obstructive pulmonary diseases or chronic infections of the respiratory tract (especially if linked to allergic rhinitis like symptoms), reactions on NSAIDs like asthma exacerbations (so called intolerance to analgesics/analgesics asthma), Quincke's oedema or urticaria are more frequent than in other patients. Therefore, special precaution is recommended in such patients (readiness for emergency). This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.
Like other medicines that inhibit prostaglandin synthase activity, BIO DICLOFENAC INJECTION and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.
Pregnancy:
The administration of Nonsteroidal anti-inflammatory drugs (NSAID's) around 20 weeks or later in pregnant patients may cause serious kidney problems in an unborn baby. This may lead to low levels of amniotic fluid because around 20 weeks of pregnancy the unborn baby's kidneys produces amniotic fluid. Amniotic fluid provides a protective cushion and helps the lungs, digestive system, and muscles of the unborn baby to develop (see section 4.3).
Medicines that inhibit prostaglandin synthesis, like NSAID's, may adversely affect pregnancy and/or the embryo or foetal's development. The risk is believed to increase with an increased dose and/or duration of therapy.
It is recommended to avoid the administration NSAIDs in pregnant woman at 20 weeks or later (see section 4.3). Unless specifically advised by a healthcare professional to administer NSAID between 20 and 30 weeks, the dose should be kept as low and the duration of treatment as short as possible. Ultrasound monitoring of amniotic fluid is recommended if NSAIDs treatment extends beyond 48 hours.
Regular use of BIO DICLOFENAC INJECTION during the third trimester of pregnancy may result in premature closure of the ductus arteriosus in utero and possibly in persistent pulmonary hypertension in the newborn. The onset of labour may be delayed and its duration increased (See section 4.6).
BIO DICLOFENAC INJECTION may cause renal dysfunction, which may progress to renal failure with oligohydroamniosis, and in some cases neonatal renal impairment. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation. Oligohydramnios may be reversible with treatment. Discontinuation and possible prolongation of bleeding time due to the anti-aggregating effect which may occur even at very low doses of BIO DICLOFENAC INJECTION.
Female fertility:
If BIO DICLOFENAC INJECTION is administered to woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and the duration of treatment as short as possible.
The use of BIO DICLOFENAC INJECTION may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of BIO DICLOFENAC INJECTION should be considered (see section 4.6)).
BIO DICLOFENAC INJECTION contains propylene glycol, benzyl alcohol and sodium metabisulphite.
BIO DICLOFENAC INJECTION contains 600 mg propylene glycol per 3 ml ampoule which is equivalent to 200 mg/ml.
BIO DICLOFENAC INJECTION contains 120 mg benzyl alcohol per 3 ml ampoule which is equivalent to 40 mg/ml. Benzyl alcohol may cause allergic reactions. Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding or if you have liver or kidney disease. This is because large amounts of benzyl alcohol can build up in your body and may cause side effects (called 'metabolic acidosis').
The sodium metabisulphite present in solution for injection may rarely cause severe hypersensitivity reactions and bronchospasm.
BIO DICLOFENAC INJECTION contains less than 1 mmol sodium (23 mg) per 3 ml ampoule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction
Methotrexate: Concurrent administration of methotrexate with BIO DICLOFENAC INJECTION may result in increased methotrexate toxicity due to the inhibition of the tubular renal clearance of methotrexate (See section 4.4).
Caution is recommended when NSAIDs, including BIO DICLOFENAC INJECTION, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increased. Cases of serious toxicity have been reported when methotrexate and NSAIDs including BIO DICLOFENAC INJECTION were given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.
Lithium or digoxin: BIO DICLOFENAC INJECTION may raise plasma concentrations of lithium or digoxin if taken together. Monitoring of the serum lithium or digoxin level is recommended.
Glucocorticoids and other NSAIDs including cyclooxygenase-2 inhibitors: Gastro-intestinal adverse effects may be exacerbated by the concomitant administration of BIO DICLOFENAC INJECTION; increased risk of gastrointestinal ulceration or bleeding. Concurrent treatment with two or more NSAIDs may increase the risk of adverse effects.
Antidiabetic medicines: BIO DICLOFENAC INJECTION may cause either hypo- or hyperglycaemia. Dosage of antidiabetic medicines may need to be changed and monitoring of the blood glucose level is recommended.
Anticoagulants: There is an increased risk of haemorrhage if BIO DICLOFENAC INJECTION is used concurrently with any anticoagulants, e.g. warfarin. Careful monitoring is necessary.
BIO DICLOFENAC INJECTION may enhance the effects of anticoagulants such as warfarin.
As with other non-steroidal anti-inflammatory agents, BIO DICLOFENAC INJECTION in a high dose can reversibly inhibit platelet aggregation.
Ciclosporin: Nephrotoxicity of ciclosporin may be increased by the effects of BIO DICLOFENAC INJECTION on renal prostaglandins.
Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.
Quinolone antibiotics: There have been isolated reports of convulsions when BIO DICLOFENAC INJECTION is administered concomitant with quinolone antibiotics and NSAIDs.
This may occur in patients with or without a previous history of epilepsy or convulsions.
Therefore, caution should be exercised when considering the use of a quinolone in patients who are already receiving an NSAID.
Anti-platelet medicines and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding.
Diuretics and antihypertensive medicines: Like other NSAIDs, concomitant use of BIO DICLOFENAC INJECTION with diuretics and antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors may cause a decrease in their antihypertensive effect via inhibition of vasodilator prostaglandin synthesis.
Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.
Medicines known to cause hyperkalaemia: Concomitant treatment with potassium sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored.
Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal anti-prostaglandin effects of both NSAID and calcineurin inhibitor.
Phenytoin: When using phenytoin concomitantly with BIO DICLOFENAC INJECTION, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.
Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of BIO DICLOFENAC INJECTION. Therefore, it is recommended to administer BIO DICLOFENAC INJECTION at least one hour before or 4 to 6 hours after administration of colestipol/cholestyramine.
Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.
Mifepristone: NSAIDs should not be used for 8 - 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.
Potent CYP2C9 inhibitors: Caution is recommended when co-prescribing BIO DICLOFENAC INJECTION with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to BIO DICLOFENAC INJECTION due to inhibition of BIO DICLOFENAC INJECTION metabolism.

