1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

DICLO-FLAM BLACKCURRANT 50,0 mg dispersible tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dispersible tablet of DICLO-FLAM BLACKCURRANT contains 46,5 mg of diclofenac free acid, equivalent to 50,0 mg of diclofenac sodium.

Contains sweetener: Saccharin sodium 0,26 mg

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Dispersible tablets

DICLO-FLAM BLACKCURRANT is a white to off-white, diamond-shaped biconvex tablet,

bisected on one side, with a blackcurrant odour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

DICLO-FLAM BLACKCURRANT is indicated for:

- Emergency treatment of acute gout attacks, subject to a maximum daily dose of 150 mg for a maximum treatment period of 3 days (see section 4.2).

4.2. Posology and method of administration

Posology

Adults

As a general recommendation, the dose should be individually adjusted.

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

Dissolve one tablet in water three times a day for acute gout attacks.

The recommended initial daily dose is 100 mg to 150 mg.

In milder cases 50 mg to 100 mg daily is usually sufficient.

The total daily dosage should generally be divided into 2 to 3 separate doses. The maximum daily dose is 150 mg for a maximum treatment period of 3 days (three DICLO-FLAM BLACKCURRANT dispersible tablets in divided doses).

Adolescents

For adolescents aged 14 years or over, a daily dose of 50 mg to 100 mg is usually sufficient.

The total daily dose should generally be divided in 2 to 3 doses.

The maximum daily dose of 150 mg should not be exceeded.

Paediatric population

DICLO-FLAM BLACKCURRANT should not be used in children and adolescents under 14 years of age.

Method of administration

Oral administration.

DICLO-FLAM BLACKCURRANT tablets should preferably be taken on an empty stomach. DICLO-FLAM BLACKCURRANT tablets should be dropped into a glass of water and the liquid stirred to aid dispersion before swallowing. Since a proportion of the active medicine may remain in the glass after swallowing, it is advisable to rinse the glass with a small amount of water and to swallow again.

The tablets must not be divided or chewed.

4.3 Contraindications

DICLO-FLAM BLACKCURRANT is contraindicated in:

- Patients with hypersensitivity to diclofenac sodium or to any excipients in DICLO-FLAM BLACKCURRANT (see section 6.1).
- Patients with hypersensitivity to other NSAIDs including aspirin.
- Patients with gastric or intestinal ulcer, bleeding or perforation.
- Patients with active or history of recurrent ulcer/haemorrhage/perforations.
- Patients with a history of gastrointestinal bleeding, ulceration or perforation (PUBs) related to previous NSAIDs including DICLO-FLAM BLACKCURRANT.
- Patients with heart failure; established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.
- Patients with hepatic or renal failure (see section 4.4).
- Asthmatic patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or by other NSAIDs or medicines with prostaglandin-synthetase inhibiting activity.
- Pregnant women from around 20 weeks of gestation or later in pregnancy (see section 4.4 and 4.6).
- Lactation (see section 4.6).
- Patients with porphyria.

4.4 Special warnings and precautions for use

General

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 dyshaemopoiesis disorders of blood coagulation.

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

The concomitant use of DICLO-FLAM BLACKCURRANT 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).

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 (see section 4.2).

Allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to DICLO-FLAM BLACKCURRANT (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 diclofenac.

Concomitant use of DICLO-FLAM BLACKCURRANT and methotrexate could result in serious interactions (see section 4.5).

DICLO-FLAM BLACKCURRANT may mask signs and symptoms of infection due to its pharmacodynamic properties.

Cardiovascular and cerebrovascular effects

Caution, appropriate monitoring and advice is required in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with DICLO-FLAM BLACKCURRANT therapy. In view of the DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT after careful consideration.

As the cardiovascular risks of DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT, particularly at high dose (150 mg daily) 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.

Hepatic impairment

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

As with diclofenac, as in DICLO-FLAM BLACKCURRANT, values of one or more liver enzymes may increase. During prolonged treatment with DICLO-FLAM BLACKCURRANT, 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 (such as eosinophilia, rash), DICLO-FLAM BLACKCURRANT should be discontinued.

