

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Diclofenac Sodium 25 mg Gastro-resistant Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 25 mg of diclofenac sodium

Excipient(s) with known effect:

Each tablet contains 68.8 mg lactose.

Each tablet contains sunset yellow (E110).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablet.

Yellow, round, biconvex, gastro-resistant tablets, printed '25' over '0518' on one side and plain on the reverse.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

Diclofenac is indicated for the relief of pain and inflammation in conditions such as rheumatoid arthritis, osteoarthritis, and low back pain; also for acute musculo-skeletal disorders and trauma such as peri-arthritis (in particular frozen shoulder), bursitis, tendinitis, tenosynovitis, strains, sprains and dislocations.

The product is also indicated for the relief of pain from fractures, ankylosing spondylitis and acute gout, and the control of pain and inflammation in dental, orthopaedic and other minor surgery.

Diclofenac Sodium 25 mg Gastro-resistant Tablets may also be used for the treatment of 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

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

Posology

Adults

75 - 150 mg daily in 2 -3 divided doses.

The recommended maximum daily dose of diclofenac sodium is 150 mg.

Paediatric population

Children (1 year or over)

1 - 3 mg/kg 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.

Renal impairment

Diclofenac is contraindicated in patients with severe renal impairment (see section 4.3). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made.

Caution is advised when administering diclofenac to patients with mild to moderate renal impairment (see section 4.3 and 4.4).

Hepatic impairment

Diclofenac is contraindicated in patients with severe hepatic impairment (see section 4.3). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering diclofenac to patients with mild to moderate hepatic impairment (see section 4.3 and 4.4).

Method of administration

For oral administration

Swallow tablets whole with some water. Do not crush or chew. To be taken preferably with or after food.

4.3. Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Active gastric or intestinal ulcer, bleeding or perforation
- History of gastrointestinal bleeding or perforation, related to previous non-steroidal anti-inflammatory drugs NSAIDs therapy.
- Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding)
- During the last trimester of pregnancy (see section 4.6).
- Severe hepatic, renal or cardiac failure (see section 4.4).
- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease
- Like other non-steroidal anti-inflammatory drugs-NSAIDs, diclofenac is also contraindicated in patients in whom attacks of asthma, urticaria, angioedema or acute rhinitis are precipitated by acetylsalicylic acid (aspirin), ibuprofen or other NSAIDs.

4.4. Special warnings and precautions for use

General

Undesirable effects may be minimised by using the minimum effective dose for the shortest possible duration necessary to control symptoms (see section 4.2 and GI and cardiovascular risks below).

The concomitant use of diclofenac with systemic NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided (see section 4.5) 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.

As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur in rare cases with diclofenac without earlier exposure to the drug (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.

Like other NSAIDs, diclofenac sodium may mask the signs and symptoms of infection due to its pharmacodynamic properties.

Gastrointestinal effects

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

the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving diclofenac, the medicinal product should be withdrawn.

As with all NSAIDs, including diclofenac, close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac in patients with symptoms indicative of gastrointestinal (GI) disorders or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation (see section 4.8).

The risk of GI bleeding ulceration or perforation is higher with increasing NSAID doses and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3) and in the 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).

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 agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low-dose acetylsalicylic acid (ASA)/aspirin or other medicinal products likely to increase gastrointestinal risk (see below and 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 medications which could increase the risk of ulceration or gastrotoxicity or bleeding, such as oral corticosteroids, systemic corticosteroids or anticoagulants such as warfarin or anti-platelet agents such as aspirin or selective serotonin-reuptake inhibitors (see section 4.5).

Close medical surveillance and caution should also be exercised in patients with ulcerative colitis or Crohn's disease, as their condition may be exacerbated (see section 4.8).

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

NSAIDs, including diclofenac, may be associated with increased risk of gastrointestinal anastomotic leak. Close medical surveillance and caution are recommended when using diclofenac after gastro-intestinal surgery.

Hepatic effects

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

As with other NSAIDs, including diclofenac, values of one or more liver enzymes may increase. During prolonged treatment with Diclofenac, 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 (e.g. eosinophilia, rash), Diclofenac should be discontinued.

Hepatitis may occur with use of diclofenac without prodromal symptoms.

Caution is called for when using Diclofenac in patients with hepatic porphyria, since it may trigger an attack.

Renal effects

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. As fluid retention and oedema have been reported in association with NSAID therapy, including diclofenac, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension and/or heart failure, the elderly, patients receiving concomitant treatment with diuretics or medicinal products 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 Diclofenac in such cases (see also section 4.3). Discontinuation of therapy is usually followed by recovery to the pre-treatment state.

Skin effects

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

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 including diclofenac.

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, particularly at high dose (150mg daily) and in long term treatment.

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.

Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration. As the cardiovascular risks of diclofenac 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.

Haematological effects

During prolonged treatment with Diclofenac, as with other NSAIDs, monitoring of the blood count is recommended.

Like other NSAIDs, Diclofenac may temporarily inhibit platelet aggregation (see section 4.5). Patients with defects of haemostasis bleeding diathesis or haematological abnormalities should be carefully monitored.

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 on 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.

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

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).

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 (see section 4.6).

Lactose warning

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sunset yellow (E110) may cause allergic reactions.

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interactions with other medicinal products and other forms of interaction

The following interactions include those observed with Diclofenac gastro-resistant tablets and/or other pharmaceutical forms of diclofenac.

Lithium: If used concomitantly, diclofenac may raise plasma concentrations of lithium. Decreased elimination of lithium. Monitoring of the serum lithium level is recommended.

Digoxin: If used concomitantly, diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended. NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents (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. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

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.

Drugs known to cause hyperkalemia: Concomitant treatment with potassium-sparing drugs may be associated with increased serum potassium levels, which should therefore be monitored frequently (see section 4.4).

Other NSAIDs and corticosteroids: Concomitant administration of diclofenac and other systemic NSAIDs including cyclooxygenase-2 selective inhibitors or corticosteroids may increase the frequency of gastrointestinal undesirable effects (see section 4.4). Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk of adverse effects (see section 4.4).

Anticoagulants and anti-platelet agents: NSAIDs may enhance the effects of anticoagulants, such as warfarin (see section 4.4). Anti-platelet agents increase risk of gastrointestinal bleeding (see section 4.4) Caution is recommended since concomitant administration could increase the risk of bleeding (see section 4.4). Although clinical investigations do not appear to indicate that diclofenac affects the action of anticoagulants, there are reports of an increased risk of haemorrhage in patients receiving diclofenac and anticoagulants concomitantly. Close monitoring of such patients is therefore recommended. As with other nonsteroidal anti-inflammatory agents, diclofenac in a high dose can reversibly inhibit platelet aggregation.

Selective serotonin reuptake inhibitors (SSRIs): Concomitant administration of systemic NSAIDs, including diclofenac, and SSRIs may increase the risk of gastrointestinal bleeding (see section 4.4).

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

Methotrexate: Diclofenac can inhibit the tubular renal clearance of methotrexate hereby decreased elimination of methotrexate and increasing methotrexate levels. Caution is recommended when NSAIDs, including diclofenac, are administered less than 24 hours before or after treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increased. Cases of serious toxicity have been reported when methotrexate and NSAIDs including diclofenac 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: Diclofenac, like other NSAIDs, may increase the nephrotoxicity of ciclosporin due to the effect on renal prostaglandins. Therefore, it should be given at doses lower than those that would be used in patients not receiving ciclosporin.

Quinolone antibacterials: Convulsions may occur due to an interaction between quinolones and NSAIDs. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions. 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.

Phenytoin: When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.

Colestipol and cholestyramine: These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol/cholestyramine.

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

Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

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

Tacrolimus: Possible increase risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostaglandin effects of both NSAID and calcineurin inhibitor.

Zidovudine: Increased risk of haematological toxicity when NSAIDs are given with zidovudine. There is evidence of an increased risk of haemarthroses and haematoma in HIV (+) haemophiliacs receiving concurrent treatment with zidovudine and ibuprofen.

4.6. Fertility, pregnancy and lactation

Pregnancy

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest 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.

From the 20th week of pregnancy onward, diclofenac use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, diclofenac should not be given unless clearly necessary. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to diclofenac for several days from gestational week 20 onward. Diclofenac should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose

- the foetus to:
 - cardiopulmonary toxicity (premature construction/closure of the ductus arteriosus and pulmonary hypertension);
 - renal dysfunction (see above);
- the mother and the neonate, at the end of pregnancy, 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.

Consequently, diclofenac is contraindicated during the third trimester of pregnancy.

Breast-feeding

Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, Diclofenac should not be administered during breast-feeding in order to avoid undesirable effects in the infant (see section 5.2).

Fertility

As with other NSAIDs, 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 (see section 4.4).

4.7. Effects on ability to drive and use machines

Patients experiencing visual disturbances, dizziness, vertigo, fatigue, somnolence or other central nervous system disturbances while taking diclofenac, should refrain from driving or using machines.

4.8. Undesirable effects

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: very common: (>1/10); common (\geq 1/100, <1/10); uncommon (\geq 1/1,000, <1/100); rare (\geq 1/10,000, <1/1,000); very rare (<1/10,000); Not known: cannot be estimated from the available data.

The following undesirable effects include those reported with either short-term or long-term use.