4.6 Fertility, pregnancy and lactation
Pregnancy
Safety and efficacy in pregnancy and lactation has not been established.
Regular use of non-steroidal anti-inflammatory medicines, such as BIO DICLOFENAC INJECTION, during the third trimester of pregnancy, may result in the following (See section 4.4):
The foetus:
- Cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension).
- Renal dysfunction, which may progress to renal failure with oligohydramnios.

The mother and the neonate (at the end of pregnancy):
- 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.

Breastfeeding
Like other NSAIDs, BIO DICLOFENAC INJECTION passes into breast milk in small amounts.
Therefore, BIO DICLOFENAC INJECTION should not be administered during lactation in order to avoid undesirable effects in the infant.
Fertility
As with other NSAIDs, the use of BIO DICLOFENAC INJECTION may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of BIO DICLOFENAC INJECTION should be considered (see section 4.4).

4.7 Effects on ability to drive and use machines
Patients who experience dizziness, visual disturbances, vertigo, somnolence, drowsiness or fatigue, or other central nervous system disturbances while BIO DICLOFENAC INJECTION is administered should refrain from driving a vehicle or operating machines.

4.8 Undesirable effects
Infections and infestations
Frequency unknown: Injection site necrosis.
Blood and the lymphatic system disorders
Less frequent: Leukopenia, thrombocytopenia, aplastic anaemia, haemolytic anaemia, agranulocytosis.
Immune system disorders
Less frequent: Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock), angioneurotic oedema (including face oedema).
Cardiac disorders
Less frequent: Palpitation, chest pain, cardiac failure, oedema, myocardial infarction.
Frequency unknown: Kounis syndrome.
Psychiatric disorders
Less frequent: Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders
Frequent: Headache, dizziness, nervousness.
Less frequent: Tiredness, disturbances of sensation (including paraesthesia), memory disturbance, convulsions, anxiety, tremor, psychotic reactions, aseptic meningitis, cerebrovascular accident, taste disturbance.
Frequency unknown: Confusion, hallucinations, malaise, disturbances of sensation.
Gastrointestinal disorders
The most commonly observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or gastrointestinal bleeding, sometimes fatal. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis, anorexia.
Frequent: Epigastric pain, nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, eructation, anorexia, local irritation.
Less frequent: Gastrointestinal bleeding, haematemesis, melaena, bloody diarrhoea, peptic ulcer with or without bleeding or perforation, lower gut disorders such as non-specific haemorrhagic colitis, exacerbation of ulcerative colitis or Crohn's proctocolitis, glossitis, aphthous stomatitis, oesophageal lesions, diaphragm-like intestinal strictures, constipation, pancreatitis, alteration in taste, gastritis.
Vascular disorders
Less frequent: Hypertension, hypotension, vasculitis.
Renal and urinary disorders
Less frequent: Acute renal failure, urinary abnormalities such as haematuria, proteinuria, interstitial nephritis, nephritic syndrome, renal papillary necrosis.
Hepato-biliary disorders
Frequent: Elevated transaminase levels (ALT, AST).
Less frequent: Hepatitis with or without jaundice, fulminant hepatitis, jaundice, liver disorder, hepatic necrosis, hepatic failure.
Eye disorders
Less frequent: Disturbances of vision (diplopia, blurred vision).
Frequency unknown: Optic neuritis.
Ear and labyrinth disorders
Frequent: Vertigo.
Less frequent: Impaired hearing, tinnitus.
Skin and subcutaneous tissue disorders
Frequent: Rash and skin reactions.
Less frequent: Urticaria, bullous eruptions, eczema, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis (Lyell's syndrome), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura, pruritus. Abscesses and local necrosis have also occurred, especially in diabetics.
Respiratory, thoracic and mediastinal disorders
Less frequent: Asthma (including dyspnoea), pneumonitis.
General disorders and administration site conditions
Frequent: Injection site reaction, injection site pain, injection site induration.
Reproductive system and breast disorders
Less frequent: Impotence.
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
(See section 4.8)
Symptoms include: headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions.
In the case of significant poisoning acute renal failure and liver damage are possible.
Treatment is symptomatic and supportive, especially for hypotension, renal failure, convulsions, gastrointestinal irritation and respiratory depression.
Specific therapies such as forced diuresis, dialysis or haemoperfusion are of little value in eliminating BIO DICLOFENAC INJECTION because of its high protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES
A.3.1 Antirheumatics (anti-inflammatory agents)
Anti-inflammatory and antirheumatic products, Non-Steroids Nonsteroidal anti-inflammatory drugs (NSAIDs). ATC code: M01AB05

5.1 Pharmacodynamic properties
Diclofenac is a non-steroidal anti-inflammatory compound (NSAID) with analgesic, antipyretic and anti-inflammatory activities. It causes decreased formation of prostaglandins and thromboxanes through inhibition of the activity of the enzyme cyclo-oxygenase. Diclofenac inhibits platelet aggregation in vitro.

5.2 Pharmacokinetic properties
Peak plasma concentrations are reached about 10 to 22 minutes after intramuscular administration. Diclofenac is extensively bound to plasma proteins (99 %) and its plasma half-life is 1 to 2 hours.
Diclofenac is excreted in the form of metabolites via the kidneys (approximately 60 %) and faeces (approximately 30 %). Less than 1 % is excreted in unchanged form.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Benzyl alcohol 4 % m/v (as preservative)
Mannitol
Propylene glycol
Sodium hydroxide (pH adjustment)
Sodium metabisulphite 0,3 % m/v (as anti-oxidant)

6.2 Incompatibilities
The ampoules used im or iv as an infusion should not be mixed with other injection solutions.
For preparation of intravenous infusion see section 6.6.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store at or below 25 °C.
Do not remove ampoules from outer carton until required for use.