Hepatitis may occur with DICLO-FLAM BLACKCURRANT without prodromal symptoms.

Renal impairment

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

Haematological effects

During prolonged treatment with DICLO-FLAM BLACKCURRANT, monitoring of blood counts is recommended.

DICLO-FLAM BLACKCURRANT may reversibly inhibit platelet aggregation (see section 4.5). Patients with defects of haemostasis, bleeding diathesis or haematological abnormalities should be carefully monitored.

Elderly

The elderly have an increased frequency of adverse reactions to NSAIDs including DICLO-FLAM BLACKCURRANT, especially gastrointestinal perforation, ulceration and bleeding (PUBs) which may be fatal.

Gastrointestinal effects

Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation, which can be fatal has been reported with diclofenac, as in DICLO-FLAM BLACKCURRANT, 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. If gastrointestinal bleeding or ulceration occurs in patients receiving DICLO-FLAM BLACKCURRANT, the medicine should be withdrawn.

Close medical surveillance is imperative and particular caution should be exercised when

prescribing DICLO-FLAM BLACKCURRANT 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 perforation, ulceration or bleeding (PUBs) is higher with increasing doses of DICLO-FLAM BLACKCURRANT, in patients with a history of ulcers, particularly if complicated with haemorrhage or perforation, and the elderly.

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 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).

DICLO-FLAM BLACKCURRANT 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 (see section 4.8).

Diclofenac, as in DICLO-FLAM BLACKCURRANT may be associated with increased risk of gastrointestinal anastomotic leak. Close medical surveillance and caution are recommended when using DICLO-FLAM BLACKCURRANT after gastrointestinal surgery.

Skin effects

Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolyis have been reported. Patients appear to be at 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. DICLO-FLAM BLACKCURRANT should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Drug reaction with eosinophillia and systemic symptoms

Drug reaction with eosinophillia and systemic symptoms (DRESS) has been reported in patients taking NSAIDs such as DICLO-FLAM BLACKCURRANT. 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 DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT 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, as in DICLO-FLAM BLACKCURRANT, and other NSAIDs can precipitate bronchospasm if administered to patients suffering from, or with a previous history of bronchial asthma.

Use in pregnancy

It is recommended that DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT, 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 DICLO-FLAM BLACKCURRANT treatment extends beyond 48 hours. Discontinue DICLO-FLAM BLACKCURRANT if oligohydramnios occurs and follow up according to clinical practice.

Female fertility

The use of DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT should be considered (see section 4.6).

Paediatric population

DICLO-FLAM BLACKCURRANT should not be used in children and adolescents under 14 years of age.

4.5. Interaction with other medicines and other forms of interaction

Methotrexate

Diclofenac, as in DICLO-FLAM BLACKCURRANT, can inhibit the tubular renal clearance of

methotrexate hereby increasing methotrexate levels

Caution is recommended when DICLO-FLAM BLACKCURRANT is administered less than 24 hours before or after treatment with methotrexate, since concurrent administration of methotrexate with DICLO-FLAM BLACKCURRANT may result in increased methotrexate toxicity and raised blood concentrations of methotrexate (see section 4.4).

Cases of serious toxicity have been reported when methotrexate and NSAIDs including diclofenac, as in DICLO-FLAM BLACKCURRANT, 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.

Lithium or digoxin

Raised plasma concentrations of lithium or digoxin may occur if taken together with DICLO-FLAM BLACKCURRANT.

Monitoring of the serum lithium or digoxin level is recommended.

Diuretics and antihypertensive medicines

Concomitant use of DICLO-FLAM BLACKCURRANT 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).

Glucocorticoids and corticosteroids

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

Other NSAIDs including cyclo-oxygenase-2 selective inhibitors

Gastrointestinal adverse effects may be exacerbated by the concomitant administration of DICLO-FLAM BLACKCURRANT and other systemic NSAIDs. Concurrent treatment with two or more NSAIDs may increase the risk of adverse effects.

Avoid concomitant use of two or more NSAIDs (see section 4.4).

