Current approved Professional Information

Scheduling status: **S3**

Except when intended for the emergency treatment of acute gout attacks and when intended for the treatment of post traumatic conditions such as pain, swelling and inflammation, for a maximum period of 5 days **S2**

Proprietary names and dosage forms:

Diclofenac 50 Oethmaan (tablets)

Composition:

Diclofenac 50 Oethmaan: Each enteric coated tablet contains diclofenac sodium 50 mg.
Sugar free.

Pharmacological classification:

A.3.1 Antirheumatics (anti-inflammatory agents)

Pharmacological 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. Prostaglandins play a major role in the cause 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*.

Pharmacokinetics:

Diclofenac is well absorbed after oral administration. Peak plasma concentrations are reached within

approximately 1 hour. Administration with food slows the rate but does not alter the extent of absorption. 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.

Diclofenac is metabolised in the liver by a cytochrome P450 isoenzyme of the CYP2C subfamily and excreted in the form of metabolites via the kidneys (approximately 60 %) and faeces (approximately 30 %). Less than 1 % is excreted in unchanged form.

Indications:

Diclofenac 50 Oethmaan is indicated as short-term treatment in the following acute conditions:

- Painful musculoskeletal conditions.
- Non-articular rheumatism.
- Acute attacks of gout.
- Painful post-operative and post-traumatic inflammation and swelling.
- Pain following dental surgery.
- Flare-up of osteoarthrosis.
- Symptomatic treatment of primary dysmenorrhoea.
- Classical migraine headaches.

Contra-indications:

- Hypersensitivity to diclofenac or to any of the ingredients.
- Hypersensitivity to other NSAIDs including aspirin.
- History of gastrointestinal bleeding or perforation (PUBs) related to previous NSAIDs.
- Active or history of recurrent ulcer or haemorrhage or perforations.
- Gastric or intestinal ulcer.
- Severe hepatic, renal or cardiac failure (see “Warnings”).
- Asthmatic patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by

acetylsalicylic acid (aspirin) or by other medicines with prostaglandin-synthetase inhibiting activity.

- Pregnancy (see “Pregnancy and lactation”).
- Porphyria.

Warnings:

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 or disorders of blood coagulation.

Gastrointestinal bleeding, ulceration or perforation, which can be fatal, have been reported with all NSAIDs such as Diclofenac 50 Oethmaan and may occur at any time during treatment, with or without warning symptoms or a previous history of serious gastrointestinal events.

The risk of gastrointestinal bleeding or perforation is higher with increasing doses of Diclofenac 50 Oethmaan, especially in patients with a history of ulcers and the elderly.

Diclofenac 50 Oethmaan 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.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with Diclofenac 50 Oethmaan (see “Side effects and special precautions”).

Diclofenac 50 Oethmaan should be used with caution in patients with hepatic or renal failure.

Concomitant use of Diclofenac 50 Oethmaan and methotrexate could result in serious interactions. (see “Interactions”).

Acetylsalicylic acid / aspirin*:*

The bioavailability of both Diclofenac 50 Oethmaan and acetylsalicylic acid may be reduced if used concurrently.

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 50 Oethmaan therapy.

Interactions:

Methotrexate:

Concurrent administration of methotrexate with Diclofenac 50 Oethmaan may result in increased methotrexate toxicity (see “Warnings”).

Lithium or digoxin:

Raised plasma concentrations of lithium or digoxin may occur if taken together with Diclofenac 50 Oethmaan. Monitoring of serum lithium and digoxin levels is recommended.

Glucocorticoids and other NSAIDs:

Gastrointestinal adverse effects may be exacerbated by the concomitant administration of Diclofenac 50 Oethmaan. Concurrent treatment with two or more NSAIDs may increase the risk of adverse effects.

Antidiabetic medicines:

Diclofenac 50 Oethmaan may cause either hypo- or hyperglycaemia. Dosage of antidiabetic medicines may need to be changed.

Anticoagulants:

There is an increased risk of haemorrhage if Diclofenac 50 Oethmaan is used concurrently with any anticoagulants. Careful monitoring is necessary. Diclofenac 50 Oethmaan may enhance the effects of anti-

coagulants such as warfarin.