6.5 Nature and contents of container
10 x 3 ml clear colourless glass, labelled ampoules in a carton box.

6.6 Special precautions for disposal and other handling
Intravenous infusions should be freshly made up and used immediately. Once prepared, the infusion should not be stored.
Intravenous Infusion
To prepare an intravenous infusion, one ampoule of BIO DICLOFENAC INJECTION should be diluted with 100 to 500 mℓ of either sodium chloride (0,9 %) or glucose solution (5 %). Both solutions should first be buffered with bicarbonate solution (0,5 mℓ 8,4 % or 1 mℓ 4,2 %). Only clear infusion solutions should be used. BIO DICLOFENAC INJECTION infusions should be freshly made up and used immediately. Once prepared, the infusion should not be stored. If crystals or precipitates are observed, the infusion solution should not be used.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Biotech Laboratories (Pty) Ltd.
Ground Floor, Block K West, Central Park
400 16th Road, Randjespark, Midrand, 1685
South Africa

8. REGISTRATION NUMBER(S)
42/3.1/0411

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION
Date of registration: 19 March 2010

10. DATE OF REVISION OF THE TEXT
12 April 2021

SKEDULERING STATUS
S3

1. NAAM VAN DIE MEDISYNE
BIO DICLOFENAC INSPUITING, 25 mg/ml

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
Elke 3 ml ampule bevat diklofenak natrium 25 mg/ml.
Hulpstowwe: Bensielalkohol 4% m/v as preserveermiddel, natriummetabisulfiet 0,3% m/v as anti-oksidant
Bevat suiker: mannitol (6 mg/ml)
Vir volledige lys hulpstowwe, sien afdeling 6.1

3. FARMASEUTIESE VORM
Inspuiting
'n Helder kleurloos tot effens geel oplossing, vry van enige deeltjies.

4. KLINIESE BESONDERHEDE
4.1 Terapeutiese indikasies
BIO DICLOFENAC INSPUITING, wanneer as binnespierse inspuiting toegedien word, is aangedui vir:
- Aanvanklike behandeling van inflammatoriese en degeneratiewe rumatiese siekte.
- Behandeling van ligte tot matige pynlike toestande as gevolge van inflammasie van nie-rumatiese oorsprong.

Binneaarse-infusie van BIO DICLOFENAC INSPUITING is aangedui vir:
- Behandeling of voorkoming van post-operatiewe ligte tot matige pyn van inflammatoriese oorsprong in die afwesigheid van infeksie.

4.2 Dosering en metode van toediening
BIO DICLOFENAC INSPUITING moet nie met ander inspuitbare oplossings gemeng word nie.
BIO DICLOFENAC INSPUITING moet nie vir meer as twee dae toegedien word. Indien nodig kan die behandeling voortgesit word met 'n orale vorm van diklofenak of met setpille. Gebruik die laagste effektiewe dosis vir die kortste moontlike duur van behandeling.
Binnespierse inspuiting
NOTA: Die aanwysings vir binnespierse inspuiting moet gevolg word om skade aan 'n senuwee of ander weefsel op die inspuitplek te voorkom.
Dit moet toegedien word as 'n diep intragluteale inspuiting in die boonste buitenste kwadrant. Nadat die naald geplaas is, moet die plunjer teruggetrek word om onbedoelde intravaskulêre inspuiting te voorkom.
Volwassenes:
75 mg een maal per dag.
In ernstige gevalle, 75 mg twee keer per dag (geskei deur 'n interval van 'n paar uur, een inspuiting in elke boud).
Alternatiewelik is dit moontlik om 75 mg BIO DICLOFENAC-INSPUITING binnespiers te kombineer met 'n orale dosis diklofenak tot 'n maksimum daaglikse dosis van 150 mg.
Intraveneuse infusie
BIO DICLOFENAC INSPUITING mag nie as intraveneuse bolus inspuiting toegedien word nie. Moet nie vir infusie gebruik word, anders as per aanbeveling nie.
Vir voorbereiding van intraveneuse infusie,sien afdeling 6.6
Twee alternatiewe dosisregimens van BIO DICLOFENAC INJECTION word aanbeveel
Matige tot ernstige postoperatiewe pyn.
75 mg moet deurlopend oor 'n periode van 30 minute tot 2 ure toegedien word. Indien nodig, kan die behandeling na 4 tot 6 uur herhaal word, maar 'n totale dosis van 150 mg binne 'n tydperk van 24 uur mag nie oorskry word nie.
Voorkoming van post-operatiewe pyn.
25 mg tot 50 mg BIO DICLOFENAC-INSPUITING kan per infusie, na sjirurgie, oor 'n typerk van 15 minute tot 1 uur toegedien word, gevolg deur 'n deurlopende infusie van ongeveer 5 mg per uur tot 'n maksimum daaglikse dosis van 150 mg.

4.3 Kontra-indikasies
NB. Die intraveneuse gebruik van BIO DICLOFENAC INSPUITING word absoluut gekontraïndikeer in pasiënte met ingeperkte nierfunksie en/of enige ander vorm van skok.
- Hipersensitiwiteit teenoor diklofenak of enige van die ander bestandele van BIO DICLOFENAC INSPUITING, veral natriummetabisulfiet.
- Hipersensitiwiteit teenoor NSAID's, insluitend aspirien.
- Gastriese of intestinale ulkus.
- Bloedingsversteurings.
- Geskiedenis van gastro-intestinale perforasie, ulserasie of bloeding (PUBs) verwant aan vorige NSAID's, insluitend BIO DICLOFENAC INSPUITING.
- Aktiewe of geskiedenis van herhalende ulserasie/bloeding perforasies (twee of meer spesifieke episodes van bewysde ulserasie of bloeding).
- Asmatiese pasiënte in wie aanvalle of asma, urtikaria of akute rinitis vererger is deur asetielsalisielsuur of enige ander medisyne met prostaglandien-sintese onderdrukkende aktiwiteit.
- Die intraveneuse gebruik van BIO DICLOFENAC INSPUITING is teenaangedui in kinders as gevolg van onvoldoende bewyse.
- Porfirie
- Swangerskap en laktasie
- Ernstige hepatiese-of hartversaking
- Matige of ernstige nierinperking (serum kreatinien > 160 µmol/l).
- Bevestigde iskemiese hartsiektes en/of serebrovaskulêre siekte (beroerte) en perifere arteriële siekte.
- Gesamentlike NSAID of anti-stollingsmiddel gebruik (insluitend lae doserings van heparien)
- Geskiedeins van hemorragiese diatese, 'n geskiedenis van bevestigde of vermeende serebro vaskulêre bloeding.
- Operasies wat verband hou met hoë risikos van bloeding.
- Hipovolemie of dehidrasie van enige oorsaak.

