APPROVED
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of Health of Ukraine
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INSTRUCTION
for medical use

DICLOTOL®

Composition:
active ingredient: aceclofenac;
1 sachet (1 g of granules) contains aceclofenac 100 mg;
excipients: sucrose, saccharin sodium, colloidal anhydrous silica, orange flavor, hydroxypropyl methylcellulose, pregelatinized maize starch, citric acid.

Pharmaceutical form. Granules.
Basic physical and chemical properties: white to off white granules.

Pharmacotherapeutic group.
Anti-inflammatory and antirheumatic products, non-steroids. Acetic acid derivatives and related substances. ATC code M01A B16.

Pharmacological properties.
Pharmacodynamics.
Aceclofenac is a non-steroidal anti-inflammatory agent with marked anti-inflammatory and analgesic effect. The mode of action of aceclofenac is believed to be largely based on the inhibition to prostaglandin synthesis.
Pharmacokinetics.
Absorption
After oral administration, aceclofenac is rapidly absorbed, its bioavailability is almost 100%. Maximal plasma concentrations are reached approximately 1.25 to 3.00 hours following ingestion. Eating slows down absorption but does not affect its degree.
Distribution
Aceclofenac is highly bound to plasma proteins (>99.7%). Aceclofenac penetrates into the synovial fluid, where the concentration reaches about 60% of the plasma concentration. Volume of distribution is approximately 30 liters.
Elimination
The average half-life is 4–4.3 hours. The clearance is 5 liters per hour. Approximately two-third of the administered dose is excreted in the urine, preferably in the form of conjugated hydroxymetabolites. Only 1% of a single oral dose is excreted unchanged.
Aceclofenac is likely to be metabolized by CYP2C9 to the major metabolite of 4-OH aceclofenac, whose clinical effect is insignificant. Diclofenac and 4-OH-diclofenac were found among many metabolites.
Special patient groups
No changes in the pharmacokinetics of aceclofenac were found in elderly patients.
Patients with impaired liver function had a slower elimination of aceclofenac after a single dose of the drug. There were no differences in pharmacokinetic parameters between patients with

mild and moderate liver cirrhosis and healthy volunteers in studies with repeated dose of 100 mg daily.
In patients with mild or moderate renal insufficiency, clinically significant differences in pharmacokinetics were not observed after single dose administration.

Clinical particulars.
Indications.
- Osteoarthritis, rheumatoid arthritis, ankylosing spondyloarthritis and other underlying diseases of musculoskeletal system accompanied by pain (e.g., scapulohumeral periarthritis and other extra-articular manifestations of rheumatism).
- In conditions accompanied by pain (including lumbago, toothache, primary dysmenorrhea).

Contraindications.
Aceclofenac is contraindicated:
- to patients with hypersensitivity to aceclofenac or to any of the excipients (see "Composition" section);
- to patients in whom acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs) cause asthma attacks, bronchospasm, acute rhinitis, angioneurotic edema or urticaria, as well as in patients with hypersensitivity to these drugs;
- to patients with a history of gastrointestinal bleeding or perforation of an ulcer associated with previous NSAID therapy;
- to patients with accompanying peptic ulcer or bleeding, including in the anamnesis (two or more separate proven episodes of ulcer or bleeding);
- to patients with acute bleeding or diseases accompanied by bleeding (haemophilia or blood coagulation disorders);
- to patients with congestive heart failure (functional class II–IV according to NYHA), coronary heart disease, diseases of peripheral arteries or with cerebrovascular disorders;
- to patients with cerebrovascular diseases who have suffered a stroke or have episodes of transient ischemic attacks;
- to patients with coronary heart disease who have angina or have suffered a myocardial infarction;
- for the treatment of perioperative pain during coronary artery bypass grafting (or when using an artificial blood circulation device);
- to patients with severe liver or kidney failure;
- during breastfeeding;
- in the last trimester of pregnancy;
- to patients under 18 years of age.

