

^{Rx}Paracetamol, Diclofenac Sodium & Chlorzoxazone Tablets

Dicloran[®] MR

COMPOSITION

Each uncoated tablet contains :

Paracetamol IP.....	325 mg
Diclofenac Sodium IP.....	50 mg
Chlorzoxazone USP.....	500 mg
Colour : Red Oxide of Iron	

PHARMACEUTICALFORM

Uncoated tablet

THERAPEUTIC INDICATION

In the treatment of acute painful musculoskeletal conditions.

DOSAGE AND ADMINISTRATION

Posology

Three recommended dose is 1-2 tablets a day or as directed by the Physician.

Method of administration: Fororal administration only.

CONTRAINDICATIONS

Known hypersensitivity to the active substance or to any of the excipients. Active gastric or intestinal ulcer, bleeding or perforation.

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

Active, or history of recurrent peptic ulcer/haemorrhage or perforation (two or more distinct episodes of proven ulceration or bleeding).

Last trimester of pregnancy Severe hepatic, renal or cardiac failure.

Like other non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac is also contraindicated in patients in whom attacks of asthma, angioedema, urticaria, or acute rhinitis are precipitated by ibuprofen, acetylsalicylic acid or other NSAIDs.

Established congestive heart failure (NYHA-II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Paracetamol

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Patients should be advised that paracetamol may cause severe skin reactions. If a skin reaction such as skin reddening, blisters, or rash occurs, they should stop use and seek medical assistance right away.

Diclofenac

General

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms. 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.

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 nonsteroidal anti-inflammatory drugs including diclofenac, allergic reactions, including anaphylactic/anaphylactoid reactions, can also occur without earlier exposure to the drug. 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 may mask the signs and symptoms of infection due to its Pharmacodynamic properties.

Gastrointestinal effects

Gastrointestinal bleeding (haematemesis, melaena), ulceration or the 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 GI 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.

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.

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 such as warfarin, selective serotonin-reuptake inhibitors (SSRIs) or anti-platelet agents such as acetylsalicylic acid.

Hepatic impairment

Close medical surveillance is required when prescribing diclofenac to patients with impairment of 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, clinical signs or symptoms consistent with liver disease develop, or if other manifestations occur (eosinophilia, rash), diclofenac should be discontinued. Caution is called for when using diclofenac in patients with hepatic porphyria, since it may trigger an attack.

Renal impairment

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, 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 4.3). Monitoring of renal function is recommended as a precautionary measure when using diclofenac in such cases.

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, including diclofenac. Diclofenac sodium tablets should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.

Cardiovascular and cerebrovascular effects

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. 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.

Hematological effects

During prolonged treatment with diclofenac, as with other NSAIDs, monitoring of the blood count is recommended. Diclofenac may reversibly inhibit platelet aggregation. Patients with defects of hemostasis, bleeding diathesis or hematological 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 I 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.

Female fertility

The use of Diclofenac may impair female fertility and is not recommended in women attempting to conceive. In women who may have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of Diclofenac should be considered.

Chlorzoxazone

Serious (including fatal) hepatocellular toxicity has been reported rarely in patients receiving chlorzoxazone. The mechanism is unknown but appears to be idiosyncratic and unpredictable. Factors predisposing patients to this rare event are not known. Patients should be instructed to report early signs and/or symptoms of hepatotoxicity such as fever, rash, anorexia, nausea, vomiting, fatigue , right upper quadrant pain, dark urine, or jaundice. Chlorzoxazone should be discontinued immediately and a physician consulted if any of these signs or symptoms develop. Chlorzoxazone use should also be discontinued if a patient develops abnormal liver enzymes (e.g., AST, ALT, alkaline phosphatase and bilirubin). The concomitant use of alcohol or other central nervous system depressants may have an additive effect.