4.4 Spesiale waarskuwings en voorsorg met gebruik
Algemeen:
Soos met ander nie-steroïdale anti-inflammatoriese medisyne insluitend BIO DICLOFENAC INSPUITING, kan allergiese reaksies, insluitend anafilaktiese reaksies, soms voorkom sonder vorige blootstelling aan die medisyne (sien afdeling 4.8)
Newe-effekte kan verminder word deur die laagste effektiewe dosis vir die kortste moontlike periode wat nodig is om simptome te beheer.
Noukeurige mediese waarneming en streng akkuraatheid van diagnose is noodsaaklik vir pasiënte met:
- Simptome aanduidend van gastro-intestinale siekte.
- Ulseratiewe colitis
- Chron se siekte
- 'n Gevallegeskiedenis wat dui op gastro-intestinale siektes.
- Ingeperkte hepatiese funksie.
- Bestaande dishematopoïesis of afwykings van bloedstolling

Gesamentlike gebruik van BIO DICLOFENAC INSPUITING en metotreksaat kan lei tot ernstige interaksies (sien afdeling 4.5)
Die gesamentlike gebruik van BIO DICLOFENAC INSPUITING met sistemiese NSAID's insluitend siklo-oksigenase-2 selektiewe remmers, moet vermy word as gevolge van die afwesigheid van enige bewyse wat sinergistiese voordele en potensiaal vir bykomende newe-effekte demonstreer (sien afdeling 4.5)
BIO DICLOFENAC INSPUITING kan tekens en simptome van infeksie verskuil.
Die teenwoordigheid van natriummetabisulfiet kan lei tot hipersensitiwiteitsreaksies, veral in pasiënte met brongiale asma en dit kan ook lei na 'n akute asma-aanval, vertroebelde bewustheid of skok.
Gastro-intestinale (GI) effekte:
Bejaardes: Bejaardes het 'n verhoogde voorkoms van nadelige reaksies teenoor NSAID's insluitend BIO DICLOFENAC INSPUITING, veral gastro-intestinale perforasie, ulserasie en bloeding (PUB's), wat fataal kan wees.
Verlaging van dosering mag nodig wees in bejaardes, veral baie verswaktes of die met 'n lae liggaamsmassa.
Die risiko van gastro-intestinale perforasie, ulserasie of bloeding (PUB's) is hoër met verhoogde dosisse van BIO DICLOFENAC INSPUITING, in pasiënte met 'n geskiedenis van ulkusse, veral wanneer gekompliseerd met bloeding of perforasie, en bejaardes.
Wanneer gastro-intestinale bloeding of ulserasie voorkom in pasiënte wat BIO DICLOFENAC INSPUITING ontvang, moet behandeling met BIO DICLOFENAC INSPUITING gestaak word.
BIO DICLOFENAC INSPUITING moet met omsigtigheid aan pasiënte met 'n geskiedenis van gastro-intestinale siekte gegee word (bv. ulseratiewe kolitis, Chron Siekte, hiatusbreuk, gastro-esofageale refluks siekte, angiodisplasie), aangesien die toestand vererger kan word.
Om die risiko van GI toksisiteit te voorkom in pasiënte met 'n geskiedenis van ulkusse, veral wanneer gekompliseerd is met bloeding of perforasie, en bejaardheid, moet aanvangsbehandeling en handhawing teen die laagste effektiewe dosis gedoen word.
Kombinasie-terapie met beskermende medisyne (bv. misopristool of protonpomp-inhibeerders), moet oorweeg word vir hierdie pasiënte, en ook in pasiënte wat gelyktydig medisyne benodig wat lae dosis asetielsalisielsuur bevat. (ASA/aspirien of medisyne geneig om gastro-intestinale risiko te verhoog (sien afdeling 4.5)).
Pasiënte met 'n geskiedenis van GI toksisiteit, veral wanneer bejaard, moet enige ongewone abnormale simptome (veral GI bloeding) aanmeld.
Omsigtigheid word aanbeveel by pasiënte wat gepaardgaande medisyne wat die risiko van ulserasie of bloeding verhoog ontvang, soos sistemiese kortikosteroïede, anti-koagulante soos warfarien, selektiewe heropname inhibeerders (SSRI's) of anti-stollingsmedisyne soos asetielsalisielsuur (sien afdeling 4.5)
Vel effekte:
Ernstige velreaksies, sommige daarvan fataal, insluitend afskilferende dermatitis, Stevens-Johnsons sindroom en toksiese epidermale nekrolise, is al aangemeld. BIO DICLOFENAC INSPUITING moet gestaak word met die eerste voorkoms van veluitstlag, mukosale letsels, of enige ander tekens van hipersensitiwiteit.
Dit blyk dat die hoogste risiko vir hierdie reaksies in pasiënte tydens die vroeë stadium van behandeling voorkom: die aanvang van die reaksie kom in die grootste hoeveelheid gevalle binne die eerste maand van behandeling voor. BIO DICLOFENAC INSPUITING moet gestaak word met die eerste verskyning van veluitslag, mukosale letsels of enige ander tekens van hipersensitiwiteit.
Hepatiese effekte:
Noukeurige mediese toesig is nodig wanneer BIO DICLOFENAC INSPUITING voorgeskryf word aan pasiënte met ingeperkte lewerfunksie omdat hul toestand vererger kan word.
Soos met ander NSAID's, insluitend BIO DICLOFENAC INSPUITING, mag die waardes van een of meer lewerensieme verhoog.
Gedurende verlengde behandeling met BIO DICLOFENAC INSPUITING, word volbloedtellings, lewer-en nierfunksie monitering aangedui. Indien abnormale lewerfunksie toetse volhou en simptome of lewersiekte ontwikkel, staak BIO DICLOFENAC INSPUITING.
Hepatitis kan voorkom met BIO DICLOFENAC INSPUITING sonder voor-kliniese simptome.
Nier-effekte:
Omdat vloeistof terughouding en edeem al aangemeld is in verband met NSAID terapie, insluitend BIO DICLOFENAC INSPUITING, moet spesifieke omsigtigheid toegepas word in pasiënte met ingeperkte hart-of nierfunksie, geskiedenis van hoë bloeddruk, bejaardes, pasiënte wat gelyktydige behandeling met diuretika of medisyne ontvang wat nierfunksie aansienlik kan beïnvloed, en daardie pasiënte met aansienlike ekstrasellulêre volume-uitputting van enige oorsaak, bv. voor of na 'n groot operasie (sien afdeling 4.3).
Monitering van nierfunksie word aanbeveel as 'n voorsorgmaatreël wanneer BIO DICLOFENAC INSPUITING gebruik word. Staking van terapie word gewoonlik gevolg deur herstel na die toestand voor die behandeling.
Sistemiese lupus erythematosus (SLE) en gemengde bindweefsel siekte:
Daar mag 'n verhoogde risiko van aseptiese meningitis wees in pasiënte met SLE en gemengde bindweefsel siekte. (sien afdeling 4.8)
Kardiovaskulêre en serebrovaskulêre effekte:
Omsigtigheid is nodig by pasiënte met 'n geskiedenis van hipertensie en/of hartversaking, aangesien vloeistofretensie en edeem in verband met BIO DICLOFENAC INJECTION-terapie gerapporteer is.
