

Section 3 - Summary of Product Characteristics

Product Summary

1. Trade Name of the Medicinal Product

Diclofenac Sodium Tablets 25mg

2. Qualitative and Quantitative Composition

Diclofenac Sodium BP 25.0mg

3. Pharmaceutical Form

Tablet

Clinical Particulars

4.1. Therapeutic Indications

Adults:

Rheumatoid arthritis, osteoarthritis, low back pain and other acute musculoskeletal disorders, acute gout, control of pain and inflammation in orthopaedic, dental and other minor surgery.

Children:

Juvenile Chronic Arthritis.

Children aged 9 yrs and above:

The short term treatment of fever related to infections of the ear, nose or throat (ENT), e.g. pharyngotonsillitis, otitis media.

As monotherapy or as adjunct therapy with morphine or other opiates (due to its opiate-sparing effect) for the relief of acute post-operative pain.

4.2. Posology and Method of Administration

For oral administration.

Adults:

A total of 75-150mg daily given in two or three divided doses.

Children:

1-3mg/kg body weight per day in divided doses.

For the short term treatment of fever related to infections of the ear, nose or throat (ENT) and post-operative pain the following dosage should be given :

Children aged 9 years (min. 35 kg BW) or over and adolescents should be given up to 2 mg/kg body weight per day in 3 divided doses, depending on the severity of the disorder.

Elderly:

The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

To be taken preferably with or after food.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4).

4.3. Contra-indications

Hypersensitivity to any of the constituents.

NSAID's are contraindicated in patients who have previously shown hypersensitivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin or other non-steroidal anti-inflammatory drugs. Severe hepatic, renal and cardiac failure (See section 4.4 – Special warnings and precautions for use).

During the last trimester of pregnancy (See section 4.6 – Pregnancy and lactation).

Active or previous peptic ulcer.

History of upper gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.

Use with concomitant NSAIDs including cyclooxygenase 2 specific inhibitors (See section 4.5 Intereactions).

4.4. Special Warnings and Precautions for Use

In all patients:

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration.

Elderly:

The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal (See section 4.2 – Posology and administration).

Respiratory disorders:

Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAID's have been reported to precipitate bronchospasm in such patients.

Cardiovascular, Renal and Hepatic Impairment:

The administration of an NSAID may cause a dose dependent reduction in

prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics and the elderly. Renal function should be monitored in these patients (See also section 4.3 – Contraindications).

Caution in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Gastrointestinal bleeding, ulceration and perforation:

GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

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

Caution should be advised in patients receiving concomitant medications which could increase the risk of gastrotoxicity or bleeding, such as corticosteroids, or anticoagulants such as warfarin or anti-platelet agents such as aspirin (see section 4.5 - Interactions).

When GI bleeding or ulceration occurs in patients receiving Diclofenac, the treatment should be withdrawn.

NSAID's should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated (See section 4.8 – Undesirable effects).

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 – Undesirable effects).

Female fertility:

The use of Diclofenac 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 should be considered.

Caution is required in patients with renal, hepatic or cardiac impairment since the use of NSAID's may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored in these patients. NSAID's should be given with care to patients with a history of heart failure or hypertension since oedema has been reported in association with NSAID administration.

Diclofenac has been reported to depress salicylate levels and vice versa. Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of diclofenac, particularly at high dose (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke).

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with diclofenac after careful consideration.

Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

4.5. Interactions with other Medicaments and other forms of Interaction

Care should be taken in patients treated with any of the following drugs as interactions have been reported in some patients.

Anti-hypertensives: reduced anti-hypertensive effect.

Diuretics: reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAID's.

Cardiac glycosides: NSAID's may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Lithium: Decreased elimination of lithium.

Digoxin: May increase plasma concentrations.

Methotrexate: Decreased elimination of methotrexate.

Cyclosporin: Increased risk of nephrotoxicity. If cyclosporin is being taken the dose of diclofenac should be halved.

Mifepristone: NSAID's should not be used for 8-12 days after mifepristone administration as NSAID's can reduce the effect of mifepristone.

Other analgesics: Avoid concomitant use of two or more NSAID's (including aspirin) as this may increase the risk of adverse effects (see section 4.3 Contraindications).

Corticosteroids: Increased risk of GI bleeding (See section 4.4 Special warnings and precautions for use).

Anticoagulants: NSAIDs may enhance the effects of anti-coagulants (See section 4.4 Special warnings and precautions for use).

Quinolone antibiotics: Animal data indicate that NSAID's can increase the risk of convulsions associated with quinolone antibiotics. Patients taking NSAID's and quinolones may have an increased risk of developing convulsions.

Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

4.6. Pregnancy and Lactation

Pregnancy:

Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of closure of the ductus arteriosus), use in the last trimester of pregnancy is contraindicated. The onset of labour may be delayed and the duration increased with an increased bleeding tendency in both mother and child (See section 4.3 – Contraindications). NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus.

Lactation:

In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations. NSAIDs should, if possible, be avoided when breastfeeding.

See Section 4.4 Special warnings and precautions for use, regarding female fertility.