DRUG INTERACTIONS

Concomitant administration of Paracetamol, Diclofenac & Chlorzoxazone Tablet should be avoided with barbiturates, carbamazepine, hydantoins, rifampicin, sulfinpyrazone, methotrexate, cyclosporine, lithium and warfarin. Lithium: If used concomitantly, diclofenac may raise plasma concentrations 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. Diuretics and Anti hypertensive 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 via inhibition of vasodilatory prostaglandin synthesis. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity. 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. Other NSAIDs including cyclo-oxygenase-2 selective inhibitors and corticosteroids: Concomitant administration of diclofenac and other systemic NSAIDs or corticosteroids may increase the risk of gastrointestinal bleeding or ulceration. Avoid concomitant use of two or more NSAIDs. 6 7 Anticoagulants and anti-platelet agents: Caution is recommended since concomitant administration could increase the risk of bleeding. 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 NSAIDs, diclofenac in 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. 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 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. Ciclosporin: Diclofenac, like other NSAIDs, may increase the risk of 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. Mifepristone: NSAIDs should not be used for B-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone. Quinolone antimicrobials: There have been isolated reports of convulsions which may have been due to concomitant use of quinolones and NSAIDs. 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 cholestyr amine: 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 8 significant increase in peak plasma concentration and exposure to diclofenac due to inhibition of diclofenac metabolism. Tacrolimus: Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostaglandin effects of both NSAID and calcineurin. Cardiac glycosides: Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure , reduce GFR and increase plasma glycoside levels. 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. Metoclopramide and Domperidone: The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided. Chloramphenicol: Increased plasma concentration of chloramphenicol.

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 postimplantation 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. During the first and second trimester of pregnancy, diclofenac sodium tablets 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. During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to: cardiopulmonary toxicity (with premature closure of the ductus arteriosus and pulmonary hypertension);

renal dysfunction, which may progress to renal failure with oligo-hydroamniosis; the mother and the neonate, at the end of pregnancy, to: possible prolongation of bleeding time, an anti-aggregating effect which mayoccurrereven at very low doses.

inhibition of uterine contractions resulting in delayed or prolonged labour. Consequently, diclofenac sodium tablets are contraindicated during the third trimester of pregnancy.

Lactation

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. 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.

UNDESIRABLE EFFECTS

Paracetamol

Fixed drug eruption (FOE) has been reported with Paracetamol

Adverse effects of paracetamol are rare. Very rare cases of serious skin reactions have been reported. There have been reports of blood dyscrasias including thrombocytopenia purpura, methaemoglobaemia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Diclofenac

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: very common: (>1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥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/long-term use.

Common

Nausea , vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia, headache, dizziness, vertigo, transaminases increased, rash.

Uncommon

Myocardial infarction, cardiac failure, palpitations, chest pain.

Rare

Hypersensitivity, somnolence, gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly), tiredness, urticaria, anaphylactic and anaphylactoid reactions (including hypotension and shock), asthma (including dyspnoea), hepatitis, jaundice, liver disorder, oedema.

Veryrare

Thrombocytopenia, leucopenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis, angioneurotic oedema (including face oedema), 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, disorientation, depression, insomnia, nightmare, 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, irritability, psychotic disorder, paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident, visual disturbance, vision blurred, diplopia, tinnitus, hearing impaired, hypertension, hypotension, vasculitis, pneumonitis, fulminant hepatitis, hepatic necrosis , hepatic failure, acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis, impotence.

Unknown

Confusion, hallucinations, disturbances of sensation, malaise, optic neuritis, kounis syndrome, ischaemic colitis.

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 (150 mg daily)and in long term treatment.

Chlorzoxazone

Occasional patients may develop gastrointestinal disturbances. It is possible in rare instances that chlorzoxazone may have been associated with gastrointestinal bleeding. Drowsiness, dizziness, lightheadedness, malaise, or overstimulation may be noted by an occasional patient. Rarely, allergic-type skin rashes, petechiae, or ecchymoses may develop during treatment. Angioneurotic edema or anaphylactic reactions are extremely rare. There is no evidence that the drug will cause

renal damage. Rarely, a patient may note discoloration of the urine resulting from a phenolic metabolite of chlorzoxazone. This finding is of no known clinical significance.

Reporting of suspected adverse reactions: Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Kindly report any suspected adverse reactions to pharmavigil@jbpharma.com

OVERDOSE

Paracetamol

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk factors:

If the patient a, Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes. Or b, regularly consumes ethanol in excess of recommended amounts. Or c , Is likely to beglutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms:

Symptoms of paracetamol overdose in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Management:

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours' post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24 h from ingestion should be discussed with the NPIS or a liver unit.

