1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

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1. NAME OF THE MEDICINE

PANAMOR GEL 1,292 g/100 g (30 g pack size)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 g of PANAMOR GEL contains 1,292 g of diclofenac hydroxyethyl pyrrolidine.

Preservative: Isopropyl Alcohol 8,0 % *m/m*

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel

PANAMOR GEL is a white to ivory-white, milky uniform gel with a characteristic odour of isopropanol and perfume.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PANAMOR GEL is indicated for :

- The symptomatic relief of localised traumatic inflammation and pain.

4.2 Posology and method of administration

Posology

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

Adults

Depending on the size of the affected area, apply 2 g to 4 g PANAMOR GEL (1 to 2 fingertips) 3 to 4 times daily. The gel should then be rubbed in gently or massaged into the skin in case of muscular pain. After application, the hands should be washed, unless they are the site being treated.

Patients should consult their doctor if the condition does not improve or worsens within 7 days of starting treatment. The duration of treatment depends on the indication and the response obtained. It is recommended that treatment be reviewed after 2 weeks.

Paediatric population

There are insufficient data on efficacy and safety available for children and adolescents below 14 years of age. In children aged 14 years and over, if this product is required for more than 7 days for pain relief or if the symptoms worsen the patient/parents of the adolescent is/are advised to consult a doctor.

Method of administration

Topical application

4.3 Contradictions

PANAMOR GEL is contraindicated in:

- Patients with hypersensitivity to diclofenac, acetylsalicylic acid (aspirin) and other non-steroidal anti-inflammatory agents (NSAIDs) or to any of the excipients in PANAMOR GEL (see section 6.1).
- Concomitant use of oral NSAIDs (see section 4.5).
- Concomitant use with other medicines containing diclofenac (see section 4.5).

- Porphyria.
- Patients with heart failure, established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease,
- Patients with history of gastrointestinal perforation, ulceration, or bleeding (PUBs) related to previous NSAIDs, including PANAMOR GEL.
- Active or history of recurrent gastric ulcer/haemorrhage/perforations.
- Patients with or without chronic asthma in whom attacks of asthma, angioedema, urticaria or acute rhinitis are precipitated by aspirin or other NSAIDs.
- Pregnant and lactating women, as safety has not been established (see section 4.4 and 4.6).

4.4 Special warnings and precautions for use

Undesirable effects

Where PANAMOR GEL is applied to relatively large areas of skin and over a prolonged period, the systemic adverse effects may occur. If they persist or are troublesome, the preparation must be discontinued.

Hypersensitivity reactions

Despite the topical application of the medicine, hypersensitivity reactions of the skin and mucous membranes e.g. asthma, angioedema and urticaria cannot be ruled out in patients who are allergic to diclofenac or certain additives. Patients suffering from asthma (intrinsic) or chronic urticaria are particularly prone to reactions.

Hypertension, heart failure and or cardiovascular events

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 PANAMOR GEL therapy. In view of PANAMOR GEL'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.

Gastrointestinal perforations/ disease
Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs, including PANAMOR GEL, especially gastrointestinal perforation, ulceration, or bleeding (PUBs) which may be fatal.

The risk of gastrointestinal perforation, ulceration, or bleeding (PUBs) is higher with increasing doses of PANAMOR GEL, in patients with a history of ulcers, and the elderly.

When gastrointestinal bleeding or ulceration occurs in patients using PANAMOR GEL, treatment with PANAMOR GEL should be stopped.

PANAMOR GEL 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 these conditions may be exacerbated.

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 (see section 4.8). PANAMOR GEL should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

The risk of occurrence of these reactions is higher at the beginning of the treatment and in most cases these reactions are manifested during the first month of treatment. Concomitant use of oral NSAID's should be cautioned as the incidence of untoward effects, particularly systemic undesirable effects, may increase.

Monitoring

During prolonged treatment with PANAMOR GEL, blood counts and monitoring of hepatic and renal function are indicated as precautionary measures.

Use in pregnancy

PANAMOR GEL is contraindicated in pregnancy and lactation (see section 4.3 and 4.6).

Bronchial asthma

Like other medicines that inhibit prostaglandin synthetase activity, diclofenac as in PANAMOR GEL, and other NSAIDs can precipitate bronchospasm if administered to patients suffering from or with a previous history of, bronchial asthma.

Hypokalaemia

Risk of renal tubular acidosis and hypokalaemia are associated with NSAID usage.

General

PANAMOR GEL should be applied only to intact non-diseased skin surfaces, and not to skin wounds or open injuries. It should not be allowed to come into contact with the eyes or with mucous membranes.

