1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

PANAMOR-25 film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet of PANAMOR-25 (which is also enteric coated) contains 25 mg diclofenac sodium.

Contains sugar: Lactose monohydrate 85,00 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

PANAMOR-25: yellowish-mustard, film-coated, shallow biconvex tablets, which are also enteric-coated.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

PANAMOR-25 is indicated for the treatment of fever or mild to moderate pain of inflammatory origin (see section 4.2).

4.2. Posology and method of administration

Posology

Use the lowest effective dose for the shortest possible duration of treatment.

Adults

Take one PANAMOR-25 tablet three times a day, for a maximum treatment period of 5 days.

Do not take more than 75 mg (three PANAMOR-25 tablets) in a day (three PANAMOR-25 tablets in divided doses).

Paediatric population

The safety and efficacy of PANAMOR-25 in children under the age of two years has not yet been established (see section 4.3).

Method of administration

For oral administration.

The tablets should be swallowed whole with a glass of water.

4.3. Contraindications

PANAMOR-25 is contraindicated in:

- Patients with hypersensitivity to diclofenac sodium or to any excipients in PANAMOR-25 (see section 6.1).
- Patients with porphyria.
- Children under the age of two years.
- Patients with a history of active gastrointestinal bleeding, ulceration or perforation

(PUBs) related to previous NSAIDs (see section 4.4).

- Patients with an active or history of recurrent ulcer/haemorrhage/perforations (see section 4.4).
- Patients with hepatic or renal failure.
- Aspirin hypersensitive patients, patients sensitive to any other non-steroidal anti-inflammatory agent.
- In asthmatic patients in whom attacks of asthma, urticaria, or acute rhinitis are precipitated by acetylsalicylic acid or by other NSAIDs.
- Patients with heart failure; established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.
- Lactation (see section 4.6).
- Pregnant women from around 20 weeks of gestation or later in pregnancy (see section 4.4 and 4.6).

4.4. Special warnings and precautions for use

General

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2).

As with other NSAIDs including diclofenac, as in PANAMOR-25, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the medicine (see section 4.8).

Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction. Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to PANAMOR-25.

Because of the possibility of cross-sensitivity due to structural relationships which exist

among non-steroidal anti-inflammatory medicines, such as PANAMOR-25, acute allergic reactions may be more likely to occur in patients who have exhibited allergic reactions to these compounds.

Diclofenac, as in PANAMOR-25, may mask the signs and symptoms of infection due to its pharmacodynamic properties.

The concomitant use of PANAMOR-25, 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 undesirable effects (see section 4.5).

Serious interactions have been reported after the use of high dose methotrexate with diclofenac, as in PANAMOR-25 (see section 4.5).

Cardiovascular and cerebrovascular effects

Appropriate monitoring, advice and 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 diclofenac, as in PANAMOR-25 therapy.

In view of PANAMOR-25's inherent potential to cause fluid retention, heart failure may be precipitated in some compromised patients.

Caution is required in patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) and should only be treated with diclofenac after careful consideration.

As the cardiovascular risks of PANAMOR-25 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 diclofenac, as in PANAMOR-25, particularly at a high dose and in long term treatment. Patients should remain alert for the signs and symptoms of serious arteriothrombotic events (e.g. chest pain, shortness of breath, weakness, slurring of speech), which can occur without warnings. Patients should be instructed to see a medical practitioner immediately in case of such an event.

PANAMOR-25 should be given with care to patients with cardiovascular disease, bleeding disorders, and in patients with impaired hepatic or renal function.

Elderly

PANAMOR-25 should be used with care as the elderly has an increased frequency of adverse reactions to NSAIDs, including PANAMOR-25, especially gastrointestinal bleeding and perforation (PUBs) which may be fatal.

Caution is indicated in the elderly on basic medical grounds. In particular, it is recommended that the lowest effective dose be used in frail elderly patients or those with a low body weight.

Gastrointestinal effects

Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation, which can be fatal has been reported with NSAIDs including diclofenac, as in PANAMOR-25, and may occur at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal (GI) events. They generally have more serious consequences in the elderly.

Close medical surveillance is imperative and particular caution should be exercised when prescribing PANAMOR-25 in patients with symptoms indicative of gastrointestinal

disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation (see section 4.8).

The risk of gastrointestinal bleeding, ulceration or perforation (PUBs) is higher with increasing doses of PANAMOR-25, in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation and the elderly (see section 4.3).

When gastrointestinal bleeding or ulceration occurs in patients receiving PANAMOR-25, treatment with PANAMOR-25 should be stopped.

