DICLOFENAC-GA PRODUCT INFORMATION

DICLOFENAC-GA (DICLOFENAC SODIUM) ENTERIC-COATED TABLETS

NAME OF THE MEDICINE
Diclofenac sodium

Molar Weight: 318.13

Chemical name: sodium 2- [(2,6- dichlorophenyl)amino]phenylacetate

CAS number: 15307-79-6

Structure:

\[
\begin{aligned}
&\text{Cl} \\
&\text{NH} \\
&\text{Cl} \\
&\text{CH}_2 - \text{C} = \text{O} \\
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\end{aligned}
\]

\(\text{Na}^+\)

: Diclofenac Sodium

DESCRIPTION
Diclofenac sodium is an odourless, yellowish-white, crystalline powder sparingly soluble in water.

In addition to diclofenac sodium, DICLOFENAC-GA tablets contain lactose, calcium hydrogen phosphate, cellulose- microcrystalline, starch-maize, sodium starch glycollate, magnesium stearate, silica-colloidal anhydrous, methacrylic acid copolymer, triethyl citrate, talc-purified, titanium dioxide and iron oxide yellow Cl 77492

PHARMACOLOGY
Diclofenac sodium, a nonsteroidal compound, exhibits pronounced antirheumatic, anti-inflammatory, analgesic and antipyretic properties.

Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is regarded as having an important bearing on its mechanism of action. Prostaglandins play a major role in the causation of inflammation, pain and fever.
In rheumatic diseases, the anti-inflammatory and analgesic properties of DICLOFENAC-GA elicit a clinical response characterised by relief from signs and symptoms such as pain at rest, pain on movement, morning stiffness, and swelling of the joints, as well as by an improvement in function.

In addition, clinical studies have revealed that in primary dysmenorrhoea diclofenac preparations are capable of relieving the pain and reducing the extent of bleeding. Low concentrations of diclofenac sodium inhibit the aggregation of platelets induced \textit{in vitro} by collagen and by adenosine diphosphate.Diclofenac sodium \textit{in vitro} does not suppress proteoglycan biosynthesis in canine cartilage at concentrations equivalent to the concentrations reached in humans. It is unknown whether or not diclofenac sodium affects the integrity of human osteoarthritic cartilage.

**Pharmacokinetics**

Diclofenac is completely absorbed from the enteric-coated tablets after their passage through the stomach. Following ingestion of one tablet with or after a meal, its passage through the stomach is slower than when it is taken before a meal, but the amount of active substance absorbed remains the same. In fasting subjects, the mean peak plasma concentration is attained on average 2 hours after ingestion of one 50 mg tablet. The plasma concentrations, as measured by the area under the time-concentration curve, are in linear relation to the size of the dose.

Following oral administration, about half the active substance is metabolised during its first passage through the liver (first-pass effect).

Diclofenac becomes bound to serum proteins to the extent of 99.7%, chiefly to albumin (99.4%).

The total systemic clearance of diclofenac in plasma is $263 \pm 56$ml/minute (mean value ± SD). The terminal half-life in plasma is 1 to 2 hours.

After administration of diclofenac for 15 days in an oral dose of 25 mg three times daily, there was no evidence of the drugs accumulation in plasma.

In a study in 16 patients with rheumatoid arthritis and knee joint effusions it was found that diclofenac enters the synovial fluid where maximum concentrations were measured 2 to 4 hours after oral administration. The apparent half-life for elimination from the synovial fluid was 3 to 6 hours. Only 4 to 6 hours after administration, therefore, concentrations of the active substance were already higher in the synovial fluid than they were in the plasma and remained higher for up to 12 hours. These results could possibly explain why the duration of clinical effect is longer than might be inferred from the plasma half-life.

The biotransformation of diclofenac partly involves glucuronidation of the intact molecule, but mainly single and multiple hydroxylation followed by glucuronidation.
About 60% of the administered dose is excreted in the urine in the form of metabolites from one of these two processes; less than 1% is excreted as unchanged substance. The remainder of the dose is eliminated as metabolites through the bile in the faeces.

No relevant age dependent differences in the drugs absorption metabolism or excretion have been observed.

In patients suffering from renal impairment, no accumulation of the unchanged active substance could be inferred from the single dose kinetics when applying the usual dosage schedule. At a creatinine clearance of less than 10 mL/minute, the theoretical steady state plasma levels of metabolites are four times higher than in normal subjects. However, the metabolites appear to be satisfactorily cleared through the bile.