PANAMOR GEL should not be taken by mouth.

Patients should be warned against excessive exposure to sunlight in order to reduce the incidence of photosensitivity.

PANAMOR GEL can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing. Occlusion can lead to an increase in the amount of, diclofenac, as in PANAMOR GEL ,absorbed and may thus cause an increase in undesirable effects.

Paediatric population

There are insufficient data on efficacy and safety available for the children and adolescents below 14 years of age.

Excipients

PANAMOR GEL contains propylene glycol which may cause skin irritation (see section 6.1).

4.5 Interaction with other medicines and other forms of interaction

Since systemic absorption of diclofenac from a topical application of PANAMOR GEL is very low, such interactions are very unlikely.

Diuretics, angiotensin converting enzyme inhibitors (ACE inhibitors) and Angiotensin II Antagonists (AAII):

NSAIDs, such as diclofenac, as in PANAMOR GEL, may decrease the effectiveness of diuretics and other antihypertensive medicines. In some patients with impaired renal function (e.g., dehydrated patients or elderly with impaired renal function) the co-administration of an ACEI or AAII and cyclooxygenase inhibitor medicines may result in the progression of renal function deterioration, including the possibility of acute renal insufficiency, which is usually reversible. The occurrence of these interactions should be considered in patients applying diclofenac, as in PANANMOR GEL, particularly if in large areas of the skin and for prolonged periods, in combination with ACEI or AAII. Consequently, diclofenac combination should be used with caution, especially in elderly patients. Patients should be properly hydrated and the need to monitor the renal function after the beginning of the concomitant therapy and periodically thereafter should be analysed.

Diuretics:

Various NSAIDs are liable to inhibit the activity of diuretics. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, hence serum potassium should be monitored.

Anti-hypertensives:

Concomitant use of NSAIDs with antihypertensive medicines (i.e. beta-blockers,

angiotensin converting enzyme (ACE) inhibitors, diuretics) may cause a decrease in their antihypertensive effect via inhibition of vasodilatory prostaglandin synthesis.

Interactions experienced with systemically absorbed diclofenac sodium

Lithium

When used concomitantly with lithium, NSAIDs like PANAMOR GEL raise the concentration of lithium in the blood. Lithium levels should be monitored more frequently.

Digoxin

Diclofenac may increase plasma concentrations of digoxin.

Other NSAIDs and corticosteroids

NSAIDs: Use of two or more NSAIDs concomitantly could result in an increase in side effects.

Corticosteroids: Increased risk of gastrointestinal perforation, ulceration, or bleeding (PUBs).

Anti-coagulants and anti-platelet medicines

The bioavailability of PANAMOR GEL is reduced by acetylsalicylic acid, (aspirin) and that of acetylsalicylic acid (aspirin), by PANAMOR GEL, when the two medicines are administered together.

PANAMOR GEL may enhance the effects of anti-coagulants such as warfarin. Anti-platelet medicines may increase risk of gastrointestinal bleeding.

Selective serotonin re-uptake inhibitors (SSRIs)

Selective serotonin re-uptake inhibitors (SSRIs) may increase risk of gastrointestinal bleeding.

Quinolone antimicrobials

Convulsions may occur due to an interaction between quinolones and NSAIDs, as in PANAMOR GEL. 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.

Mifepristone

NSAIDs should not be used for 8 to12 days after mifepristone administration as NSAIDs can reduce the effects of mifepristone.

4.6 Fertility, pregnancy, and lactation

Pregnancy

PANAMOR GEL, should not be used during pregnancy, as safety and efficacy in pregnancy has not been established (see section 4.3).

For NSAIDs, such as PANAMOR GEL, with systemic uptake:

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. An increased risk of miscarriage and of cardiac malformation and gastroschisis has been reported after use of a prostaglandin synthesis inhibitor in early pregnancy. The risk is believed to increase with dose and duration of therapy.

Use of NSAIDs during the third trimester of pregnancy may result in premature closure of the foetal ductus arteriosus in utero and possibly in persistent pulmonary hypertension of the newborn. The onset of labour may be delayed, and its duration increased.

Use of NSAIDs, such as PANAMOR GEL, around 20 weeks gestation or later in pregnancy may cause a rare but serious foetal renal dysfunction leading to oligohyramnios and, in some cases, neonatal renal impairment.
Complications of prolonged oligohydramnios include limb contractures and delayed lung maturation, which may require invasive procedures such as exchange transfusion or dialysis, in some cases.

