For the use of a Registered Medical Practitioner or a Hospital or a Laboratory or a Specialist only

℞

Diclofenac Sodium and Paracetamol Tablets IP

Diclosal™-P 50 mg + 325 mg

COMPOSITION
Each uncoated tablet contains :
Diclofenac Sodium IP.....50 mg
Paracetamol IP .....325 mg

DOSAGE FORM
Uncoated Tablet

THERAPEUTIC INDICATION
Indicated for the symptomatic treatment of acute pain and inflammation in patients with osteoarthritis, rheumatoid arthritis and ankylosing spondylitis.

DOSGAE AND METHOD OF ADMINISTRATION
Posology
The recommended dose is 1 tablet to be taken with food, two or three times daily or as directed by the Physician.
Method of administration: For oral administration only.
Patient should be advised to swallow the tablet whole, not be chewed or crushed.

CONTRAINDICATIONS
The Paracetamol/diclofenac tablets are contraindicated in patients with the following conditions:
- Hypersensitivity to diclofenac and/ or paracetamol and/or other constituents.
- Patients with active peptic ulcer/haemorrhage or perforation or who have active GI bleeding or other active bleedings, e.g. cerebrovascular bleedings.
- Pregnant women and in women planning a pregnancy.
- Women of childbearing potential who are not using effective contraception
- Patients with a known hypersensitivity to diclofenac, acetylsalicylic acid, other NSAIDs, misoprostol, other prostaglandins, or any other ingredient of the product.
- Patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or other NSAIDs.
- Treatment of peri-operative pain in the setting of CABG surgery.
- Patients with severe renal and hepatic failure.
- Established congestive heart failure (NYHA II–IV), ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Black Box Warning
Cardiovascular Risk
Non-steroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction and stroke, which can be fatal. This risk may increase with duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk. Diclofenac Potassium tablets are contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.
Gastrointestinal Risk
NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events, including inflammation, bleeding, ulceration and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious GI events.
Paracetamol
Warning
Taking more than daily dose may cause serious liver damage or allergic reactions (e.g. swelling of the face, mouth and throat, difficulty in breathing, itching or rash).
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.
Do not take with any other paracetamol-containing products. If symptoms persist for more than 3 days or get worse consult with the physician.
Do not exceed the recommended dose.
Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.
Hepatotoxicity
Acetaminophen (Paracetamol) has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4,000 milligrams per day, and often involve more than one acetaminophen-containing product.
Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index are chronic heavy users of alcohol or have sepsis. In patients with glutathione depleted states the use of paracetamol may increase the risk of metabolic acidosis.
Paracetamol should be given with care to patients with impaired kidney or liver function.
Where analgesics are used long-term (>3 months) with administration every two days or more frequently, headache may develop or worsen. Headache induced by overuse of analgesics (MOH medication-overuse headache) should not be treated by dose increase. In such cases, the use of analgesics should be discontinued in consultation with the doctor.
Care is advised in the administration of paracetamol to patients with alcohol dependency, severe renal or severe hepatic impairment. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
Acetaminophen provides symptomatic relief only, additional therapy to treat the cause of the pain or fever should be instituted when necessary.
Diclofenac
Paracetamol/diclofenac tablets cannot be expected to substitute for corticosteroids or to treat corticosteroid insufficiency. Abrupt discontinuation of corticosteroids may lead to disease exacerbation. Patients on prolonged corticosteroid therapy should have their therapy tapered slowly if a decision is made to discontinue corticosteroids.
The pharmacological activity of Paracetamol/diclofenac tablets in reducing fever and inflammation may diminish the utility of these diagnostic signs in detecting complications of presumed non-infectious, painful conditions.
The use of Paracetamol/diclofenac tablets with concomitant systemic NSAIDs, including COX-2 inhibitors, should be avoided, except in patients requiring low-dose acetylsalicylic acid – caution is advised in such patients along with close monitoring. Concomitant use of a systemic NSAID and another systemic NSAID may increase the frequency of gastrointestinal ulcers and bleeding.
Undesirable effects may be minimized 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 non-steroidal anti-inflammatory drugs (NSAIDs) 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 Potassium 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, and 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.
Haematological 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 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 Potassium 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.

