SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

FLENODIC IM, 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 antioxidant.

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

FLENODIC IM, 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 FLENODIC IM 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

FLENODIC IM should not be mixed with other injection solutions.

FLENODIC IM 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 FLENODIC IM intramuscularly with an oral dose of diclofenac up to a maximum daily dosage of 150 mg.

Intravenous Infusion

FLENODIC IM 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 FLENODIC IM 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 FLENODIC IM 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.

Special populations

Elderly:

The elderly have an increased frequency of adverse reactions to NSAIDs including FLENODIC IM. A reduction in dosage may be required in the elderly, especially the very frail or those with a low body mass (see section 4.4).

Paediatric population

FLENODIC IM is not recommended for use in children (see section 4.3).

Method of administration

Intramuscular injection or intravenous infusion.

4.3 Contraindications

NB. The intravenous use of FLENODIC IM is absolutely contraindicated in patients with impaired renal function and/or any form of shock.

- Hypersensitivity to diclofenac or to any of the excipients of FLENODIC IM, especially sodium metabisulphite, listed in section 6.1.

- 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 FLENODIC IM.
- 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 FLENODIC IM 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 FLENODIC IM, 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 FLENODIC IM and methotrexate could result in serious interactions (see section 4.5).

The concomitant use of FLENODIC IM 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).

FLENODIC IM 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 FLENODIC IM, 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 (see section 4.2).

The risk of gastrointestinal perforation, ulceration or bleeding (PUBs) is higher with increasing doses of FLENODIC IM, 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 FLENODIC IM, treatment with FLENODIC IM should be stopped.

FLENODIC IM 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).

Serious skin reactions:

Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN)

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. FLENODIC IM 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. FLENODIC IM should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as FLENODIC IM. 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. Eosinophilia 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 FLENODIC IM and evaluate the patient immediately.

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).

Hepatic effects:

Close medical surveillance is required when prescribing FLENODIC IM to patients with impairment of hepatic function as their condition may be exacerbated.

As with other NSAIDs, including FLENODIC IM, values of one or more liver enzymes may increase. During prolonged treatment with FLENODIC IM, 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 FLENODIC IM.

Hepatitis may occur with FLENODIC IM without prodromal symptoms.

Renal effects:

As fluid retention and oedema have been reported in association with NSAIDs therapy, including FLENODIC IM, 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 medicines 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 FLENODIC IM in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.

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 FLENODIC IM therapy. In view of the FLENODIC IM'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 FLENODIC IM after careful consideration.

The cardiovascular risks of FLENODIC IM 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 FLENODIC IM, particularly at high dose (150 mg daily) and in long term treatment.

Haematological effects:

During prolonged treatment with FLENODIC IM, as with other NSAIDs, monitoring of the blood count is recommended.

FLENODIC IM 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, FLENODIC IM 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 FLENODIC IM 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).
FLENODIC IM 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 FLENODIC IM.

FLENODIC IM contains propylene glycol, benzyl alcohol and sodium metabisulphite.

FLENODIC IM contains 600 mg propylene glycol per 3 ml ampoule which is equivalent to 200 mg/ml.

FLENODIC IM 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.

FLENODIC IM 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 FLENODIC IM 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 FLENODIC IM, 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 FLENODIC IM 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: FLENODIC IM 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 FLENODIC IM; increased risk of gastrointestinal ulceration or bleeding. Concurrent treatment with two or more NSAIDs may increase the risk of adverse effects.

Antidiabetic medicines: FLENODIC IM 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 FLENODIC IM is used concurrently with any anticoagulants, e.g. warfarin. Careful monitoring is necessary. FLENODIC IM may enhance the effects of anticoagulants such as warfarin.

As with other non-steroidal anti-inflammatory agents, FLENODIC IM in a high dose can reversibly inhibit platelet aggregation.

Ciclosporin: Nephrotoxicity of ciclosporin may be increased by the effects of FLENODIC IM 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 FLENODIC IM 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 FLENODIC IM with diuretics and antihypertensive medicines (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 FLENODIC IM, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Colestipol and cholestyramine: These medicines can induce a delay or decrease in absorption of FLENODIC IM. Therefore, it is recommended to administer FLENODIC IM 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 FLENODIC IM with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak

plasma concentrations and exposure to FLENODIC IM due to inhibition of FLENODIC IM metabolism.

4.6 Fertility, pregnancy and lactation

Pregnancy

FLENODIC IM is contraindicated during pregnancy (see section 4.3).

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors such as FLENODIC IM 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 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

FLENODIC IM passes into breast milk in small amounts. FLENODIC IM is contraindicated in lactation (see section 4.3).

Fertility

The use of FLENODIC IM 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 FLENODIC IM should be considered.

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 FLENODIC IM 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.
Frequency unknown	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4)
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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

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.

Prolonged use at higher than recommended doses may result in severe hypokalaemia and renal tubular acidosis. Symptoms may include reduced level of consciousness and generalised weakness (see section 4.4 and section 4.8).

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 FLENODIC IM 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

Mechanism of action

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

Absorption

Peak plasma concentrations are reached about 10 to 22 minutes after intramuscular administration.

Distribution

Diclofenac is extensively bound to plasma proteins (99 %).

Biotransformation and elimination

Diclofenac 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 antioxidant)

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

30 months

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

5 x 3 ml clear colourless glass, labelled ampoules in a carton box.

10 x 3 ml clear colourless glass, labelled ampoules in a carton box.

100 x 3 ml clear colourless glass, labelled ampoules in a carton box.

All pack sizes may not necessarily be marketed at one time.

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 FLENODIC IM 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. FLENODIC IM 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

Tel: +27 (0) 11 848 3050

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

06 November 2025