Breastfeeding

Diclofenac passes into breast milk in small amounts. PANAMOR GEL should not be used during lactation, as safety and efficacy in lactation has not been established (see section 4.3).

Fertility

There are no data available on the use of topical formulations of diclofenac, such as PANAMOR GEL, and its effect on fertility in humans.

4.7 Effects on ability to drive and use machines

Cutaneous application of PANAMOR GEL has no or negligible influence on the ability to drive and use machines.
Since adverse reactions such as dizziness and headache have been reported in patients using PANAMOR GEL, patients should not drive, use machinery, or

perform any tasks that require concentration, until they are certain that PANAMOR GEL does not adversely affect their ability to do so (see section 4.8).

4.8 Undesirable effects

a) *Tabulated list of adverse reactions*

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Infections and infestations		Pustular rash	
Blood and lymphatic system disorders		Bone marrow suppression, (leucopenia, thrombocytopenia, aplastic anaemia)	
Immune system disorders		Hypersensitivity reactions (bronchospasm, anaphylactic/anaphylactoid systemic reactions including urticaria), angioedema	
Nervous system disorders		Headache, slight dizziness	
Cardiac disorders		Peripheral oedema, cardiac failure	
Vascular disorders		Hypertension	
Respiratory, thoracic, and mediastinal disorders		Asthma	
Gastrointestinal disorders*	Peptic ulcers, gastritis, perforation vomiting, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease	Gastrointestinal ulceration or haemorrhage, sometimes fatal	Eructation, epigastric pain, nausea, diarrhoea
Hepato-biliary disorders		Jaundice, hepatitis	Elevated transaminase levels
Skin and subcutaneous tissue disorders	Skin rash, eczema, erythema, dermatitis (including contact dermatitis), pruritus	Bullous dermatitis including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), photosensitivity reactions	Burning sensation at the application site, dry skin, itching, reddening, or smarting of the skin, urticaria.

			desquamation, skin discolouration
Renal and urinary disorders			Renal failure, nephrotic syndrome

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. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/ +27 (0)11 239-6200

4.9 Overdose

Symptoms

The low systemic absorption of topical diclofenac renders overdoses very unlikely. However, undesirable effects similar to those observed following an overdose of diclofenac containing tablets can be expected if topical diclofenac preparations, such as PANAMOR GEL is inadvertently ingested.

Treatment

Treatment is symptomatic and supportive.

In the event of significant systemic adverse events occurring as a result of improper use, accidental ingestion or overdosage (e.g. in children), general therapeutic

measures of the kind normally adopted in order to treat poisoning with non-steroidal anti-inflammatory agents should be resorted to.

The use of activated charcoal should be considered, especially within a short time of ingestion.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

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

Pharmacotherapeutic group: Topical products for joint and muscular pain, anti-inflammatory preparations, non-steroids for topical use.

ATC code: M02AA15

Mechanism of action

Diclofenac gel has anti-inflammatory and analgesic properties designed for external application.

Inhibition of prostaglandin synthesis, by cyclo-oxygenase 2 (COX-2) is the primary mechanism of action of diclofenac.

5.2. Pharmacokinetic properties

The amount of diclofenac absorbed through the skin is relative to the contact time and the area covered with PANAMOR GEL application.

Protein binding: 99,7 %.

Absorption

Following the local application of diclofenac, the active ingredient is absorbed through the skin. The percutaneous absorption of diclofenac, estimated in healthy volunteers by measuring the metabolised fraction in the urine, is about 6 % of the applied dose.

Distribution

After local application, the active ingredient enters the skin and penetrates the underlying tissues where it attenuates the acute and chronic inflammatory reactions. The anti-inflammatory and analgesic properties of diclofenac in traumatic and rheumatic inflammation result in a decrease in swelling and a reduction in pain on pressure and movement.

Elimination

The mean terminal elimination half-life of the unchanged diclofenac is 1 to 2 hours. Diclofenac and its metabolites are excreted mainly in the urine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isopropyl alcohol, Lanol, perfume (Dalin pH), polyethylene glycol, polyethylene glycol monostearate, purified water, Synthalen KP, Synthalen MP, triethanolamine.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C, in a dry place

6.5 Nature and contents of container

30 g is packed into a white aluminium collapsible tube, sealed with a white, smooth polypropylene screw cap, and placed in a unit cardboard carton together with a leaflet.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

33/3.1/0058

9. DATE OF FIRST AUTHORISATION

06 August 2002

10. DATE OF REVISION OF TEXT

28 April 2024

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

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