DRUG INTERACTIONS
Paracetamol
The hepatotoxicity of Paracetamol, particularly after overdosage, may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, and alcohol.
Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolize large doses of paracetamol, the plasma half-life of which can be prolonged.
Cholestyramine
The speed of absorption of paracetamol is reduced by cholestyramine. Therefore, the cholestyramine should not be taken within one hour if maximal analgesia is required.
Metoclopramide and Domperidone
The absorption of paracetamol is increased by metoclopramide and domperidone. However, concurrent use need not be avoided.
Imatinib
Restriction or avoidance of concomitant regular paracetamol use should be taken with imatinib.
Warfarin
The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Chloramphenicol
Increased plasma concentration of chloramphenicol.
Antivirals
Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).
The use of drugs that induce hepatic microsomal enzymes such as anticonvulsants and oral contraceptives may increase the extent of metabolism of paracetamol resulting in reduced plasma concentrations of the drug and a faster elimination rate.
Diclofenac
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. 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, 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, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.
Drugs known to cause hyperkalemia
Concomitant treatment with potassium-sparing diuretics, ciclosporin, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored frequently.
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. Therefore, to be certain that no change in anticoagulant dosage is required, close monitoring of such patients is required. As with other nonsteroidal anti-inflammatory agents, diclofenac in high dose can reversibly inhibit platelet aggregation.
Other NSAIDS including cyclo-oxygenase-2selective inhibitors and corticosteroids
Co-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.
Selective serotonin reuptake inhibitors (SSRIs)
Concomitant administration of SSRIs may increase the risk of gastrointestinal bleeding.
Antidiabetics
There have been isolated reports of 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 advised when NSAIDs, including diclofenac, are administered less than 24 hours before treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increased. Interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of NSAIDs.
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.
Tacrolimus
Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus. This might be mediated through renal antiprostagladin effects of both NSAID and calcineurin inhibitor.
Quinolone antimicrobials
Convulsions may occur due to an interaction between 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 concomitant use.
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 4-6 hours after administration of colestipol/cholestyramine.
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.
Potent CYP2C9 inhibitors
Caution is recommended when co-prescribing the diclofenac with potent CYP2C9 inhibitors (such as sulfinpyrazone and voriconazole), which could result in a significant increase in peak plasma concentration and exposure to diclofenac due to inhibition of diclofenac metabolism.

USE IN SPECIAL POPULATION
Paracetamol
Pregnancy
A large amount of data on pregnant women indicates neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.
It is considered to be the analgesic of choice in pregnant patients. Although it crosses placenta, paracetamol is considered to be safe in normal therapeutic doses for short-term use as a minor analgesic/antipyretic in pregnancy.
Lactation
It is not recommended for use by lactating mothers. It is excreted in breast milk. Maternal ingestion of paracetamol in normal therapeutic doses does not appear to present a risk to the nursing infant. Available published data do not contraindicate breast feeding.
Labour and Delivery
In rat studies with NSAIDs, as with other drugs known to inhibit prostaglandin synthesis, an increased incidence of dystocia, delayed parturition, and decreased pup survival occurred. The effects of diclofenac on labour and delivery in pregnant women are unknown.
Lactating Women
It is not known whether diclofenac is excreted in human milk. Paracetamol is excreted in breast milk but not in clinically significant amount. Available published data do not contraindicate breastfeeding. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from Paracetamol/diclofenac tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
Paediatric Patients
Safety and effectiveness in paediatric patients have not been established.
Geriatric Patients
As with any NSAIDs; caution should be exercised in treating the elderly (65 years of age and older).
Diclofenac
Teratogenic Effects: Pregnancy Category C.
Reproductive studies conducted in rats and rabbits have not demonstrated evidence of developmental abnormalities. However, animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women.
Non-Teratogenic Effects: Because of the known effects of NSAIDs on the foetal CV system (closure of ductus arteriosus), use during pregnancy (particularly late pregnancy) should be avoided.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
Patients who experience dizziness or other central nervous system disturbances while taking NSAIDs should refrain from driving or operating machinery.