Interaction with other medicinal products and other types of interaction.
Interaction studies have not been performed, except for interactions with warfarin.
Aceclofenac is metabolized by cytochrome P450 2C9 and *in vitro* data suggest that aceclofenac may be an inhibitor of this enzyme. Thus, the risk of pharmacokinetic interactions is possible when co-administered with phenytoin, cimetidine, tolbutamide, phenylbutazone, amiodarone, miconazole and sulfaphenazole. As with other NSAIDs, there is an increased risk of pharmacokinetic interactions with other drugs that are excreted by active renal secretion, such as methotrexate and lithium. Aceclofenac is almost completely bound to plasma albumin, so it may interact with other protein-binding drugs.
Due to the lack of pharmacokinetic interaction studies with aceclofenac, the following information is based on data from other NSAIDs.
Concurrent use should be avoided:

Methotrexate. NSAIDs inhibit tubular secretion of methotrexate; in addition, a slight metabolic interaction may occur, which leads to a decrease in methotrexate clearance. Therefore, during the use of high doses of methotrexate use of NSAIDs should always be avoided.
Cardiac glycosides, digoxin. NSAIDs can increase heart failure, reduce glomerular filtration rate (GFR), and inhibit renal glycoside clearance, leading to increased plasma levels of glycosides. Concomitant use should be avoided unless frequent monitoring of digoxin concentration is performed.
Lithium and digoxin preparations. Some NSAIDs inhibit the renal clearance of lithium and digoxin leading to increased serum concentrations of both substances. Concomitant use should be avoided unless frequent monitoring of lithium and digoxin concentrations is performed.
Anticoagulants. NSAIDs inhibit platelet aggregation and damage the mucous membrane of gastrointestinal tract (GIT), which can lead to increased anticoagulants and increase the risk of gastrointestinal bleeding in patients receiving anticoagulants. Concomitant use of aceclofenac and oral anticoagulants of coumarin, ticlopidine and thrombolytics and heparin should be avoided unless careful monitoring of the patient is carried out.
Quinolone antibiotics. Animal studies show that NSAIDs increase the risk of convulsions related to the use of quinolone antibiotics. Patients taking NSAIDs and quinolone antibiotics are at increased risk of developing seizures.
Antiplatelet agents and selective serotonin reuptake inhibitors (SSRIs). With concomitant use with NSAIDs, they increase the risk of GI bleeding (see "Special warnings and precautions for use" section).
Combinations requiring dose selection and precautionary use:
Methotrexate. Possible interaction of NSAIDs and methotrexate should be considered, even with low dose methotrexate, especially in patients with impaired renal function. At the same time, it is necessary to monitor the indicators of kidney function. Caution is required, if NSAIDs and methotrexate was taken within 24 hours, as the concentration of methotrexate may increase that will increase the toxicity of this medicinal product.
Cyclosporine, tacrolimus. A simultaneous administration of NSAIDs with cyclosporine or tacrolimus, the risk of increased nephrotoxicity by reducing renal formation of prostacyclin should be taken into consideration. Therefore, during simultaneous administration, the kidney function should be carefully controlled.
Other analgesics, NSAIDs, including selective cyclooxygenase-2 inhibitors. The simultaneous use of two or more NSAIDs (including acetylsalicylic acid) should be avoided as this increases the incidence of adverse events.
Mifepristone. NSAIDs should not be taken for 8–12 days after receiving mifepristone as they may reduce the effect of mifepristone.
Corticosteroids. The risk of ulceration or GI bleeding increases (see "Special warnings and precautions for use" section).
Diuretics. Aceclofenac, like other NSAIDs, can suppress the activity of diuretics, may reduce the diuretic effect of furosemide and bumetanide and the antihypertensive effect of thiazides. Simultaneous use with potassium-sparing diuretics can lead to increased potassium content; therefore, serum potassium content should be monitored regularly.
Antihypertensive medicinal products. NSAIDs can also reduce the effect of antihypertensive medicinal products. Simultaneous administration of ACE inhibitors or angiotensin II receptor antagonists and NSAIDs may impair renal function. The risk of acute renal failure, which is usually reversible, is increased in some patients with impaired renal function, for example, elderly or dehydrated patients. Therefore, caution should be exercised when administering NSAIDs, especially to elderly patients. Patients should consume the required amount of fluid and be supervised (renal function monitoring at the beginning of concomitant use and periodically during treatment).
Aceclofenac did not affect blood pressure control when used with benzofluazide, although interactions with other diuretics cannot be excluded.