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 (aspirin), or other medicines likely to increase gastrointestinal risk (see section 4.5).

Patients with a history of GI toxicity, particularly the elderly, should report any unusual abdominal symptoms (especially GI bleeding).

Caution is recommended in patients receiving concomitant medicines which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors (SSRIs) or anti-platelet medicines such as acetylsalicylic acid (see section 4.5).

PANAMOR-25 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.

PANAMOR-25, may be associated with increased risk of gastrointestinal anastomotic leak. Close medical surveillance and caution are recommended when using PANAMOR-25 after gastrointestinal surgery.

Hepatic impairment

Close medical surveillance is required when prescribing PANAMOR-25 to patients with impairment of hepatic function, as their condition may be exacerbated.

As with diclofenac, as in PANAMOR-25, values of one or more liver enzymes may increase. During prolonged treatment with PANAMOR-25, regular monitoring of hepatic function is indicated as a precautionary measure.

If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease develop, or if other manifestations occur (eosinophilia, rash), PANAMOR-25 should be discontinued.

Hepatitis may occur with PANAMOR-25 without prodromal symptoms.

Renal impairment

As fluid retention and oedema have been reported in association with NSAID therapy, including diclofenac as in PANAMOR-25, 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 in 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 PANAMOR-25 in such cases. Discontinuation of therapy is usually followed by recovery to the pre-treatment state.

Skin effects

Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have been reported. Patients appear to be at highest risk for 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. PANAMOR-25 should be discontinued at the first appearance of skin rash, mucosal

lesions, or any other sign of hypersensitivity (see section 4.8).

Drug reaction with eosinophillia and systemic symptoms

Drug reaction with eosinophillia and systemic symptoms (DRESS) has been reported in patients taking NSAIDs such as PANAMOR-25. 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 PANAMOR-25 and evaluate the patient immediately.

SLE and mixed connective tissue disease

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

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 to PANAMOR-25 such as 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 medicines, e.g. with skin reactions, pruritus or urticaria.

Diclofenac sodium, as in PANAMOR-25, can precipitate bronchospasm if administered to

patients suffering from, or with a previous history of bronchial asthma.

Therefore, PANAMOR-25, should be used with caution in patients with asthma or bronchoconstriction.

Haematological effects

It is advisable to perform and monitor blood counts in patients undergoing prolonged treatment.

Diclofenac, as in PANAMOR-25, may reversibly inhibit platelet aggregation and decreased platelet aggregation with increased bleeding time may occur (see section 4.5). Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Use in pregnancy

It is recommended that PANAMOR-25 is avoided in pregnant women at 20 weeks or later in pregnancy (see section 4.3 and 4.6).

The use of NSAIDs, such as diclofenac, as in PANAMOR-25, around 20 weeks gestation or later in pregnancy may cause foetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may include limb contractures and delayed lung maturation. In some post marketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

Healthcare professionals should consider ultrasound monitoring of amniotic fluid if PANAMOR-25 treatment extends beyond 48 hours. Discontinue PANAMOR-25 if oligohydramnios occurs and follow up according to clinical practice.

Female fertility

The use of PANAMOR-25 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 PANAMOR-25 should be considered (see section 4.6).

Paediatric population

The safety and efficacy of PANAMOR-25 in children under the age of two years has not yet been established (see section 4.3).

Excipients

PANAMOR-25 contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, total lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take PANAMOR-25.

4.5. Interaction with other medicines and other forms of interaction

Diuretics and anti-hypertensive medicines

Concomitant use of PANAMOR-25 with diuretics or antihypertensive medicines (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory 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 and periodically thereafter, particularly for diuretics

and ACE inhibitors due to the increased risk of nephrotoxicity.

Medicines known to cause hyperkalemia

Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently (see section 4.4).

Other NSAIDs including cyclo-oxygenase-2 selective inhibitors

Co-administration of PANAMOR-25 and other systemic NSAIDs may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs as concurrent use of two or more NSAIDs could result in an increase in side effects (see section 4.4).

Corticosteroids

Increased risk of gastrointestinal perforation, ulceration or bleeding (PUBs). Concomitant administration of glucocorticoids or other non-steroidal anti-inflammatory medicines may aggravate gastrointestinal side effects.

Anti-coagulants and anti-platelet medicines

PANAMOR-25 may enhance the effects of anti-coagulants such as warfarin, therefore PANAMOR-25 should be given with care to patients who are receiving coumarin anticoagulants.