UNDESIRABLE EFFECTS
Paracetamol
Fixed drug eruption (FDE) has been reported with Paracetamol
The information below lists reported adverse reactions, ranked using the following frequency classification: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).
Immune System Disorders
Hypersensitivity, including skin rash, may occur. Not Known: anaphylactic shock, angio-oedema.
Blood and Lymphatic System Disorders
Not Known: blood dyscrasias, including thrombocytopaenia and agranulocytosis.
Skin and Subcutaneous Disorders
Very rare cases of serious skin reactions such as toxic epidermal necrolysis, Stevens-Johnson syndrome, acute generalised exanthematous pustulosis, and fixed drug eruption have been reported.
Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage. Allergic reactions occur occasionally.
Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods.
A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal. Low level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol; these are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol.
Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.
Post-marketing data:
Blood and lymphatic system disorders
Very rare: Thrombocytopaenia.
Immune System disorders:
Very rare: Anaphylaxis cutaneous hypersensitivity reactions including, among others, skin rashes, angioedema, Stevens-Johnson syndrome and Toxic Epidermal Necrolysis.
Hepatobiliary disorders
Very rare: Hepatic dysfunction.
Respiratory, thoracic and mediastinal disorders
Very rare: Bronchospasm in patients sensitive to aspirin and other NSAIDs.
Diclofenac
In patients taking diclofenac Potassium tablets, or other NSAIDs, the most frequently reported adverse experiences occurring in approximately 1–10% of patients are as follows:
GI Events
These include abdominal pain, constipation, diarrhoea, dyspepsia, flatulence, gross bleeding / perforation, heartburn, nausea, GI ulcers (gastric/duodenal) and vomiting.
Other
Abnormal renal function, anaemia, dizziness, oedema, elevated liver enzymes, headaches, increased bleeding time, pruritus, rashes and tinnitus.
Additional adverse experiences reported occasionally include the following:
Body as a Whole
fever, infection, sepsis.
CV System
congestive heart failure, hypertension, tachycardia, syncope.
Digestive System
dry mouth, oesophagitis, gastric/peptic ulcers, gastritis, GI bleeding, glossitis, haematemesis, hepatitis, jaundice.
Haemic and Lymphatic System
ecchymosis, eosinophilia, leucopaenia, melaena, purpura, rectal bleeding, stomatitis, thrombocytopaenia.
Metabolic and Nutritional
weight changes.
Nervous System
anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paraesthesia, somnolence, tremors, vertigo.
Respiratory System
asthma, dyspnoea.
Skin and Appendages
alopecia, photosensitivity, sweating increased.
Special Senses:
blurred vision.
Urogenital System
cystitis, dysuria, haematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure.
Other adverse reactions, which occur rarely, are as follows:
Body as a Whole
anaphylactic reactions, appetite changes, death.
CV System
arrhythmia, hypotension, myocardial infarction, palpitations, vasculitis.
Digestive System
colitis, eructation, fulminant hepatitis with and without jaundice, liver failure, liver necrosis, pancreatitis.
Haemic and Lymphatic System
agranulocytosis, haemolytic anaemia, aplastic anaemia, lymphadenopathy, pancytopaenia.
Metabolic and Nutritional
hyperglycaemia.
Nervous System
convulsions, coma, hallucinations, meningitis.
Respiratory System
respiratory depression, pneumonia.
Skin and Appendages
angio-oedema, toxic epidermal necrolysis, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria
Special Senses
conjunctivitis, hearing impairment
Nicolau's syndrome, also known as livedo-like dermatitis or embolia cutis medicamentosa, is a rare complication reported following intramuscular diclofenac Potassium injection.
Reporting of side effects or suspected adverse reaction: If you experience any side effects, talk to your doctor or pharmacist or report to indiadrugsafety@akums.in. You can also report side effects directly by calling on toll free no. **1800-313-3363**. By reporting side effects, you can help provide more information on the safety of this product.