In a study of patients with impaired hepatic function (chronic hepatitis, non decompensated cirrhosis), the kinetics and metabolism of diclofenac were the same as in patients without hepatic disease.

**INDICATIONS**

Inflammatory and degenerative forms of rheumatism; rheumatoid arthritis, osteoarthritis. Relief of acute or chronic pain states in which there is an inflammatory component. Symptomatic treatment of primary dysmenorrhoea.

**CONTRAINDICATIONS**

Peptic ulcer, gastrointestinal bleeding.
Known hypersensitivity to the active substance and any of the excipients.
Last trimester of pregnancy (see Precautions, Use in pregnancy).
Severe hepatic, renal or cardiac failure (see Precautions).
Patients in whom diclofenac, aspirin or other NSAIDs induce asthma, urticaria, or other allergic-type reactions because severe, rarely fatal, anaphylactic type reactions to diclofenac have been reported in such patients.

**PRECAUTIONS**

Use with caution in the following circumstances

*Cardiovascular Thrombotic Events* – Observational studies have indicated that non-selective NSAIDS may be associated with an increased risk of serious cardiovascular events, including myocardial infarction and stroke, which may increase with dose or duration of use.
Patients with cardiovascular disease or cardiovascular risk factors may also be at greater risk. To minimize the potential risk of an adverse cardiovascular event in patients taking an NSAID, especially in those with cardiovascular risk factors, the lowest effective dose should be used for the shortest possible duration (see Dosage and Administration).
There is no consistent evidence that the concurrent use of aspirin mitigates the possible increased risk of serious cardiovascular thrombotic events associated with NSAID use.

_Hypertension_ - NSAIDs may lead you to the onset of new hypertension or worsening of pre-existing hypertension and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals thereafter.

_Heart failure_ – Fluid retention and oedema have been observed in some patients taking NSAIDs, including diclofenac, therefore caution is advised in patients with fluid retention or heart failure.

_Gastrointestinal effects_ - All NSAIDS can cause gastrointestinal discomfort and serious, potentially fatal gastrointestinal effects such as ulcers, bleeding and perforation which may increase with dose or duration of use, but can occur at any time without warning. Studies to date have not identified any subset of patients who are not at risk of developing these problems. Upper GI ulcers, gross bleeding or perforation caused by NSAIDs including diclofenac, occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. These trends continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short term therapy is not without risk.

Close medical surveillance during treatment with DICLOFENAC-GA is imperative in patients with symptoms indicative of gastrointestinal disorders or with a history suggestive of gastrointestinal ulceration, bleeding or perforation (see Adverse Effects). The risk of GI bleeding is higher with increasing NSAID doses and in patients with the history of ulcer, particularly if complicated with haemorrhage or perforation and in the elderly. Close medical surveillance and caution should be exercised in patients with ulcerative colitis or with Crohn's disease, as well as in patients suffering from severe impairment of hepatic function or with pre-existing dyshaemopoeisis or disorders of blood coagulation, as their condition may be exacerbated (see Adverse Effects).

Gastric or duodenal ulceration and gastrointestinal bleeding have been reported in patients receiving diclofenac. Studies to date have not identified any subset of patients who are not at risk of developing these problems. Except for a history of serious gastrointestinal events and other risk factors known to be associated with gastrointestinal ulceration, such as alcoholism, smoking, etc. no risk factors (eg age, sex) have been associated with increased risk.

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. Gastrointestinal bleeding or ulcerations/perforations in general have more serious consequences in the elderly. They can occur at any time during treatment with or without warning symptoms or a previous history. Where gastrointestinal bleeding or ulcerations occur in patients receiving diclofenac, the drug should be withdrawn immediately. Physicians should warn patients about the signs and symptoms of serious gastrointestinal toxicity and what steps to take if they occur.
Combination therapy with protective agents (e.g. proton pump inhibitors or misoprostol) 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.

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, e.g. systemic corticosteroids, anticoagulants, antiplatelet agents or selective serotonin reuptake inhibitors (see Precautions - Interactions With Other Medicines).

Skin reactions – Severe 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, including DICLOFENAC-GA (see Adverse Effects). 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. DICLOFENAC-GA should be discontinued at the first appearance of skin rash, mucosal lesions or any other sign of hypersensitivity, and Diclofenac should be discontinued.

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 NSAIDs 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. This is applicable as well for patients who are allergic to other substances, e.g. with skin reactions, pruritus or urticaria.