Aangesien Bio DICLOFENAC INSPUITING inherente potensiaal het om vogretensie te veroorsaak, mag hartversaking voorkom in gekompromitteerde pasiënte.
Toepaslike monitering en advies is nodig vir hierdie pasiënte.
Omsigtigheid is nodig by pasiënte met beduidende risikofaktore vir kardiovaskulêre gebeure (bv. onbeheerde hipertensie, hiperlipidemie, diabetes mellitus, rook, kongestiewe hartversaking, gevestigde iskemiese hartsiektes, perifere arteriële siekte en / of serebrovaskulêre siekte) en moet slegs behandel word met BIO DICLOFENAC INSPUITING na deeglike oorweging.
Die kardiovaskulêre risiko van BIO DICLOFENAC INSPUITING mag verhoog met dosis en tydperk van blootstelling, die korste moontlike tydperk en die laagste effektiewe daaglikse dosis moet gebruik word.
Die pasiënte se behoefte vir simptomatiese verligting en respons teenoor terapie moet perdiodiek herevalueer word.
Kliniese proefnemings en epidemiologiese data dui deurgaans op 'n verhoogde risiko vir arteriële trombotiese gebeure (byvoorbeeld miokardiale infarksie of beroerte) wat verband hou met die gebruik van BIO DICLOFENAC INSPUITING, veral met 'n hoë dosis (150 mg per dag) en tydens langtermynbehandeling.
Hematologiese effekte:
Tydens langdurige behandeling met BIO DICLOFENAC INSPUITING, soos met NSAID's, word monitering van bloedtelling aanbeveel.
BIO DICLOFENAC INSPUITING kan plaatjie aggregasie omkeerbaar onderdruk (sien afdeling 4.5). Pasiënte met versteurings van hemostase, bloeiende diastase of hematologiese abnormaliteite moet versigtig gemonitor word.
Bestaande asma:
In pasiënte met asma, seisoenale allergiese rinitis, swelling van die nasale slymvlies (d.w.s neuspoliepe), kroniese obstruktiewe pulmonêre siekte of kroniese infeksies van die respiratoriese kanaal (veral as dit verbind word met allergiese rinitis-tipe simptome), is reaksies soos asma-verergerings teenoor NSAID's, (sogenaamde onverdraagsaamheid teenoor analgetika/ analgetiese asma) , Quincke se edeem of urtikaria, meer algemeen as in ander pasiënte. Daarom word spesiale voorsorg aanbeveel in hierdie pasiënte (gereedheid vir noodgeval). Dit is ook van toepassing op pasiënte wat allergies is vir ander middels, bv. met velreaksies, pruritis, urtikaria.
Soos ander medisyne wat prostaglandiensintese aktiwiteit beheer, kan BIO DICLOFENAC INSPUITING en ander NSAID's brongospasma vererger as dit toegedien word aan pasiënte wat daaraan ly, of met 'n vorige geskiedenis van brongiale asma.
Swangerskap:
Die toediening van nie-steroïdale anti-inflammatoriese middels (NSAID's) ongeveer 20 weke of later by swanger pasiënte kan ernstige nierprobleme by 'n ongebore baba veroorsaak. Dit kan lei tot lae vlakke van vrugwater, want die niere van die ongebore baba produseer dit tydens ongeveer 20 weke van swangerskap. Amniotiese vloeistof bied 'n beskermende kussing en help die longe, spysverteringstelsel en spiere van die ongebore baba om te ontwikkel (sien afdeling 4.3).
Medisyne wat prostaglandiensintese inhibeer, soos NSAID's, kan swangerskap en/of die ontwikkeling van die embrio of fetus nadelig beïnvloed. Daar word geglo dat die risiko toeneem met 'n verhoogde dosis en/of die duur van die behandeling.
Die aanbeveling is om die toediening van NSAID's in swanger vroue teen 20 weke of later te vermy. (sien afdeling 4.3)
Tensy spesifiek deur 'n gesondheidswerker aangeraai word om NSAID tussen 20 en 30 weke toe te dien, moet die dosis laag gehou word en die duur van die behandeling so kort as moontlik gehou word. Ultraklankmonitering van vrugwater word aanbeveel as die behandeling met NSAID's langer as 48 uur duur.
Gereelde gebruik van BIO DICLOFENAC-inspuiting gedurende die derde trimester van die swangerskap kan lei tot voortydige sluiting van die ductus arteriosus in die baarmoeder en moontlik aanhoudende pulmonale hipertensie by die pasgeborene. Die aanvang van kraam kan vertraag word en die duur daarvan kan toeneem (sien afdeling 4.6).
BIO DICLOFENAC INSPUITING kan nierdisfunksie veroorsaak, wat kan lei tot nierversaking met oligohidroamniose, en in sommige gevalle neonatale nierinperking. Komplikasies van langdurige oligahidroamniose kan ledemaat-kontraksie en vertraagde long maturasie insluit.
Oligahidroamniose kan omgekeer word met behandeling. Staking van en moontlike verlenging van bloedingtyd as gevolg van die anti-stollingseffek wat mag voorkom, selfs teen lae dosisse van BIO DICLOFENAC INSPUITING.
Vroulike vrugbaarheid:
Indien BIO DICLOFENAC INSPUITING toegedien word aan vrouens wat poog om swanger raak, of gedurende die eerste en tweede trimester van swangerskap, moet die dosering so laag as en vir die kortste duur as moontlik gehou word.
Die gebruik van BIO DICLOFENAC INSPUITING kan vroulike vrugbaarheid benadeel, en word nie aanbeveel in vroue wat poog om swanger te raak nie. In vroue wat probleme ondervind om swanger te raak, of wat ondersoeke oor vrugbaarheid ondergaan, moet ontrekking van BIO DICLOFENAC INSPUITING oorweeg word. (sien afdeling 4.6)
BIO DICLOFENAC INSPUITING bevat propileenglikol, bensielalkohol en natriummetabisulfiet.
BIO DICLOFENAC INSPUITING bevat 600 mg propileenglikol per 3 ml ampule wat gelykstaande is aan 200 mg/ml.
BIO DICLOFENAC INSPUITING bevat 120 mg bensielalkohol per 3 ml wat gelykstaande is aan 40 mg/ml. Bensielalkohol kan allergiese reaksies veroorsaak. Vra u dokter of apteker vir raad indien u swanger is of borsvoed, of indien u aan lewer of niersiekte ly. Dit is omdat groot hoeveelhede bensielalkohol kan opbou in u liggaam en ernstige newe-effekte kan veroorsaak (genaamd 'metaboliese asidose')
Die natriummetabisulfiet teenwoordig in die oplossing vir inspuiting veroorsaak selde ernstige hipersensitiwiteitsreaksies en brongospasma.
BIO DICLOFENAC INSPUITING bevat minder as 1 mmol natrium (23 mg) per 3 ml ampule, dit is so te sê in wese 'natriumvry'.