Caution is recommended since concomitant administration could increase the risk of bleeding and gastrointestinal bleeding (see section 4.4). Although clinical investigations do not appear to indicate that diclofenac, as in PANAMOR-25, affects the action of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving diclofenac, as in PANAMOR-25, and anticoagulants concomitantly (see section 4.4). Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. PANAMOR-25 in high dose can reversibly inhibit platelet aggregation.

Selective serotonin reuptake inhibitors (SSRIs)

Concomitant administration of SSRIs may increase the risk of gastrointestinal bleeding (see section 4.4).

Aspirin

Plasma concentrations are significantly decreased by the concomitant administration of therapeutic doses of aspirin.

The bioavailability of PANAMOR-25 is reduced by acetylsalicylic acid, and that of acetylsalicylic acid by PANAMOR-25, when the two medicines are administered together.

Lithium

If used concomitantly, PANAMOR-25 may raise plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.

Digoxin

If used concomitantly, PANAMOR-25 may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended.

Probenecid

PANAMOR-25 may increase the half-life of probenecid.

Antidiabetics

Clinical studies have shown that diclofenac, as in PANAMOR-25, can be given together with oral antidiabetic medicines without influencing their clinical effect. However, there have been reports of hypoglycaemic and hyperglycaemic effects necessitating changes in the dosage of the antidiabetic medicines during treatment with diclofenac, as in PANAMOR-25. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

Methotrexate

Diclofenac, as in PANAMOR-25 can inhibit the tubular renal clearance of methotrexate hereby increasing methotrexate levels. Caution is recommended when PANAMOR-25 is

administered less than 24 hours before or after treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this medicine may be increased.

Cases of serious toxicity have been reported when methotrexate and NSAIDs including diclofenac, as in PANAMOR-25, are 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.

Ciclosporin

PANAMOR-25 may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, PANAMOR-25 should be given at doses lower than those that would be used in patients not receiving ciclosporin.

Tacrolimus

Possible increased risk of nephrotoxicity when NSAIDs, such as diclofenac as in PANAMOR-25, are given with tacrolimus. This might be mediated through renal antiprostaglandin effects of both NSAID and calcineurin inhibitor.

Quinolone antimicrobials

Convulsions may occur due to an interaction between quinolones and NSAIDs, such as diclofenac as in PANAMOR-25. 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 PANAMOR-25.

Phenytoin

When using phenytoin concomitantly with PANAMOR-25, 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 diclofenac, as in PANAMOR-25. Therefore, it is recommended to administer PANAMOR-25 at least one

hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.

Cardiac glycosides

Concomitant use of cardiac glycosides and NSAIDs, such as diclofenac as in PANAMOR-25, in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Mifepristone

NSAIDs, including diclofenac as in PANAMOR-25, should not be used for 8 to 12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Potent CYP2C9 inhibitors

Caution is recommended when co-prescribing diclofenac, as in PANAMOR-25, with potent CYP2C9 inhibitors (such as sulfinpyrazone and voriconazole), which could result in a significant increase in peak plasma concentration and exposure to diclofenac due to inhibition of diclofenac metabolism.

Other protein-bound medicines

Use with care together with other protein-bound medicines e.g. tolbutamide, coumarin and hydantoin.

4.6. Fertility, pregnancy and lactation

Pregnancy

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 %. The risk is believed to increase with dose and duration of therapy. 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, such as PANAMOR-25, may expose the foetus to:

- cardiopulmonary toxicity (with premature closure of the foetal ductus arteriosus *in utero*, and in persistent pulmonary hypertension of the newborn;
- renal dysfunction, which may progress to renal failure with oligo-hydramniosis (see section 4.4);

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 (see section 4.4).

It is recommended that PANAMOR-25 is avoided in pregnant women at 20 weeks or later in pregnancy (see section 4.3 and 4.4).

Breastfeeding

Diclofenac, as in PANAMOR-25, passes into the breastmilk in small amounts. Therefore, PANAMOR-25 should not be administered during breastfeeding in order to avoid undesirable effects in the infant (see section 4.3).

Fertility

PANAMOR-25 may impair female fertility and is not recommended in women attempting

to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of PANAMOR-25 should be considered (see section 4.4).

4.7. Effects on ability to drive and use machines

PANAMOR-25 has minor influence on the ability to drive or use machines.