Hepatic function - Close medical surveillance is required when prescribing DICLOFENAC-GA to patients with impaired hepatic function, as their condition may be exacerbated (see Contraindications).

As with other NSAIDs, including diclofenac, elevations of one or more hepatic enzymes may occur during diclofenac therapy. These laboratory abnormalities may progress, remain unchanged, or revert to normal despite continued therapy. Borderline elevations (i.e. 1.2 to 3 times the upper limit of normal), or greater elevations of Transaminases occurred in about 15% of diclofenac treated patients. In clinical trials, meaningful elevations (i.e. more than 3 times the upper limit of normal) of AST and/or ALT occurred in about 4% of patients treated for several months, including marked elevations (i.e. more than 8 times the upper limit of normal) in about 1% of patients. Transaminase elevations were seen more frequently in patients with osteoarthritis than in those with rheumatoid arthritis (see Adverse Effects).

Transaminase elevations were reversible on cessation of therapy, and even among patients with marked elevations, signs and symptoms of hepatic disease occurred only in isolated cases. Most patients with borderline elevations did not have therapy interrupted, and transaminase elevations in most of these cases disappeared or did not progress. There were no identifying features to distinguish those patients who developed marked elevations from those who did not.
In addition to the enzyme elevations seen in clinical trials, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, have been reported.

Severe hepatotoxicity may develop without prodromal symptoms, so transaminases should be measured periodically in patients receiving long-term therapy with diclofenac. The optimum times for making the measurements are not known. In most patients who have developed marked transaminase elevations, abnormal tests occurred during the first 2 months of therapy with diclofenac. Based on this experience the first transaminase measurement should be made no later than 8 weeks after the start of diclofenac treatment. As with other NSAIDs, including diclofenac, if abnormal liver tests persist or worsen, if clinical signs and/or symptoms consistent with hepatic disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash) diclofenac should be discontinued.

To minimise the possibility of hepatic injury becoming severe between transaminase measurements, physicians should inform patients of the warning signs and symptoms of hepatotoxicity (e.g. nausea, fatigue, lethargy, pruritus, jaundice, abdominal tenderness in the right upper quadrant and flu-like symptoms) and the appropriate action to take should these signs and symptoms appear.

Caution should be exercised when using diclofenac in patients with hepatic porphyria, since diclofenac may trigger an attack.

**Kidney** – As a class, NSAIDs have been associated with renal papillary necrosis and other pathology during long-term administration in animals. Fluid retention and oedema have been reported in association with NSAID therapy including diclofenac. Owing to the importance of prostaglandins for maintaining renal blood flow, particular caution is called for in patients with impaired cardiac or renal function, history of hypertension, in the elderly, in patients being treated with diuretics or medicinal products that can significantly impact renal function and in those with extracellular volume depletion from any cause, e.g. in the peri- or postoperative phase of major surgical operations (see Contraindications). Monitoring of renal function as a precautionary measure is therefore recommended when using diclofenac in such cases. Discontinuation of therapy is typically followed by recovery to the pre-treatment state.

**Infection** – Like other NSAIDs, diclofenac may mask the usual signs and symptoms of infection due to its pharmacodynamic properties.

**Haematological effects** – Like other NSAIDs, diclofenac may temporarily inhibit platelet aggregation. Patients with haemostatic disorders should be carefully monitored.

During prolonged treatment, a slight reduction in haemoglobin has been noted in some patients. On rare occasions, blood dyscrasias have been reported. Periodic blood counts are therefore recommended.

**Perioperative bleeding** - Preoperative administration of DICLOFENAC-GA may increase the risk of postoperative bleeding. Since DICLOFENAC-GA may temporarily inhibit platelet aggregation, children undergoing minor procedures such as tonsillectomy, myringotomy, circumcision, orchidopexy and strabismus surgery should be carefully monitored.
**Hypersensitivity** – As with other NSAIDs, allergic reactions, including anaphylactic/anaphylactoid reactions, have been reported with diclofenac. These reactions can occur without earlier exposure to the drug.

**Lactose** – DICLOFENAC-GA tablets contain lactose and therefore are not recommended for patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or glucose/ galactose malabsorption.

**Use in the elderly** - In addition to the above precautions, in elderly patients who are generally more prone to side effects, particular caution should be exercised. It is recommended that the lowest effective dosage be used in elderly patients or those with a low bodyweight.

**Effects on ability to drive or use machines** - Patients experiencing visual disturbances, dizziness, vertigo, somnolence or other CNS disturbances should refrain from driving a vehicle or operating machines.