4.5 Interaksies met ander medisyne en ander vorms van interaksie
Metotreksaat: Gesamentlike toediening van metotreksaat met BIO DICLOFENAC INSPUITING kan lei tot verhoogde metotreksaat toksisiteit as gevolg van die nierbuisuitskeiding onderdrukking van metotreksaat. (sien afdeling 4.4)
Omsigtigheid word aanbeveel wanneer NSAID's, insluitend BIO DICLOFENAC INSPUITING, toegedien word minder as 24 uur voor behandeling met metotreksaat, aangesien bloedkonsentrasies van metotreksaat kan verhoog en die toksisiteit van die stof kan verhoog.
Gevalle van ernstige toksisiteit is al aangemeld wanneer metotreksaat en NSAID's, insluited BIO DICLOFENAC INSPUITING, gegee is binne 24 uur na mekaar.
Hierdie interaksie word bemiddel deur ophoping van metotreksaat as gevolg van inkorting van die nieruitskeiding in die teenwoordigheid van die NSAID.
Litium of digoksien: BIO DICLOFENAC INSPUITING kan plasmakonsentrasies van litium of digoksien verhoog indien saam geneem word. Monitering van serum litium of digoksien word aanbeveel.
Glukokortikoïede en ander NSAID's insluitend siklo-oksigenase-2 onderdrukkers: Gastrointestinale newe-effekte kan vererger word deur die gesamentlike toediening van BIO DICLOFENAC INSPUITING, verhoogde risiko van gastrointestinale ulserasie of bloeding. Gesamentlike behandeling met twee of meer NSAID's verhoog ook die risiko van newe-effekte.
Anti-diabetiese medisyne: BIO DICLOFENAC INSPUITING kan hipo- of hiperglukemie veroorsaak. Die dosis van antidiabetiese medisyne moet moontlik gewysig word en die monitering van die bloedglukosevlak word aanbeveel.
Anti-stollingsmiddels: Daar is 'n verhoogde risiko vir bloeding as BIO DICLOFENAC INSPUITING gelyktydig met enige antistolmiddels gebruik word, bv. warfarin. Noukeurige monitering is nodig.
BIO DICLOFENAC-INSPUITING kan die effekte van antistolmiddels soos warfarien verhoog.
Soos met ander nie-steroïdale anti-inflammatoriese middels, kan BIO DICLOFENAC INSPUITING in 'n hoë dosis plaatjie-aggregasie omkeerbaar inhibeer.
Siklosporien: Nefrotoksisiteit van siklosporien kan verhoog word deur die uitwerking van BIO DICLOFENAC INSPUITING op nierprostaglandiene.
Daarom moet dit toegedien word in dosisse laer as dié wat gebruik sal word by pasiënte wat nie siklosporien ontvang nie.
Kinolone-antibiotika: Daar is geïsoleerde aanmelding van stuiptrekkings wanneer BIO DICLOFENAC INSPUITING gelyktydig met kinoloonantibiotika en NSAID's toegedien word. Dit kan voorkom by pasiënte met of sonder 'n vorige geskiedenis van epilepsie of stuiptrekkings. Daarom moet daar omsigtigheid wees wanneer die gebruik van 'n kinoloon oorweeg word by pasiënte wat reeds 'n NSAID ontvang.
Anti-plaatjie medisyne en selektiewe serotonien heropname remmers (SSRI's): Verhoogde risiko van gastrointestinale bloeding.
Diuretika en antihipertensiewe medisyne: Soos ander NSAID's, kan gelyktydige gebruik van BIO DICLOFENAC INSPUITING met diuretika en antihipertensiewe middels (bv. beta-blokkers, angiotensienomskakelende ensiem- (ACE) –remmers) 'n afname in hul antihipertensiewe effek veroorsaak deur die inhibisie van vasodilator prostaglandien sintese.
Daarom moet die kombinasie met versigtigheid toegedien word, en pasiënte, veral bejaardes, moet hul bloeddruk gereeld monitor. Pasiënte moet voldoende gehidreer word en daar moet gereeld oorweeg word om die nierfunksie te monitor na die aanvang van die gepaardgaande behandeling, veral vir diuretika en ACE-remmers weens die verhoogde risiko vir nefrotoksisiteit.
Medisyne wat bekend is dat dit hiperkalemie veroorsaak:
Gelyktydige behandeling met kaliumsparende diuretika, siklosporien, takrolimus of trimetoprim kan geassosieer word met verhoogde serumkaliumvlakke, wat dus gemonitor moet word.
Takrolimus: Moontlike verhoogde risiko vir nefrotoksisiteit wanneer NSAID's saam met takrolimus toegedien word. Dit kan bemiddel word deur nier-anti-prostaglandien-effekte van beide NSAID en kalsineurienremmer.
Fenitoïen: Wanneer fenitoïen gelyktydig met BIO DICLOFENAC-INSPUITING gebruik word, word monitering van plasmakonsentrasies van fenitoïen aanbeveel as gevolg van 'n verwagte toename in blootstelling aan fenitoïen.
Kolestipol en cholestiramien: Hierdie middels kan 'n vertraging of afname in die opname van BIO DICLOFENAC-INSPUITING veroorsaak. Daarom word aanbeveel om BIO DICLOFENAC INSPUITING toe te dien, minstens een uur voor of 4 tot 6 uur na toediening van kolestipol/ cholestiramien.
Hartglikosiede: Die gebruik van hartglikosiede en NSAID's by pasiënte kan hartversaking vererger, die GFR verminder en die plasmaglikosiedvlakke verhoog.
Mifepristoon: NSAID's moet nie 8 - 12 dae na toediening van mifepristoon gebruik word nie, aangesien NSAID's die effek van mifepristoon kan verminder.
Kragtige CYP2C9 –remmers: Versigtigheid word aanbeveel wanneer BIO DICLOFENAC INSPUITING saam met kragtige CPY2C9-remmers (soos vorikonasool) voorgeskryf word, wat kan lei tot 'n beduidende toename in piekplasmakonsentrasies en blootstelling aan BIO DICLOFENAC INSPUITING as gevolg van inhibisie van die metabolisme van BIO DICLOFENAC INSPUITING.