Cyclosporin:

Nephrotoxicity of cyclosporin may be increased by the effects of Diclofenac 50 Oethmaan on renal prostaglandins. Diclofenac 50 Oethmaan should be given at doses lower than those that would be used in patients not receiving cyclosporin.

Quinolone antibiotics:

There have been isolated reports of convulsions which may have been due to concomitant use of quinolone antibiotics and NSAIDs.

Diuretics and antihypertensive medicines:

Concomitant use of Diclofenac 50 Oethmaan with diuretics or antihypertensive medicines (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. 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. Concomitant treatment with potassium-sparing medicines may be associated with increased serum potassium levels, which should therefore be monitored frequently.

Anti-platelet agents and Selective serotonin reuptake inhibitors (SSRIs):

Concomitant administration of Diclofenac 50 Oethmaan with anti-platelet agents and SSRIs may increase the risk of gastrointestinal bleeding.

Pregnancy and lactation:

Safety and efficacy in pregnancy and lactation has not been established.

***Pregnancy*:**

Use of Diclofenac 50 Oethmaan 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 “Contra-indications”).

Lactation:

Diclofenac 50 Oethmaan passes into breast milk in small amounts.Therefore,Diclofenac 50 Oethmaan should not be administered during breast feeding in order to avoid undesirable effects in the infant.

***Fertility*:**

The use of Diclofenac 50 Oethmaan 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 Diclofenac 50 Oethmaan should be considered.

Dosage and directions for use:

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

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

Adults:

Initial daily dose:

100 to 150 mg in two to three divided doses, with a maximum daily dose of 150 mg in divided doses.

Milder cases:

75 to 100 mg daily in divided doses.

Primary dysmenorrhoea:

50 to 150 mg daily in divided doses. Dosage should be individually determined. Treatment should be initiated at onset of symptoms and continued for a few days, depending on the intensity of pain.

Classical migraine:

50 mg taken at first signs of an impending attack. If pain relief is not sufficient within 2 hours after the first dose, a second dose of 50 mg may be taken. A third dose may be taken after 4 to 6 hours if necessary but the total daily dose of 150 mg must not be exceeded.

Side effects and special precautions:

Side effects:

Side effects are listed using the following convention:

Very common (≥ 1/10); Common (≥ 1/100, < 1/10);

Uncommon (≥ 1/1000, < 1/100); Rare (≥ 1/10 000, < 1/1000);

Very rare (< 1/10 000), including isolated reports.

Blood and lymphatic system disorders:

Very rare: Leucopenia, thrombocytopenia, anaemia (including aplastic, haemolytic anaemia), agranulocytosis.

Immune system disorders:

Rare: Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).

Very rare: Angioneurotic oedema (including face oedema).

Psychiatric disorders:

Very rare: Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.

Cardiac disorders:

Very rare: Palpitation, chest pain, cardiac failure, myocardial infarction.

Vascular disorders:

Very rare: Hypertension, vasculitis.

Nervous system disorders:

Common: Headache, dizziness.

Rare: Somnolence.

Very rare: Taste disturbances, paraesthesia, memory impairment, convulsions, anxiety, tremor, aseptic meningitis, cerebrovascular accident.

Respiratory, thoracic and mediastinal disorders:

Rare: Asthma (including dyspnoea).

Very rare: Pneumonitis.

Gastrointestinal disorders:

Common: Nausea, vomiting, diarrhoea, abdominal pain , dyspepsia, flatulence, anorexia.

Rare: Gastritis, gastrointestinal bleeding, haematemesis, melaena, bloody diarrhoea, gastrointestinal ulcer with or without bleeding or perforation.

Very rare: Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, ulcerative stomatitis, glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.

Renal and urinary disorders:

Very rare: Acute renal failure, urinary abnormalities such as haematuria, proteinuria, interstitial nephritis, nephrotic syndrome, renal papillary necrosis.

Hepato-biliary disorders:

Common: Transaminases increased.

Rare: Hepatitis, jaundice, liver disorder.

Very rare: Fulminant hepatitis.

Eye disorders:

Very rare: Disturbances of vision (diplopia, blurred vision).