Hypoglycemic agents. Clinical studies show that diclofenac can be used together with oral hypoglycemic agents without affecting their clinical effect. However, there is separate reports on hypoglycemic and hyperglycemic effects of the medicinal product. Thus, during administration of aceclofenac doses of medicinal products that may cause hypoglycemia should be corrected.
Zidovudine. With simultaneous administration of NSAIDs and zidovudine, hematological toxicity risk increases. There is evidence of an increased risk of hemarthrosis and hematoma in HIV(+) patients with hemophilia receiving zidovudine and ibuprofen.

Special warnings and precautions for use.
The simultaneous use of aceclofenac drug and NSAIDs, including selective cyclooxygenase-2 inhibitors, should be avoided.
Undesirable effects can be minimized by lower use for a short time of effective dose for symptom control (see "Administration and dosage" section and the risks associated with the GIT and the cardiovascular system see below).
Effects on the gastrointestinal tract (GIT)
GI bleeding, ulceration, or perforation with lethal outcome were observed with administration of all NSAIDs during any treatment period, both with and without dangerous symptoms, regardless of the history of serious gastrointestinal pathology.
The risk of bleeding, ulceration, and gastrointestinal perforation increases with increase of NSAID doses in patients with a history of ulcer, especially if accompanied by hemorrhage or perforation (see "Contraindications" section) and in elderly patients. These patients should receive the lowest effective dose of the medicinal product. They need combination therapy with use of protective medicinal products (e.g., misoprostol or proton pump inhibitors); also similar therapy is required for patients who use low doses of acetylsalicylic acid or other medicinal products that have a negative effect on the GIT (see "Interaction with other medicinal products and other types of interactions" section).
GI patients, including elderly patients, should report any unusual symptoms associated with GIT (especially gastrointestinal bleeding), including at the initial stage of treatment. Particular caution should be followed in patients receiving concomitant medicinal products that increase the risk of bleeding or ulcers, such as systemic corticosteroids, anticoagulants (e.g., warfarin), selective inhibitors of serotonin reuptake or antiplatelet agents (such as acetylsalicylic acid) (see "Interaction with other medicinal products and other types of interaction" section).
If bleeding or GI ulcers occur in patients receiving aceclofenac, treatment should be discontinued.
Cardiovascular and cerebrovascular effects.
Patients with hypertension and/or mild or moderate congestive heart failure require appropriate monitoring and special instructions as reported fluid retention in the body and edema associated with NSAIDs use.
There is insufficient data to exclude this risk when taking aceclofenac.
Clinical studies and epidemiological data suggest that some NSAIDs (especially when administered high doses and prolonged use) slightly increase the risk of arterial thrombotic events (such as myocardial infarction or stroke).
Patients with congestive heart failure (NYHA functional class I) with factors of risk for the cardiovascular system (e.g., hypertension, hyperlipidemia, diabetes and smoking) should only be treated with aceclofenac after careful consideration. As the adverse effect on the cardiovascular system increases with increasing dose and duration of treatment, the minimum effective daily dose should be used throughout the shortest period of treatment. The need for further symptomatic treatment of the patient and the effectiveness of therapy should be reviewed periodically.
Aceclofenac should be used with caution and close medical attention in patients with history of cerebrovascular hemorrhage.
Aceclofenac should be used with caution and under close medical supervision in patients with the

following conditions (as there is a risk of exacerbation of the disease) (see “Adverse reactions” section):

– symptoms indicating the presence of GIT disorders involving either the upper or lower gastrointestinal tract;
– history of ulceration, bleeding or perforation of the GIT;
– ulcerative colitis;
– Crohn’s disease;
– bleeding tendency, systemic lupus erythematosus (SLE), porphyria and disorders of hematopoiesis and hemostasis.