**Carcinogenicity/mutagenicity**
Dietary administration of diclofenac to mice and rats at doses up to 0.5 mg/kg/day revealed no carcinogenic activity. However, the plasma concentration of diclofenac at this dose level was 20 to 100 times lower than that in humans. Administration of higher doses to rats and mice resulted in increased mortality due to gastrointestinal ulceration. Diclofenac showed no mutagenic or carcinogenic effects in the studies conducted.

**Effects on fertility**
The use of DICLOFENAC-GA 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-GA should be considered.

**Use in pregnancy (Category C)**
NSAIDs have an inhibitory effect on prostaglandin synthesis and, when given in the latter part of pregnancy, may cause premature closure of the fetal ductus arteriosus, foetal/renal impairment, inhibition of platelet aggregation and delayed labour and birth.

The safety of diclofenac sodium in pregnancy has not been established. Therefore diclofenac should not be used in pregnant women or those likely to become pregnant unless the expected benefits are likely to outweigh any possible risk.

Use of DICLOFENAC-GA during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus (see Contraindications).

**Use in lactation**
Following oral doses of 50 mg administered every eight hours, the active substance passes into the breast milk. As with other drugs which are excreted in milk, diclofenac is not recommended for use in lactation.
Use in children
Diclofenac is not recommended for use in children as safety and efficacy in this age group have not been established.

INTERACTIONS WITH OTHER MEDICINES

Combination use of ACE inhibitors or angiotensin receptor antagonists, anti-inflammatory drugs and thiazide diuretics
The use of an ACE inhibiting drug (ACE-inhibitor or angiotensin receptor antagonist), an anti-inflammatory drug (NSAID or COX-2 inhibitor) and a thiazide diuretic at the same time increases the risk of renal impairment. This includes use in fixed-combination products containing more than one class of drug. Combined use of these medications should be accompanied by increased monitoring of serum creatinine, particularly at the institution of the combination. The combination of drugs from these three classes should be used with caution particularly in elderly patients or those with pre-existing renal impairment.

Lithium/Digoxin
When given together with preparations containing lithium or digoxin, diclofenac may raise their plasma concentrations and these concentrations should be monitored during treatment with GN-DICLOFENAC.

Diuretics
Various NSAIDs are liable to inhibit the activity of diuretics. 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. 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, ACE inhibitors or angiotensin II receptor antagonists due to the increased risk of nephrotoxicity. Concomitant treatment with potassium-sparing diuretics may be associated with increased serum potassium levels, thus making it necessary to monitor the latter (see Precautions – Kidney).

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

Other NSAIDs
Other nonsteroidal anti-inflammatory drugs and corticosteroids. The concomitant use of diclofenac 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.
Concomitant administration of systemic NSAIDs may increase the occurrence of side effects. Concurrent treatment with aspirin lowers the plasma concentration, peak plasma levels and AUC values of diclofenac. The use of both drugs concurrently is not recommended.

**Warfarin**
Caution is recommended since concomitant administration could increase the risk of bleeding (see Precautions, Gastrointestinal effects). The concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage. The exact mechanism of the interaction between NSAIDs and warfarin is unknown, but may involve enhanced bleeding from NSAID-induced gastrointestinal ulceration or an additive effect of anticoagulation by warfarin and inhibition of platelet function by NSAIDs. DICLOFENAC-GA should be used with caution in combination with warfarin and such patients should be closely monitored.

**Selective serotonin reuptake inhibitors (SSRIs)**
Concomitant administration of systemic NSAIDs including diclofenac and SSRIs may increase the risk of gastrointestinal bleeding (see Precautions, Gastrointestinal effects).

**Antidiabetics**
Diclofenac can be given together with oral antidiabetic agents without influencing their clinical effect. However there are isolated reports of both hypoglycaemic and hyperglycaemic effects in the presence of diclofenac, which necessitated changes in the dosage of hypoglycaemic agents. For this reason, monitoring of the blood glucose level is recommended as a precautionary measure during concomitant therapy.

**Methotrexate**
Caution should be exercised when NSAIDs including diclofenac are administered less than 24 hours before or after treatment with methotrexate, since the blood concentration of methotrexate may rise and the toxicity of this substance be increased.

**Cyclosporin and Glucocorticoids**
Increased nephrotoxicity of ciclosporin may occur through effects of NSAIDs including diclofenac on renal prostaglandins. Therefore, diclofenac should be given at doses lower than those that would be used in patients not receiving ciclosporin. The addition of glucocorticoids to NSAIDs, though sometimes necessary for therapeutic reasons, may aggravate gastrointestinal side effects.