Diclofenac

Symptoms

There is no typical clinical picture resulting from diclofenac overdose. Over dosage can cause symptoms such as headache, nausea, vomiting, epigastric pain, gastrointestinal haemorrhage, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In the case 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 haemoperfusion are probably of no help in eliminating NSAIDs, including diclofenac, due to the high protein binding and extensive metabolism. Activated charcoal may be considered after ingestion of a potentially toxic overdose, and gastric decontamination (e.g. vomiting, gastric lavage) after ingestion of a potentially life threatening overdose.

Chlorzoxazone

Symptoms

Initially, gastrointestinal disturbances such as nausea, vomiting, or diarrhea together with drowsiness, dizziness, light-headedness or headache may occur. Early in the course there may be malaise or sluggishness followed by marked loss of muscle tone making voluntary movement impossible. The deep tendon reflexes may be decreased or absent. The sensorium remains intact, and there is no peripheral loss of sensation. Respiratory depression may occur with rapid, irregular respiration and intercostal substernal retraction. The blood pressure is lowered, but shock has not been observed.

Treatment

Gastric lavage or induction of emesis should be carried out, followed by administration of activated charcoal. Thereafter, treatment is entirely supportive. If respirations are depressed, oxygen and artificial respiration should be employed and a patent airway assured by use of an oropharyngeal airway or endotracheal tube. Hypotension may be counteracted by use of dextran, plasma, concentrated albumin or a vasopressor agent such as norepinephrine. Cholinergicdrugs or analeptic drugs are of no value and should not be used.

PHARMACOLOGICALPROPERTIES

PHARMACODYNAMIC PROPERTIES

Paracetamol

Paracetamol is an analgesic and antipyretic.

Diclofenac

Pharmacotherapeutic group: Non-steroidal anti-inflammatory drugs (NSAIDs).

Diclofenac is a phenylacetic acid derivative and non-steroidal anti-inflammatory drug (NSAID). NSAIDs inhibit cyclooxygenase (COX)-1 and-2 which are the enzyme responsible for producing prostaglandins (PGs). PGs contribute to inflammation and pain signaling. Diclofenac reduces inflammation and by extension reduces nociceptive pain and combats fever.

Diclofenac sodium in vitro does not suppress proteoglycan biosynthesis incartilage at concentrations equivalent to the concentrations reached in human beings.

Chlorzoxazone

Chlorzoxazone is a centrally acting agent for painful musculoskeletal conditions. Data available from animal experiments as well as human study indicate that chlorzoxazone acts primarily at the level of the spinal cord and subcortical areas of the brain where it inhibits multisynaptic reflex arcs involved in producing and maintaining skeletal muscle spasm of varied etiology. The clinical result is a reduction of the skeletal muscle spasm withrelief of pain and increased mobility of the involved muscles.

PHARMACOKINETIC PROPERTIES

Paracetamol

Paracetamol is readily absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine, mainly as glucuronide and sulphate conjugates.

Diclofenac

Absorption

Absorption is complete but onset is delayed until passage through the stomach, which may be affected by food which delays stomach emptying. The mean peak plasma diclofenac concentration reached at about 2 hours (50mg dose produces 1511 ± 466 ng/ml).

Distribution

The active substance is 99.7% protein bound, mainly to albumin (99.4%). Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after the peak plasma values have been attained. Diclofenac was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose.

Metabolism

Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Elimination

The total systemic clearance of diclofenac in plasma is 263 ± 56 mL/min (mean value $\pm$ SD). The terminal half-life in plasma is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. About 60% of the administered dose is excreted in the urine in the form of the glucuronide conjugate of the intact molecule and as metabolites, most of which are also converted to glucuronide conjugates. Less than 1% is excreted as unchanged substance. The rest of the dose is eliminated as metabolites through the bile in the faeces.

Chlorzoxazone

Blood levels of chlorzoxazone can be detected in people during the first 30 minutes and peak levels may be reached, in the majority of the subjects, in about 1 to 2 hours after oral administration of chlorzoxazone. Chlorzoxazone is rapidly metabolized and is excreted in the urine, primarily in a conjugated form as the glucuronide. Less than one percent of a dose of chlorzoxazone is excreted unchanged in the urine in 24 hours.

INCOMPATIBILITY

Not known.

STORAGE CONDITIONS

Store protected from light & moisture, at a temperature not exceeding 30°C.

Keep out of reach of children.



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Note: This prescribing information is applicable for India Market only

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