Impact on the liver and kidneys

Administration of NSAIDs can cause dose-dependent reduction in prostaglandin and sudden renal failure. The importance of prostaglandins in providing renal blood flow should be considered when administering the medicinal product to patients with cardiac, renal, or liver disorders, patients on diuretics, patients after surgery, and elderly patients.

Caution should be followed when administering aceclofenac to patients with liver or kidney disorders of mild or moderate degree, as well as to patients with other conditions accompanied by fluid retention in the body. In these patients, use of NSAIDs can lead to impaired renal function and fluid retention. Caution should also be followed when administering aceclofenac to patients receiving diuretics or those at increased risk of hypovolemia. A minimal effective dose and regular medical monitoring of renal function are required. Kidney effects are usually reversible upon discontinuation of aceclofenac.

If abnormal liver function tests persist or worsen, clinical signs or symptoms consistent with liver disease develop or if other manifestations occur (eosinophilia, rash), aceclofenac should be discontinued. Close medical surveillance is necessary in patients suffering from mild to moderate impairment of hepatic function. Hepatitis may occur without prodromal symptoms. Use of NSAIDs in patients with hepatic porphyria may trigger an attack.

Hypersensitivity and skin reactions

Like other NSAIDs, aceclofenac can cause allergic reactions, including anaphylactic/anaphylactoid reactions, even if the medicinal product is taken for the first time. Severe skin reactions (some of which can be fatal), including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rare after NSAIDs use (see “Adverse reactions” section). The highest risk of these reactions in patients is observed at the beginning of administration of the medicinal product, and the development of these adverse reactions is observed mainly during the first month of the medicinal product use. Aceclofenac should be discontinued if skin rashes, damage to the oral mucosa or other signs of hypersensitivity occur.

Exceptionally, varicella can trigger serious cutaneous and soft tissues infections complications. To date, the contributing role of NSAIDs in the worsening of these infections cannot be ruled out. Thus, it is advisable to avoid use of aceclofenac in case of varicella.

Systemic lupus erythematosus (SLE) and mixed connective tissue disease

In patients with (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see “Adverse reactions” section).

Hematological disorders

Aceclofenac may cause reversible inhibition of platelet aggregation (see “Interaction with other medicinal products and other types of interaction” section).

Respiratory system disorders

Caution should be followed when administering the medicinal product to patients with bronchial asthma, including in anamnesis, as NSAIDs may provoke the development of sudden bronchospasm in such patients.

Elderly patients

Caution should be followed when administering the medicinal product to elderly patients (65 years of age and older) as they are more likely to experience side effects (especially bleeding,

gastrointestinal perforation) when receiving NSAIDs. Complications can be fatal. Also, elderly patients are more likely to suffer from kidney, liver or cardiovascular disease.

Long-term use

All patients using NSAIDs for a long time should be under careful medical monitoring (general blood test, functional liver and kidney tests).

Excipients.

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

In case of intolerance to some sugars, you should consult your doctor before taking this medicine, as this medicine contains sucrose.

Use during pregnancy or breastfeeding.

Pregnancy

There is no information on the use of aceclofenac during pregnancy.

Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/fetal development.

Data from epidemiological studies suggest an increased risk of miscarriage, cardiac malformation or gastroschisis after use of prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5%. The risk is believed to increase with dose and duration of therapy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.

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

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

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors:

- may expose the fetus to cardiopulmonary toxicity (with premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- may expose the fetus to renal dysfunction, which may progress to renal failure with oligohydroamniosis (see above).

The woman (at the end of pregnancy) and the neonate may be exposed to:

- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labor.

Consequently, aceclofenac is contraindicated during the third trimester of pregnancy (see "Contraindications" and "Special warnings and precautions for use" sections).

Breastfeeding

There is no information on the secretion of aceclofenac to breast milk; there was however no notable transfer of radio labelled (14C) aceclofenac to the milk of lactating rats.