OVERDOSE
Paracetamol
Liver damage is possible in adults who have taken 10g or more of paracetamol. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors.
Symptoms of paracetamol overdosage 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.
Treatment: In cases of overdose, methods of reducing the absorption of ingested drug are important. Gastric lavage is essential even if several hours have elapsed. Prompt administration of 50g activated charcoal and 500ml iced mannitol 20% by mouth, may reduce absorption. If the history suggests that 15g Paracetamol or more has been ingested, administer one of the following antidotes:
Administer intravenously, 20% acetlcysteine immediately without waiting for positive urine test or plasma level results: initial dose of 150mg/kg over 15 minutes, followed by continuous infusion of 50mg/kg in 500ml 5% glucose/dextrose over 4 hours and 100mg/kg in 1L 5% glucose/dextrose over 16 hours; or
Oral Methionine 2.5g; immediately followed by three further doses of 2.5g at four hourly intervals. For a 3 year old child, 1g methionine every four hours for four doses has been used; or
Oral Acetylcysteine (5%): 140mg/kg as a loading dose, then 70mg/kg every 4 hours for a total of 17 maintenance doses. If more than ten hours have elapsed since the overdosage was taken, the antidote may be in ineffective.
Diclofenac
Symptoms: There is no typical clinical picture resulting from diclofenac over dosage. 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 haemo-perfusion 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.

PHARMACOLOGICAL PROPERTIES
Mechanism of action
Paracetamol/Diclofenac tablets contain diclofenac Potassium and paracetamol. Diclofenac Potassium is a NSAID (non-steroidal anti-inflammatory drug) that exhibits anti-inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of diclofenac Potassium, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition. Paracetamol has analgesic and antipyretic actions.
Pharmacodynamic properties
Pharmacotherapeutic group: Non-steroidal anti-inflammatory drugs (NSAIDs).
Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (specifically COX-2) and, to a lesser extent, through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitize pain receptors to mechanical or chemical stimulation. Paracetamol act centrally on the hypothalamic heat-regulating center to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. Paracetamol reduces fever by inhibiting the formulation and release of prostaglandins in the CNS and by inhibiting endogenous pyrogens at the hypothalamic thermo-regulator center.Diclofenac Potassium is a NSAID that has been shown to have anti-inflammatory and analgesic properties and is effective in treating the signs and symptoms of arthritic conditions.
Paracetamol is an aniline derivative with analgesic and antipyretic actions similar to those of aspirin, but with no demonstrable anti-inflammatory activity. The mechanism of analgesic action has not been fully determined.
Pharmacokinetic properties
Paracetamol
Paracetamol is readily absorbed from the GI tract, with peak plasma levels occurring about 30 minutes to 2 hours after ingestion.
It is metabolised in the liver (90–95%) and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted unchanged.
The elimination half-life of paracetamol varies from about 1 to 4 hours. Plasma protein-binding is negligible at usual therapeutic doses but increases with increasing concentrations.
A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine), which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione, may accumulate following paracetamol overdosage and cause liver damage.
The time to peak plasma concentration of paracetamol is 0.5-2 hours, the time to peak effect 1-3 hours, and the duration of action is 3-4 hours.
Diclofenac
Absorption
Diclofenac is 100% absorbed after oral administration compared to intravenous (IV) administration as measured by urine recovery. However, due to first-pass metabolism, only about 50% of the absorbed dose is systemically available. Food has no significant effect on the extent of diclofenac absorption. However, there is usually a delay in the onset of absorption of 1-4.5 hours and a reduction in peak plasma levels of <20%.
Distribution
The apparent volume of distribution (V/F) of diclofenac Potassium is 1.4 L/kg. Diclofenac is more than 99% bound to human serum proteins, primarily to albumin. Serum protein-binding is constant over the concentration range (0.15–105 µg/mL) achieved with recommended doses. Diclofenac diffuses into and out of the synovial fluid. Diffusion into the joint occurs when plasma levels are higher than those in the synovial fluid, after which the process reverses and synovial fluid levels are higher than plasma levels. It is not known whether diffusion into the joint plays a role in the effectiveness of diclofenac.
Metabolism
Five diclofenac metabolites have been identified in human plasma and urine. The metabolites include 4'-hydroxy-, 5-hydroxy-, 3'-hydroxy-, 4',5-dihydroxy- and 3' hydroxy-4'-methoxy-diclofenac. The major diclofenac metabolite, 4'-hydroxy-diclofenac, has very weak pharmacologic activity. The formation of 4'-hydroxy- diclofenac is primarily mediated by CPY2C9. Both diclofenac and its oxidative metabolites undergo glucuronidation or sulphation followed by biliary excretion. Acylglucuronidation mediated by UGT2B7 and oxidation mediated by CPY2C8 may also play a role in diclofenac metabolism. CYP3A4 is responsible for the formation of minor metabolites, 5-hydroxyand 3'-hydroxy-diclofenac. In patients with renal dysfunction, peak concentrations of the metabolites, 4'-hydroxy- and 5-hydroxy-diclofenac, were approximately 50% and 4% of the parent compound after single oral dosing compared with 27% and 1%, respectively, in normal healthy subjects.
Excretion
Diclofenac is eliminated through metabolism and subsequent urinary and biliary excretion of the glucuronide and the sulphate conjugates of the metabolites. Little or no free unchanged diclofenac is excreted in the urine. Approximately 65% of the dose is excreted in the urine and approximately 35% in the bile as conjugates of unchanged diclofenac plus metabolites. Because renal elimination is not a significant pathway of elimination for unchanged diclofenac, dosing adjustment in patients with mild-to-moderate renal dysfunction is not necessary. The terminal half-life of unchanged diclofenac is approximately 2 hours.