Table 1

Blood and lymphatic system disorders	
Very rare	Thrombocytopenia, leukopenia, anaemia (including haemolytic and aplastic anaemia), Agranulocytosis.
Immune system disorders	
Rare	Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock). Angioneurotic oedema (including face oedema).
Very rare	
Psychiatric disorders	
Very rare	Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders	
Common	Headache, dizziness. Somnolence, tiredness. Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, Confusion, hallucinations, disturbances of sensation, malaise.
Rare	
Very rare	
Not known	
Eye disorders	
Very rare	Visual disturbance, vision blurred, diplopia.
Not known	Optic neuritis.
Ear and labyrinth disorders	
Common	Vertigo. Tinnitus, hearing impaired.
Very rare	
Cardiac disorders	
Very rare	Palpitations, chest pain, cardiac failure, myocardial infarction.
Not known	Kounis syndrome
Vascular disorders	
Very rare	Hypertension, hypotension, vasculitis.
Respiratory, thoracic and mediastinal disorders	
Rare	Asthma (including dyspnoea). Pneumonitis.
Very rare	
Gastrointestinal disorders	

Common	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia. Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer (with or without bleeding or perforation, sometimes fatal, particularly in the elderly, may occur (see section 4.4)). Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, Stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Rare	
Very rare	
Not known	
Hepatobiliary disorders	
Common	Transaminases increased (ALT, AST).
Rare	Hepatitis, jaundice, liver disorder.
Very rare	Fulminant hepatitis, hepatic necrosis, hepatic failure.
Skin and subcutaneous tissue disorders	
Common	Rash. Urticaria. Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.
Rare	
Very rare	
Renal and urinary disorders	
Very rare	Acute renal failure, Nephrotoxicity in various forms, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis.
General disorders and administration site conditions	
Rare	Oedema
Reproductive system and breast disorders	
Not known:	Impotence

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, particularly at high dose (150mg daily) and in long term treatment. (see section 4.3 and 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Symptoms

There is no typical clinical picture resulting from diclofenac overdosage. Overdosage can cause symptoms such as headache, nausea, epigastric pain, disorientation, hypotension, respiratory depression, excitation, coma, drowsiness, fainting, vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible.

Therapeutic measures

Management of acute poisoning with NSAIDs, including diclofenac, 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 NSAIDs, including diclofenac, due to the high protein binding and extensive metabolism.

Within one hour of ingestion of a potentially toxic overdose, activated charcoal should be considered. Alternatively, in adults, gastric decontamination (e.g. vomiting, gastric lavage) should be considered within one hour of ingestion of a potentially life-threatening overdose.

Good urine output should be closely monitored.

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

Frequently or prolonged convulsions should be treated with intravenous diazepam.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: SO1B C03 Anti-inflammatory agents, non-steroids.

Diclofenac has analgesic, antipyretic and anti-inflammatory properties; it is an inhibitor of prostaglandin synthetase (cyclo-oxygenase).

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

Diclofenac is absorbed from the gastro-intestinal tract but is subject to first-pass metabolism. Peak plasma concentrations occur about one to four hours after ingestion of gastro-resistant tablets. At therapeutic concentrations it is more than 99% bound to plasma proteins. The terminal half-life is about 1-2 hours. Diclofenac is excreted primarily in the form of metabolites, mainly in the urine but also in the bile.

5.3 Pre clinical safety data

Preclinical information has not been included because the safety profile of diclofenac has been established after many years of clinical use. Please refer to section 4.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet contains:

Lactose monohydrate
Maize starch
Povidone (E1201)
Sodium starch glycolate (Type A)
Colloidal anhydrous silica
Magnesium stearate (E572)

Coating contains:

Hypromellose (E464)
Citric acid monohydrate (E330)
Methacrylic acid copolymer
Purified talc (E553b)
Polyethylene glycol (E1520)
Sunset yellow (E110)
Titanium dioxide (E171)
Iron oxide yellow (E172)
Quinoline yellow (E104)

Printing ink contains:

Shellac
Iron oxide black (E172)
Propylene Glycol (E1520).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Blister: Do not store above 25°C. Store in the original package.
HDPE containers: Do not store above 25°C. Keep the container tightly closed.

6.5 Nature and content of container

HDPE or polypropylene containers with caps or child resistant closures in packs of 28, 30, 50, 56, 60, 100, 250, 500, or 1000 tablets.

Blister strips in packs of 10, 20, 28, 30, 56, 60, 84 or 100 tablets.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Not applicable.

7. MARKETING AUTHORISATION HOLDER

Teva UK Limited,
Ridings Point,
Whistler Drive,
Castleford, WF10 5HX,
United Kingdom.

8. MARKETING AUTHORISATION NUMBER

PL 00289/0738

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

26/09/2006

10. DATE OF REVISION OF THE TEXT

28/02/2023

POM