Antidiabetic medicines

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

Anticoagulants and anti-platelet medicines

Caution is recommended since concomitant administration could increase the risk of bleeding

(see section 4.4).

There is an increased risk of haemorrhage if DICLO-FLAM BLACKCURRANT is used concurrently with any anticoagulants such as warfarin. Therefore, to be certain that no change in anticoagulant dosage is required, careful monitoring of such patients is necessary. Diclofenac, as in DICLO-FLAM BLACKCURRANT, in high dose can reversibly inhibit platelet aggregation.

Selective serotonin reuptake inhibitors (SSRIs):

Increased risk of gastrointestinal bleeding.

Ciclosporin

Nephrotoxicity of ciclosporin may be increased by the effects of DICLO-FLAM BLACKCURRANT on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.

Tacrolimus

Possible increased risk of nephrotoxicity when DICLO-FLAM BLACKCURRANT is given with tacrolimus. This might be mediated through renal antiprostaglandin effects of both DICLO-FLAM BLACKCURRANT and calcineurin inhibitor.

Quinolone antibiotics

There have been reports of convulsions which may have been due to concomitant use of quinolone antibiotics and NSAIDs, such as diclofenac, as in DICLO-FLAM BLACKCURRANT.

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.

Acetylsalicylic acid/aspirin

The bioavailability of both DICLO-FLAM BLACKCURRANT and acetylsalicylic acid may be reduced if used concurrently.

Phenytoin

When using phenytoin concomitantly with DICLO-FLAM BLACKCURRANT, 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 and DICLO-FLAM BLACKCURRANT. Therefore, it is recommended to administer and DICLO-FLAM BLACKCURRANT at least one hour before or 4 to 6 hours after administration of colestipol/ cholestyramine.

Cardiac glycosides

Concomitant use of cardiac glycosides and DICLO-FLAM BLACKCURRANT in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Mifepristone

DICLO-FLAM BLACKCURRANT should not be used for 8 to 12 days after mifepristone administration as DICLO-FLAM BLACKCURRANT can reduce the effect of mifepristone.

Potent CYP2C9 inhibitors

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

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 DICLO-FLAM BLACKCURRANT, may expose the foetus to:

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

At the end of pregnancy, the mother and the neonate may be exposed to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour (see section 4.4).

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

Breastfeeding

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

Fertility

The use of DICLO-FLAM BLACKCURRANT 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 DICLO-FLAM BLACKCURRANT should be considered (see section 4.4).

4.7 Effects on ability to drive and use machines

DICLO-FLAM BLACKCURRANT has a minor influence on the ability to drive or use machines.

Since adverse reactions such as dizziness or visual disturbances have been reported in patients receiving DICLO-FLAM BLACKCURRANT, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that DICLO-FLAM BLACKCURRANT 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		Leucopenia, thrombocytopenia, aplastic anaemia, haemolytic anaemia, agranulocytosis.	
Immune system disorders		Hypersensitivity reactions (such as bronchospasm, anaphylactoid and anaphylactic systemic reactions including hypotension and shock), angioneurotic oedema (including face oedema).	
Psychiatric disorders		Disorientation, depression, insomnia, nightmares, irritability, psychotic reactions.	

Nervous system disorders	Headache, dizziness, nervousness.	Tiredness, disturbances of sensation (including paraesthesia), memory disturbance, convulsions, anxiety, tremor, aseptic meningitis, somnolence, cerebrovascular accident, alteration in taste, confusion, hallucinations, malaise.	
Eye disorders		Disturbances of vision (diplopia, blurred vision).	Optic neuritis.
Ear and labyrinth disorders	Vertigo.	Impaired hearing, tinnitus.	
Cardiac disorders		Palpitations, chest pain, congestive heart failure, cardiac failure, myocardial infarction.	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, constipation, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease, gastritis, epigastric pain, nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, eructation, anorexia, local irritation.	Gastrointestinal bleeding, bloody diarrhoea, peptic ulcer with or without bleeding or perforation, lower gut disorders such as non-specific haemorrhagic colitis, glossitis, aphthous, stomatitis, oesophageal lesions, diaphragm-like intestinal strictures, pancreatitis, diarrhoea haemorrhagic.	Ischaemic colitis.
Hepatobiliary disorders	Elevated transaminase levels (ALT, AST).	Hepatitis with or without jaundice, fulminant hepatitis, liver disorder, hepatic necrosis, hepatic failure.	