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

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

**ADVERSE EFFECTS**

**Gastrointestinal.** Up to 20%: epigastric pain, other gastrointestinal disorders such as nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence, anorexia. Less than 2%:
gastrointestinal bleeding, haematemesis, melaena, peptic ulcer with or without bleeding or perforation, bloody diarrhoea. In isolated cases: lower gut disorders such as nonspecific haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn’s proctocolitis; aphthous stomatitis, glossitis, oesophageal lesions, constipation, diaphragm-like intestinal strictures, pancreatitis.

*Dermatological.* More than 1%: rashes or skin eruptions. Less than 1%: urticaria. In isolated cases: bullous eruptions, eczema, erythema multiform, Stevens-Johnson syndrome, Lyell's syndrome (acute toxic epidermolyisis), erythroderma (exfoliative dermatitis), loss of hair, photosensitivity reaction, purpura, including allergic purpura, pruritus.

*Renal.* Less than 1%: oedema
In isolated cases: acute renal failure, urinary abnormalities such as haematuria, proteinuria, interstitial nephritis, nephrotic syndrome, papillary necrosis.

*Hepatic.* Up to 2%: elevation of serum aminotransferase enzymes (ALT, AST). Less than 1%: hepatitis with or without jaundice. In isolated cases: fulminant hepatitis, hepatic necrosis, hepatic failure.

*Central nervous system.* More than 1%: headache, dizziness or vertigo. Less than 1%: drowsiness. In isolated cases: disturbances of sensation, including paraesthesia, memory disturbance, disorientation, disturbances of vision (blurred vision, diplopia), impaired hearing, tinnitus, insomnia, irritability, convulsions, depression, anxiety, nightmares, tremor, psychotic reactions, taste alteration disorders, cerebrovascular accident, myoclonic encephalopathy (described in two patients), aseptic meningitis.

*Haematological.* In isolated cases: thrombocytopenia, leucopenia, anaemia (haemolytic anaemia, aplastic anaemia), agranulocytosis, positive Coombs' test.

*Hypersensitivity.* Less than 1% bronchospasm; anaphylactic/anaphylactoid systemic reactions, including hypotension.
In isolated cases: vasculitis, pneumonitis.

*Other.* In isolated cases: impotence (association with diclofenac intake is doubtful), palpitation, chest pain, hypertension, cardiac failure, myocardial infarction, congestive heart failure, asthma. Toxic shock syndrome has been reported in patients administered NSAIDs postoperatively.

**DOSAGE AND ADMINISTRATION**
Initial dosage is 75 to 150 mg daily. For long-term therapy, 75 to 100 mg daily is usually sufficient. The daily dose should generally be prescribed in two or three divided doses.

In primary dysmenorrhoea the daily dosage, which should be individually adapted, is generally 50 to 150 mg. Initially, a dose of 50 to 100 mg should be given and, if necessary, raised in the course of several menstrual cycles up to a maximum of 200 mg/day. Treatment should be started upon appearance of the first symptoms and, depending on the symptomatology, continued for a few days.
The tablets should be swallowed whole with liquid.

**OVERDOSE**

Symptoms: There is no typical clinical picture resulting from an overdosage of diclofenac.

Treatment: Management of acute poisoning with NSAIDs including diclofenac consists essentially of supportive and symptomatic measures. Overdosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible. The therapeutic measures to be taken in cases of overdosage are as follows. Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.

Supportive and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal irritation and respiratory depression. Haematological and biochemical parameters, and the presence or absence of blood in the stools, should be monitored.

Specific therapies such as forced diuresis, dialysis or haemoperfusion are probably of no help in eliminating nonsteroidal antirheumatic agents, because of their high protein binding rate and extensive metabolism.

Contact the Poisons Information Centre (Telephone no: 131126) for advice on management of overdosage.

**PRESENTATION AND STORAGE CONDITIONS**

Tablets.

- 25 mg (enteric coated) blister of 50
- 50 mg (enteric coated) blister of 50

Store below 25 degrees Celsius

**POISON SCHEDULE OF THE MEDICINE**

S4

**NAME AND ADDRESS OF THE SPONSOR**

Ascent Pharma Pty Ltd
151-153 Clarendon Street
South Melbourne
VIC 3205
www.ascentpharma.com.au
Date of TGA Approval: 31 March 2008
Date of most recent amendment: 24 January 2011.