INCOMPATIBILITIES
Not known.

STORAGE INSTRUCTIONS
Store protected from light & moisture, at a temperature not exceeding 30°C.
Keep all medicines out of reach of children.

Warning : Not for veterinary use.

Mfg. Lic. No. : 4/UA/LL/2014

Manufactured by:
Akums Drugs & Pharmaceuticals Ltd.
At: Plot No. 26A, 27-30, Sector-8A, I.I.E.,
SIDCUL, Ranipur, Haridwar-249 403,
Uttarakhand.

Marketed by:
Mylan Pharmaceuticals Private Limited
Plot No. 564/A/22, Road No. 92,
Jubilee Hills, Hyderabad, Telangana-500096.

TM - Trademark Under Registration.

DATE OF IMPLEMENTATION
April 2026

4063557

Smartdose™ Technology

Current Version - Diclosal-P 50 mg + 325 mg_AKUMS_R0

Mylan

20297610

Diclofenac Sodium and Paracetamol Tablets IP

Diclofenac Sodium and Paracetamol Tablets IP
Diclosal™-P 50 mg + 325 mg

Product Name	Diclofenac Sodium and Paracetamol Tablets IP_R0 Diclosal™-P 50 mg + 325 mg
Strength	50 mg + 325 mg
Counts	NA
Component	Pack Insert
Design & Style	NA
Size	NA
Material Code	20297610(TWCC No. 4063557)
Supersedes Code	..
Printing Pantone No's	1 BLACK; 2 PANTONE 2603 C; 3 PANTONE 2756 C; 4 PANTONE 306 C; 5 PANTONE RED 032 C; 6 NA; 7 NA; 8 NA; 9 NA
Non Printing	1 KEYLINE; 2 INFO; 3 NA

Generic name font size: 21 pt
Brand name font size: 19 pt

TEXT SIZE CONTAINED IN THIS ARTWORK
Body text size: 5pt
Smallest text size: 5pt
Microtext: No

Reason of artwork : New (Domestic) (R0)
Substrate: 40 ±5% GSM, BIBLE PAPER with 1 Vertical & 4 Horizontal Fold as equal distance

PREPARED BY	REVIEWED BY				APPROVED BY
Marketing Dept	Packaging Development	Regulatory Affairs	Marketing Dept	Medical Affairs	Regional Quality Assurance
Signature & Date	Signature & Date	Signature & Date	Signature & Date	Signature & Date	Signature & Date

SOP-00364271O/FORM-00364273A_00