Skin and subcutaneous tissue disorders	Rash and skin reactions.	Urticaria, bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal, necrolysis, (lyell's syndrome acute toxic epidermolysis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura, pruritus.	Drug Reaction with Eosinophillia and Systemic Symptoms (DRESS) (see section 4.4).
Renal and urinary disorders		Acute renal failure, urinary abnormalities such as haematuria, proteinuria, interstitial nephritis, nephritic syndrome, papillary necrosis.	
Reproductive system and breast disorders		Impotence.	
General disorders and administrative site conditions		Oedema.	

c) Description of selected adverse reactions

Cardiac disorders

Clinical trial and epidemiological data consistently point towards an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, as in DICLO-FLAM BLACKCURRANT, particularly at high dose (150 mg daily) and in long term treatment (see sections 4.3 and 4.4).

General

Vasculitis and pneumonitis may occur without prior exposure to DICLO-FLAM BLACKCURRANT. Discontinue treatment immediately.

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 DICLO-FLAM BLACKCURRANT overdosage. Overdosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal haemorrhage, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.
(See section 4.4 and 4.8).

Treatment

Treatment is symptomatic and supportive, especially for hypotension, renal failure, convulsions, gastrointestinal irritation and respiratory depression.

Absorption should be prevented as soon as possible after an overdose by means of activated charcoal.

Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting) after ingestion of a potentially life-threatening overdose.

Specific therapies such as forced diuresis, dialysis or haemoperfusion are of little value in eliminating DICLO-FLAM BLACKCURRANT because of its high protein binding and extensive metabolism.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

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

Pharmacotherapeutic group: Acetic acid derivatives and related substances

ATC code: M01AB05

Mechanism of action

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) with antirheumatic, analgesic, antipyretic and anti-inflammatory activities. It causes decreased formation of prostaglandins and thromboxanes through inhibition of the activity of the enzyme cyclo-oxygenase. Prostaglandins play a major role in the causation of inflammation, pain and fever and the inhibition of prostaglandin synthesis may have an important bearing on diclofenac's mechanism of action.

Diclofenac inhibits platelet aggregation *in vitro*.

5.2 Pharmacokinetic properties

Absorption

Diclofenac is well absorbed after oral administration.

Absorption of diclofenac from DICLO-FLAM BLACKCURRANT tablets sets in rapidly after administration. The plasma concentrations show a linear relationship to the size of the dose.

Peak plasma concentrations are attained in 20 to 60 minutes after ingestion on an empty stomach. Administration with food slows the rate but does not alter the extent of absorption.

Distribution

There is a substantial first-pass effect (only 50 % of diclofenac is available systemically).

Diclofenac is extensively bound to plasma proteins (99 %) and its plasma half-life is 1 to 2 hours.

Biotransformation

Diclofenac is metabolised in the liver by a cytochrome P-450 isozyme of the CYP2C subfamily.

Elimination

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

Blackcurrant flavour, croscarmellose sodium, glycerol distearate, microcrystalline cellulose, purified talc, saccharin sodium, sodium starch glycolate.

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 light and moisture.

Keep the blister in the carton until required for use.

6.5. Nature and contents of container

9 dispersible tablets are packed in a clear polyvinylchloride, polyethylene and polyvinylidene chloride film sealed with an aluminium foil backing. One blister strip is packed into an outer cardboard carton 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

37/3.1/0607

9. DATE OF FIRST AUTHORISATION

03 June 2005

10. DATE OF REVISION OF TEXT

28 November 2021

Die Afrikaanse Professionele Inligting is op versoek beskikbaar.

Mediese Blitslyn: 0800 118 088.

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