Ear and labyrinth disorders:

Common: Vertigo.

Very rare: Tinnitus, hearing impaired.

Skin and subcutaneous tissue disorders:

Common: Rash.

Rare: Urticaria.

Very rare: Bullous eruptions, eczema, erythema, erythema multiforme, Steven's-Johnson syndrome, Lyell's syndrome (acute toxic epidermal necrolysis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura, pruritus.

General disorders and administration site conditions:

Rare: Oedema.

Special precautions:

Patients who experience visual disturbances, dizziness, vertigo, somnolence or other central nervous system disturbances while taking Diclofenac 50 Oethmaan should refrain from driving a vehicle or operating machinery.

Diclofenac 50 Oethmaan may mask signs and symptoms of infection due to its pharmacodynamic properties.

The concomitant use of Diclofenac 50 Oethmaan 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.

Diclofenac 50 Oethmaan, should be used with caution in elderly patients. It is recommended that the lowest effective dose be used in the elderly, especially in the very frail or those with a low body mass, for the shortest possible duration.

In patients with asthma, seasonal allergic rhinitis, swelling of the mucosa (i.e. nasal polyps), chronic obstructive pulmonary disease or chronic infections of the respiratory tract (especially if linked to allergic rhinitis-like symptoms), reactions to 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.

Close medical surveillance is imperative and particular caution should be exercised when prescribing Diclofenac 50 Oethmaan in patients with symptoms indicative of gastrointestinal (GI) disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation. The risk of GI bleeding is higher with increasing Diclofenac 50 Oethmaan doses and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation and in 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.

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 medications which could increase the risk of ulceration or bleeding, such as systemic corticosteroids, anticoagulants, anti-platelet

agents or selective serotonin-reuptake inhibitors (see “Interactions”).

Close medical surveillance and caution should also be exercised in patients with ulcerative colitis or Crohn’s disease, as their condition may be exacerbated.

Heart failure may be precipitated in some compromised patients, due to the inherent potential of Diclofenac 50 Oethmaan to cause fluid retention.

As fluid retention and oedema have been reported in association with Diclofenac 50 Oethmaan therapy, particular caution is called for in patients with impaired renal, hepatic or cardiac function, history of hypertension, the elderly, patients being treated with diuretics or medicinal products that can significantly impact renal function, or in those patients with substantial extracellular volume depletion from any cause. Monitoring of renal function is recommended.

Close medical surveillance is required when prescribing Diclofenac 50 Oethmaan to patients with impaired hepatic function, as their condition may be exacerbated.

Values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac 50 Oethmaan, blood counts and monitoring of hepatic and renal function are indicated.

If abnormal liver function tests persist or worsen, if symptoms of hepatic disease develop, or if other manifestations occur (e.g. eosinophilia, rash), discontinue Diclofenac 50 Oethmaan. Hepatitis may occur without prodromal symptoms.

Known symptoms of overdosage and particulars of its treatment:

(See “Side effects and special precautions”).

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 gastric lavage and activated charcoal.

Specific therapies such as forced diuresis, dialysis or haemoperfusion are of little value in eliminating Diclofenac 50 Oethmaan because of its high protein binding and extensive metabolism.

Identification:

Diclofenac 50 Oethmaan: Light brown, round, slightly biconvex, enteric-coated tablet.

Presentations:

Diclofenac 50 Oethmaan:

Packs of 21, 30 or 100 tablets in amber glass bottles.

Packs of 21, 30, 100 or 500 tablets in securitainers.

Blister packs of 15, 20, 21, 30, 100 or 500 tablets.

Sealed aluminium bags with 15, 21, 30 or 100 tablets.

Storage instructions:

Store below 25 °C. Protect from moisture.

KEEP OUT OF THE REACH OF CHILDREN.

Registration numbers:

Diclofenac 50 Oethmaan: V/3.1/137

Name and business address of the holder of the registration certificates:

Oethmaan Biosims (Pty) Ltd

Office 207A, 1st floor, Sherwood House

Greenacres Office Park, Cnr Victory & Rustenburg Roads

Victory Park, 2195

Johannesburg, RSA

Date of publication of this package insert:

14 August 2009