4.6 Fertiliteit, swangerskap en laktasie
Swangerskap
Veiligheid en effektiwiteit tydens swangerskap en laktasie is nog nie vasgestel nie.
Die gereelde gebruik van nie-steroïedale anti-inflammatoriese medisyne, soos BIO DICLOFENAC INSPUITING, gedurende die derde trimester van swangerskap, kan lei na die volgende (Sien afdeling 4.4).
Die fetus:
- Kardiopulmonale toksisiteit (met premature sluiting van die ductus arteriosus en pulmonale hipertensie)
- Nierdisfunksie, wat kan vorder tot nierversaking met oligohidramniose.

Die moeder en die neonaat (aan die einde van swangerskap):
- Moontlike verlenging van bloedingstyd, 'n 'n anti-stollings effek wat selfs by baie lae dosisse kan voorkom
- Onderdrukking van baarmoeder kontraksies wat lei tot vertraging of verlenging van kraam.

Borsvoeding
Soos met ander NSAID's, versprei BIO DICLOFENAC INSPUITING na borsmelk in klein hoeveelhede. Daarom, moet BIO DICLOFENAC INSPUITING nie toegedien word tydens laktasie nie, om ongewenste newe-effekte op die baba te vermy.
Fertiliteit
Soos met ander NSAID's, kan die gebruik van BIO DICLOFENAC INSPUITING vroulike vrugbaarheid benadeel, en is daarom nie aanbeveel in vroue wat poog om swanger te raak nie. In vroue wat probleme ondervind om swanger te raak, of wat ondersoek instel na onvrugbaarheid, moet die onttrekking van BIO DICLOFENAC INSPUITING oorweeg word.(sien afdeling 4.4)

4.7 Effek op vermoë om te bestuur en masjinerie te gebruik
Pasiënte wat duiseligheid, visuele versteurings, vertigo, slaperigheid, lomerigheid of moegheid, of ander sentrale senuweesisteem afwykings ondervind, terwyl BIO DICLOFENAC INSPUITING toegedien word, moet hul daarvan weerhou om 'n voertuig of masjinerie te bestuur.

4.8 Ongewenste effekte
Infeksies en besmettings
Voorkoms onbekend: Nekrose op die inspuitplek
Bloed en limfstelsel siekte
Minder algemeen: Leukopenie, trombositopenie, aplastiese anemie, hemolitiese anemie, agranulositose.
Immuunsisteem versteurings
Minder algemeen: Hipersensitiwiteit, anafilaktiese en anafilaktoïede reaksies (insluitend hipotensie en skok), angioneurotiese edeem (insluitend gesig edeem).
Hart versteurings
Minder algemeen: Hartkloppings, borspyn, hartversaking, edeem, miokardiale infarksie.
Voorkoms onbekend: Kounis-sindroom.
Psigiatriese versteurings
*Minder algemeen:*bDisoriëntasie, depressie, slapeloosheid, nagmerries, prikkelbaarheid, psigotiese versteuring.
Senuweesisteem versteurings
Algemeen: Hoofpyn, duiseligheid en senuagtigheid.
Minder algemeen: Moegheid, sensasieversteurings (insluitend parestesie), geheueversteuring, stuiptrekkings, angs, bewing, psigotiese reaksies, aseptiese meningitis, serebrovaskulêre ongeluk, smaakversteuring.
Voorkoms onbekend: Verwarring, hallusinasies, malaise, sensasieversteurings.
Gastrointestinale versteurings
Die mees algemene newe-effekte is gastro-intestinaal van aard. Maagsere, perforasie of gastro-intestinale bloeding, soms dodelik. Naarheid, braking, diarree, winderigheid, hardlywigheid, dispepsie, buikpyn, melena, haematemese, ulseratiewe stomatitis, verergering van kolitis en Crohn se siekte, gastritis, anoreksie.
Algemeen: Epigastriese pyn, naarheid, braking, diarree, abdominale krampe, dispepsie, winderigheid, erektasie, anoreksie, plaaslike irritasie
Minder algemeen: Gastrointestinale bloeding, haematemese, melena, bloederige diarree, peptiese ulkus met of sonder bloeding of perforasie, afwykings in die laer ingewande soos nie-spesifieke hemorragiese kolitis, verergering van ulseratiewe kolitis of Chron's proktokolitis, glossitis, apteuse stomatitis, oesofageale letsels, diafragma-agtige intestinale vernouings, konstipasie, pankreatitis, verandering in smaak, gastritis.
Vaskulêre versteurings
Minder algemeen: Hipertensie, hipotensie, vaskulitis.
Nier en urinêre versteurings
Minder algemeen: Akute nierversaking, urinêre abnormaliteite soos hematurie, proteïenurie, interstisiële nefritis, nefritiese sindroom, nierpapillêre nekrose.
Lewer en gal versteurings
Algemeen: Verhoogde transaminase vlakke (ALT, AST).
Minder algemeen: Hepatitis met of sonder geelsug, fulminante hepatitis, geelsug, lewerafwyking, lewernekrose, lewerversaking.
Oog versteurings
Minder algemeen: Visie versteurings (diplopia, versteurde sig)
Voorkoms onbekend: Optiese neuritis
Oor- en labirint versteurings
Algemeen: Vertigo.
Minder algemeen: Gestremde gehoor, tinnitis
Vel en subkutane-weefsel versteurings
Algemeen: Uitslag en vel reaksies
Minder algemeen: Urtikaria, uitbreek van blase, ekseem, erythema multiforme, Stevens-Johnson sindroom en toksiese epidermale nekrolise (Lyell sindroom), erythroderma (afskilferende dermatitis), haarverlies, fotosensitiwiteit reaksie, purpura, insluited allergiese purpura, pruritis. Absesse en locale nekrose het al voorgekom, veral in diabete.
Asemhalings-, torakale en mediastinum-afwykings
Minder akgemeen: Asma (insluited dispnee), longontsteking
Algemene afwykings en toedieningsplek toestande
Algemeen: Inspuitplek reaksie, pyn op inspuitplek, verharding van die inspuitplek.
Voortplantingstelsel en borsversteurings
Minder algemeen: Impotensie.
Aanmelding van vermeende newe-effekte
Aanmelding van vermeende newe-effekte na goedkeuring van die medisyne is belangrik. Dit maak aanhoudende monitering van die voor-en-nadeel risiko balans van die medisyne moontlik. Gesondheidsorgwerkers word gevra om enige vermeende ongewenste reaksies aan te meld by SAHPRA via die *"6.04 Adverse Drug Reactions Reporting Form"*, wat aanlyn gevind kan word onder SAHPRA publikasies: https://www.sahpra.org.za/Publications/Index/8