Like other NSAIDs, aceclofenac is excreted in breast milk in small amounts, so the drug is contraindicated for women who are breastfeeding to avoid unwanted effects on the baby.

Fertility
Aceclofenac, like other cyclooxygenase/prostaglandin inhibitors, may reduce fertility and is therefore not recommended in women planning a pregnancy. Aceclofenac should be discontinued in women who have difficulty conceiving or are undergoing fertility testing.

Effects on ability to drive and use machines.
Patients who experience symptoms such as weakness, dizziness, vertigo, or other symptoms of the central nervous system should not drive motor vehicles or use other dangerous mechanisms when receiving NSAIDs.

Administration and dosage.
Method of administration
Diclotol® granules are intended for oral use. The contents of the sachets should be dissolved in about 40–60 ml of water and taken immediately.
Simultaneous consumption with food slows the rate of absorption of the active substance, but does not reduce the degree of absorption from the gastrointestinal tract.
Posology
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see "Special warnings and precautions for use" section).
Adults. The recommended dose is one sachet 2 times a day (one sachet in the morning and one sachet in the evening).
Elderly patients. Usually no dose reduction is required, however, the precautions listed in the "Special warnings and precautions for use" section should be considered.
These patients should be closely monitored as they frequently have impaired renal function, liver, cardiovascular disorders, they are also more likely to receive concomitant therapy for other diseases, which increases the risk of serious adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. Usually no dose reduction is required. Patients should be closely monitored for timely detection of gastrointestinal bleeding with NSAID therapy, and it is advisable to follow the recommendations in the "Special warnings and precautions for use" section.
Hepatic insufficiency. Aceclofenac dose should be reduced for patients with mild or moderate hepatic impairment. The recommended starting dose is 100 mg per day (see "Special warnings and precautions for use" section).
Renal insufficiency. There is no information that patients with mild renal insufficiency require a dose adjustment of aceclofenac, but these patients should be following caution when using the medicinal product (see "Special warnings and precautions for use" section).

Children.
The safety and efficacy of aceclofenac in children and adolescents have not been established, so this product is not recommended for use in this age group (see "Contraindications" section).

Overdose.
There are no data on aceclofenac overdose in humans.
Possible symptoms
Headache, nausea, vomiting, epigastric pain, dizziness, drowsiness, gastrointestinal irritation, gastrointestinal bleeding, diarrhea, disorientation, agitation, coma, tinnitus, hypotension, respiratory depression, loss of consciousness, convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.
Treatment

Treatment of acute NSAID poisoning consists of the use of antacids (if necessary) and other supportive symptomatic therapy for complications such as arterial hypotension, renal failure, cramps, irritation of the gastrointestinal mucosa, and respiratory depression.
Treatment of acute poisoning with aceclofenac ingestion is to prevent absorption of the medicinal product by gastric lavage and the use of activated charcoal (repeated doses) as soon as possible after overdose. Forced diuresis, dialysis or hemoperfusion are unlikely to help eliminate NSAIDs because of their high protein binding rate and extensive metabolism.
Good urine output should be ensured.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts.
In case of frequent or prolonged convulsions, patients should be treated with intravenous diazepam.
Other measures may be indicated by the patient's clinical condition.