Since adverse reactions such as drowsiness, dizziness, blurred vision and other ocular reactions have been reported in patients receiving PANAMOR-25, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that PANAMOR-25 does not adversely affect their ability to do so (see section 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

The most commonly observed adverse events are gastrointestinal in nature.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders		Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.	
Immune system disorders		Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock), angioneurotic oedema (including face oedema).	Sensitivity reactions.
Psychiatric disorders		Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.	Drowsiness, nervousness, agitation.
Nervous system disorders	Headache, dizziness	Somnolence, tiredness, paraesthesia, memory impairment, convulsion,	Confusion, hallucinations, malaise.

		anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, disturbances of sensation.	
Eye disorders		Blurred vision, visual disturbance, diplopia.	Optic neuritis, other ocular reactions.
Ear and labyrinth disorders	Vertigo.	Tinnitus, hearing impaired.	Minor hearing disorders.
Cardiac disorders		Myocardial infarction, cardiac failure, palpitations, chest pain.	Kounis syndrome.
Vascular disorders		Hypertension, hypotension, vasculitis.	
Respiratory, thoracic and mediastinal disorders		Asthma (including dyspnoea), pneumonitis.	
Gastrointestinal disorders	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.	Diarrhoea haemorrhagic, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly), colitis (including haemorrhagic colitis), stomatitis, glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis	Ischaemic colitis.
Hepatobiliary disorders	Transaminases increased.	Hepatitis, jaundice, liver disorder, fulminant hepatitis, hepatic necrosis, hepatic failure.	Abnormalities of liver function tests.
Skin and subcutaneous tissue disorders	Rash.	Urticaria, bullous reactions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.	Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) (see section 4.4).
Renal and urinary disorders		Acute renal failure, haematuria, proteinuria, nephrotic syndrome,	Impairment of renal function.

		interstitial nephritis, renal papillary necrosis.	
Reproductive system and breast disorders		Impotence.	
General disorders and administrative site conditions		Oedema.	

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: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.9. Overdose

Symptoms

There is no typical clinical picture resulting from PANAMOR-25 over dosage. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal haemorrhage, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the case of significant poisoning acute renal failure and liver damage are possible.

See section 4.4 and 4.8.

Treatment

Management of acute poisoning with PANAMOR-25 essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression.

Special measures such as forced diuresis, dialysis or haemo-perfusion are probably of no help in eliminating PANAMOR-25 due to the high protein binding and extensive metabolism.

Activated charcoal may be considered after ingestion of a potentially toxic overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 3.1 Anti-rheumatics (anti-inflammatory agents)

Pharmacotherapeutic group: Acetic acid derivatives and related substances

ATC code: M01AB05

Mechanism of action

Diclofenac sodium is a non-steroidal anti-inflammatory compound with analgesic, anti-inflammatory, antirheumatic and antipyretic properties.

In vitro its active substance strongly inhibits prostaglandin-synthetase and also has an inhibitory effect on platelet aggregation.

Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is regarded as having an important bearing on its mechanism of action. Prostaglandins play a major role in the causation of inflammation, pain and fever.

5.2. Pharmacokinetic properties

Absorption

Diclofenac is absorbed after passage through the stomach. Following ingestion of one tablet on an empty stomach, absorption occurs more rapidly than when the tablet is taken

during or after a meal, but bioavailability remains the same.

Distribution

Plasma concentrations show a linear relationship to the size of the dose. Peak levels are attained in 1 to 4 hours with the tablets.

Protein binding is 99,7 %.

Biotransformation

Diclofenac is subject to first-pass metabolism.

Diclofenac sodium is eliminated principally by metabolism and subsequent urinary and biliary excretion of glucuronide and sulphate conjugates of the metabolites. The principal metabolite in man is the 4-hydroxy derivative of diclofenac sodium.

Elimination

Approximately 60 % of the dose administered is excreted via the kidneys in the form of metabolites, and less than 1 % in unchanged form. About 30 % of the dose is excreted in metabolised form in the faeces.

The amount excreted in the urine accounts for 20 % to 30 % of the dose, and that in bile for 10 % to 20 %. The mean terminal elimination half-life is 1,2 to 1,8 hours.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Colloidal anhydrous silica, iron oxide yellow (C.I. 77492), lactose monohydrate, magnesium stearate, methacryclic acid copolymer, microcrystalline cellulose, simethicone, sodium lauryl sulfate, sodium starch glycolate, starch maize, talc (purified), titanium dioxide (C.I. 77891), triethyl citrate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

Protect from moisture.

Do not remove the blisters from the carton until required for use.

6.5. Nature and contents of container

15 tablets are packed in a clear polyvinyl chloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer carton of printed cardboard together with a leaflet.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

R/3.1/49

9. DATE OF FIRST AUTHORISATION

21 November 1985

10. DATE OF REVISION OF TEXT

29 November 2021

Die Afrikaanse Professionele Inligting is op versoek beskikbaar.

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Botswana: B9322605 S2

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