4.9 Oordosering
(Sien afdeling 4.8)
Simptome sluit in: hoofpyn, naarheid, braking, epigastriese pyn, gastrointestinale bloeding, diarree, duiseligheid, disoriëntasie, eksitasie, koma, slaperigheid, tinnitis, floute of konvulsies. In geval van beduidende vergiftiging, is akute nierversaking en lewerskade moontlik.
Behandeling is simptomaties en ondersteunend, veral vir hipotensie, nierversaking, konvulsies, gastrointestinale irritasie en asemhalingsonderdrukking.
Spesifieke behandeling soos gedwonge diurese, dialise of hemoperfusie is van weinig waarde om BIO DICLOFENAC-INSPUITING uit te skakel, vanweë die hoë proteïenbinding en uitgebreide metabolisme.

5. FARMAKOLOGIESE EIENSKAPPE
A.3.1 Anti-reumatika (anti-inflammatoriese middels)
Anti-inflammatoriese en anti-reumatiese produkte, Nie-steroïedale anti-inflammatoriese middels (NSAID) (NSAIDs). ATC code: M01AB05

5.1 Farmakodinamiese eienskappe
Diklofenak is 'n nie-steroïdale anti-inflammatoriese verbinding (NSAID) met pynstillende, koorswerende en anti-inflammatoriese aktiwiteite.
Dit veroorsaak verminderde vorming van prostaglandiene en tromboksane deur inhibisie van die aktiwiteit van die ensiem siklo-oksigenase. Diklofenak inhibeer plaatjie-aggregasie in vitro.

5.2 Farmakokinetiese Eienskappe
Piek plasmakonsentrasie word bereik ongeveer 10 tot 22 minute na binnespierse toediening.
Diklofenak het hoë binding aan plasmaproteïene (99%) en die plasmahalfleeftyd is 1 tot 2 uur.
Diklofenak word uitgeskei in die vorm van metaboliete deur die niere (ongeveer 60%) en deur ontlasting (ongeveer 30%). Minder as 1% word uitgeskei in onveranderde vorm.

6. FARMASEUTIESE BESONDERHEDE
6,1 Lys van hulpstowwe:
Bensielalkohol 4% m/v (as preserveermiddel)
Mannitol
Propileenglukol
Natriumhidroksied (pH aanpassing)
Natrium metabisulfiet 0,3% m/v (as anti-oksidant)

6.2 Teenaanduiding
Die ampules gebruik as im of iv as infusie moet nie met ander inspuitbare oplossings gemeng word nie.
Vir voorbereiding van binneaarse infusie, sien afdeling 6.6

6.3 Rakleeftyd
2 jaar

6.4 Spesiale voorsorg met bewaring
Bewaar teen of benede 25°C
Moet nie die ampules uit die kartonhouer haal voor benodig word vir gebruik nie

6.5 Aard en inhoud van die houer
10 x 3 ml helder kleurlose glas, gemerkte ampules in 'n kartonhouer

6.6 Spesiale voorsorgmaatreëls vir wegdoening en ander hantering
Intraveneuse infusies moet vars opgemaak word en onmiddellik gebruik word. Sodra dit voorberei is, moet die infusie nie gestoor word nie.

Intraveneuse Infusie
Om 'n intraveneuse infusie voor te berei, moet een ampule BIO DICLOFENAC INSPUITING verdun word met 100 tot 500 ml natriumchloried (0,9%) of glukose-oplossing (5%). Albei oplossings moet eers met bikarbonaatoplossing gebuffer word (0,5 ml 8,4% of 1 ml 4,2%). Slegs helder infusie-oplossings moet gebruik word. BIO DICLOFENAC-inspuitings moet vars opgemaak en onmiddellik gebruik word. Sodra dit voorberei is, moet die infusie nie gestoor word nie. As kristalle of neerslae waargeneem word, moet die infusie-oplossing nie gebruik word nie.

7. HOUER VAN DIE REGISTRASIE SERTIFIKAAT
Biotech Laboratories (Edms) Bpk.
Grond Vloer, Blok K Wes, Central Park
400 16de Weg, Randjespark, Midrand, 1685
Suid Afrika

8. REGISTRATION NOMMER(S)
42/3.1/0411

9. DATUM VAN DIE EERSTE REGISTRATION/HERNUWING VAN DIE REGISTRASIE
Datum van registrasie: 19 Maart 2010

10. DATUM VAN HERSIENING VAN DIE TEKS
12 April 2021