Adverse reactions.
Gastrointestinal disorders: the most commonly-observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see "Special warnings and precautions for use" section). Nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, abdominal pain, melaena, hematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see "Special warnings and precautions for use" section) have been reported following administration. Less frequently, gastritis has been observed.
Cardiovascular and cerebrovascular disorders: oedema, hypertension and cardiac failure have been reported in association with NSAID treatment.
Aceclofenac is both structurally related and metabolised to diclofenac for which a greater amount of clinical and epidemiological data consistently point towards an increased risk of general arterial thrombotic events (e.g., myocardial infarction or stroke, particularly at high doses or in long treatment). Epidemiological data has also found an increased risk of acute coronary syndrome and myocardial infarction associated with the use of aceclofenac (see "Contraindications" and "Special warnings and special precautions for use" sections).
Hypersensitivity and skin reactions: the use of NSAIDs may develop non-specific allergic reactions, manifested in the form of anaphylactic reactions, respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnea, various skin reactions, including rashes of various types, itching, urticaria, purpura, angioedema, less often – exfoliative and bullous dermatitis (including epidermal necrolysis and erythema multiforme).
Neurological disorders and disorders of the senses: optic neuritis, cases of aseptic meningitis (especially in patients with autoimmune disorders such as SLE, mixed connective tissue disease) with symptoms such as numbness (stiffness) of the neck muscles, fever, disorientation, confusion, hallucinations, malaise.
Hematological disorders: agranulocytosis, aplastic anemia.
Clinical studies and epidemiological data show that some NSAIDs (especially at high doses and with long-term use) increase the risk of arterial thrombotic events (e.g., myocardial infarction or stroke) (see "Special warnings and precautions for use" section).
The table below shows adverse reactions reported with aceclofenac use grouped by system organ class and frequency: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1000, <1/100); rare (≥1/10000, <1/1000); very rare (<1/10000).

MedDRa SOC	Common ≥1/100, <1/10	Uncommon ≥1/1000, <1/100	Rare ≥1/10000, <1/1000	Very rare <1/10000

Blood and lymphatic system disorders			anemia	bone marrow depression, granulocytopenia, thrombocytopenia, neutropenia, hemolytic anemia
Immune system disorders			anaphylactic reaction (including shock), hypersensitivity	
Metabolism and nutrition disorders				hyperkalemia
Psychiatric disorders				depression, abnormal dreams, insomnia
Nervous system disorders	dizziness			paresthesia, tremor, somnolence, headache, dysgeusia (abnormal taste)
Eye disorders			visual disturbance	
Ear and labyrinth disorders				vertigo, tinnitus
Cardiac disorders			cardiac failure	palpitations
Vascular disorders			hypertension, worsening of hypertension	flushing, hot flush, vasculitis
Respiratory, thoracic and mediastinal disorders			dyspnea	bronchospasm, stridor
Gastrointestinal disorders	dyspepsia, abdominal pain, nausea, diarrhea	flatulence, gastritis, constipation, vomiting, mouth ulceration	melaena, gastrointestinal ulcers, hemorrhagic diarrhea, gastrointestinal hemorrhage	stomatitis, bloody vomiting, intestinal perforations, gastrointestinal bleeding, exacerbation of Crohn's disease and ulcerative colitis, pancreatitis
Hepatobiliary disorders	hepatic enzyme increased			hepatic injury (including hepatitis), blood alkaline phosphatase increased, jaundice
Skin and subcutaneous tissue disorders		itching, rash, dermatitis, urticaria	angioneurotic edema	purpura, eczema, severe skin and mucous membrane reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis)

Renal and urinary disorders		increase in concentration of urea in blood, increase in content of creatinine in blood		nephrotic syndrome, renal failure
General disorders and administration site conditions				edema, fatigue, muscle cramps (in the legs)
Investigations				weight gain

Other undesirable effects observed with NSAIDs.
Rare:
Renal and urinary tract disorders: interstitial nephritis.
Skin and subcutaneous tissue disorders: bullous reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis (very rare), photosensitization.
In particular cases, severe skin and soft tissue infections were observed with NSAIDs during chickenpox disease (see also "Special warnings and precautions for use" and "Interaction with other medicinal products and other types of interactions" sections).
Reporting suspected adverse reactions.
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Medical and pharmaceutical workers, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of effectiveness of the medicinal product through the Pharmacovigilance Automated Information System at: https://aisf.dec.gov.ua.

Shelf life.
3 years.

Storage conditions.
Store in original packing at temperature below 25°C.
Keep out of reach of children.

Package.
1 g of granules in a sachet. 20 sachets in a carton package.

Conditions of supply.
By prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of business activity.
Plot No. M-3, Indore Special Economic Zone, Phase-II, Pithampur, Distt. Dhar, Madhya Pradesh, Pin 454774, India.

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