4.7. Effects on Ability to Drive and Use Machines

Dizziness, drowsiness, fatigue, visual disturbances or headaches are possible undesirable effects after taking NSAID's, if affected, patients should not drive or operate machinery.

4.8. Undesirable Effects

Gastrointestinal: The most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (See section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (See section 4.4 Special warnings and precautions for use), and gastrointestinal haemorrhage have been reported following administration. Less frequently, gastritis, duodenal ulcer, gastric ulcer and gastrointestinal perforation have been observed.

Hypersensitivity: Hypersensitivity reactions have been reported following treatment with NSAID's. These may consist of (a) non-specific allergic reactions and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders, including rashes of various types, pruritis, urticaria, purpura, angioedema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis, erythema multiforme).

Cardiovascular: Oedema has been reported in association with NSAID treatment.

Other adverse events reported less commonly include:

Renal: Nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome and renal failure.

Hepatic: abnormal liver function, hepatitis and jaundice.

Neurological and special senses: Visual disturbances, optic neuritis, headaches, paraesthesia, reports of aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (See section 4.4) depression, confusion, hallucinations, tinnitus, vertigo, dizziness, malaise, fatigue and drowsiness.

Haematological: Thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and haemolytic anaemia.

Dematological: photosensitivity.

Clinical trial and epidemiological data suggest that use of diclofenac, particularly at high doses (150mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4).

4.9 Overdose

(a) Symptoms

Symptoms include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely, diarrhoea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible. Gastric lavage and correction of severe electrolyte abnormalities may need to be considered.

(b) Therapeutic measure

Patients should be treated symptomatically as required.

Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be ensured.

Renal and liver function should be closely monitored.

Patients should be observed for at least four hours after ingestion of potentially toxic amounts.

Frequent or prolonged convulsions should be treated with intravenous diazepam.

Other measures may be indicated by the patient's clinical condition.

Pharmacological Properties

5.1. Pharmacodynamic Properties

Diclofenac Sodium is a non-steroidal agent with marked analgesic/antiinflammatory and anti-pyretic properties. Like most other drugs in this class, it is an inhibitor of prostaglandin synthetase.

There is limited clinical trial experience of the use of diclofenac in JRA/JIA paediatric patients. In a randomised, double-blind, 2-week, parallel group study in children aged 3-15 years with JRA/JIA, the efficacy and safety of daily 2-3 mg/kg BW diclofenac was compared with acetylsalicylic acid (ASS, 50-100 mg/kg BW/d) and placebo - 15 patients in each group. In the global evaluation, 11 of 15 diclofenac patients, 6 of 12 aspirin and 4 of 15 placebo patients showed improvement with the difference being statistically significant ($p < 0.05$). The number of tender joints decreased with diclofenac and ASS but increased with placebo. In a second randomised, double-blind, 6-week, parallel group study in children aged 4-15 years with JRA/JIA, the efficacy of diclofenac (daily dose 2-3 mg/kg BW, n=22) was comparable with that of indomethacin (daily dose 2-3 mg/kg BW, n=23).

5.2. Pharmacokinetic Properties

The reference and the test drugs are quickly absorbed from the gastrointestinal tract giving adequate levels of Diclofenac one hour after treatment.

With both formulations peak plasma concentrations are attained in all subjects

after two hours, with mean values of 460ng/ml for Rhumalgan and 452ng/ml for Voltaren 25.

The results indicate that Rhumalgan tablets 25mg and Volteran tablets 25mg are bioequivalent since the plasma levels and the urinary excretion of active drug obtained with the two formulations are superimposable and no significant differences can be demonstrated.

5.3. Preclinical Safety Data

Diclofenac Sodium was considered to be unsafe in patients with acute porphyria because it has been shown to be porphyrinogenic in animals or invitro systems.

Pharmaceutical Particulars

6.1. List of Excipients

Anhydrous Lactose EP

Microcrystalline Cellulose BP

Maize Starch EP

Magnesium Stearate EP (E572)

Colloidal Silicon Dioxide USP (E551)

Coating:

Cellulose Acetate Phthalate EP

Carbowax 6000 HSE

Castor Oil EP

Opaspray, K-1-2433 HSE or Orange Dispersion F00223 HSE

Acetone BP (ND)

Methylene Chloride EP (ND)

6.2. Incompatibilities

None stated

6.3. Shelf Life

3 years: polypropylene containers

2 years: blister strips

6.4. Special Precautions for Storage

Store in a dry place below 25°C.

6.5. Nature and Contents of Container

Polypropylene tamper evident containers: 100 84, 70, 56, 42, 28, 21, 15 and 14 tablets.

Blister pack (composed of PVdC coated PVC and aluminium foil): 84, 70, 56, 42, 28, 21, 15 and 14 tablets.

6.6. Instruction for Use/Handling

None

Administrative Data

7. Marketing Authorisation Holder

Goldshield Pharmaceuticals Limited
NLA Tower, 12-16 Addiscombe Road
Croydon, Surrey, CR0 0XT
United Kingdom

8. Marketing Authorisation Number

PL 12762/0420

9. Date of First Authorisation/Renewal of Authorisation

4th July 1995

10. Date of (Partial) Revision of the Text

15/02/2011