INSTRUCTION
for medical use of medicinal product
LEKFENAC®

Composition:
active ingredient: diclofenac sodium;
1 ml of solution contains 25 mg of diclofenac sodium;
excipients: mannitol (E 421), sodium metabisulphite (E 223), benzyl alcohol, propylene glycol, sodium hydroxide, water for injections.

Pharmaceutical form. Solution for injections.

Pharmacotherapeutic group. Nonsteroidal anti-inflammatory and anti-rheumatic products. Acetic acid derivatives and related substances. ATC code M01A B05.

Pharmacological properties.
Pharmacodynamics.
Lekfenac® is a non-steroidal drug with strong analgesic/anti-inflammatory properties. It is an inhibitor of prostaglandine synthase (cyclooxygenase). Diclofenac sodium *in vitro* does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to those reached in humans. If used in combination with opioids for postoperative pain Lekfenac® significantly reduces the opioid consumption.
Pharmacokinetics.
Absorption.
After administration of 75 mg of diclofenac by intramuscular injection absorption sets in immediately, and mean peak plasma concentrations of about 2.558±0.968 μg/ml (2.5 μg/ml=8 μmol/l) are reached after about 20 minutes. The amount absorbed is in linear proportion to the size of the dose.
When 75 mg of diclofenac is administered as an intravenous infusion over 2 hours, mean peak plasma concentrations are about 1.875±0.436 μg/ml (1.9 μg/ml=5.9 μmol/l). Shorter infusions result in higher peak plasma concentrations, while longer infusions give plateau concentrations proportional to the infusion rate after 3 to 4 hours. This is in contrast to the rapid decline in plasma concentrations seen after peak levels have been achieved with oral, rectal or i.m. administration.
Bioavailability.
The area under the concentration curve (AUC) after intramuscular or intravenous administration is about twice as large as it is following oral or rectal administration as this route avoids «first-pass» metabolism.
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 to 4 hours after peak plasma values have been attained. The apparent half-life for elimination from the synovial fluid is 3 to 6 hours. Two hours after reaching peak plasma values, concentrations of the active substance are already higher in the synovial fluid than in the plasma, and they remain higher for up to 12 hours.
Diclofenac sodium 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 of these phenolic metabolites are biologically active, but to a much smaller extent than diclofenac.
Elimination.

Total systemic clearance of diclofenac from plasma is 263±56 ml/min (mean value ±SD). The terminal half-life in plasma is 1 to 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 as 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.
Special patient groups.
Elderly. No relevant age-dependent differences in the drug's absorption, metabolism or excretion have been observed, other than the finding that in five elderly patients, a 15 minute intravenous infusion resulted in 50% higher plasma concentrations than expected with young healthy subjects.
Patients with renal impairment. In patients suffering from renal impairment, no accumulation of the unchanged active substance can be inferred from the single-dose kinetics when applying the usual dosage schedule. At a creatinine clearance of <10 mL/min, the calculated steady-state plasma levels of the hydroxy metabolites are about 4 times higher than in normal subjects. However, the metabolites are ultimately cleared through the bile.
Patients with hepatic impairment. In patients with chronic hepatitis or non-decompensated cirrhosis, the pharmacokinetics and metabolism of diclofenac are the same as in patients without liver disease.

Clinical particulars.
Indications.
In intramuscular administration the product is used for the treatment of:
– inflammatory and degenerative forms of rheumatism, rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, spondylitis, vertebral pain, extra-articular rheumatism;
– acute gout;
– renal and hepatic colic;
– pain and swelling after injuries and surgery;
– severe migraine.
When administered in intravenous infusion the product is used for treatment or prevention of post-operative pain.

Contraindications.
Known hypersensitivity to the active substance, sodium bisulphite or any of the excipients.
History of gastrointestinal bleeding or perforation, relating to previous nonsteroidal anti-inflammatory drug (NSAID) therapy.
Active, or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
Last trimester of pregnancy.
Like other 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 nonsteroidal anti-inflammatory drugs.
Inflammatory bowel disease (e.g. Crohn’s disease or ulcerative colitis).
Hepatic impairment.
Renal impairment.
Congestive Heart Failure (NYHA II-IV).
High risk of postoperative bleeding, blood incoagulability, haemostasis disorders, hematopoietic disorders or cerebrovascular bleeding.
Treatment of peri-operative pain in coronary artery bypass grafting (or using cardiopulmonary bypass).
Coronary heart disease in patients with angina pectoris, myocardial infarction.
Cerebrovascular disease in patients with previous stroke or episodes of transient ischemic attacks.
Peripheral arterial diseases.

This dosage form is contraindicated in children.
For intravenous use only.
Concomitant NSAID or anticoagulant use (including low dose heparin).
History of haemorrhagic diathesis, a history of confirmed or suspected cerebrovascular bleeding.
Operations associated with a high risk of haemorrhage.
A history of bronchial asthma.
Moderate or severe renal impairment (serum creatinine >160 µmol/l).
Hypovolaemia or dehydration from any cause.

Interactions with other medicinal products and other forms of interaction
The following interactions include those observed with Lekfenac® solution for injection and/or other pharmaceutical forms of diclofenac.
Lithium. If used concomitantly, diclofenac may increase 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-hypertensives. Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity.
Drugs known to cause hyperkalaemia. Concomitant treatment with potassium-sparing diuretics, cyclosporine, tacrolimus or trimethoprim may be associated with increased serum potassium levels, which should therefore be monitored more often.
Anticoagulants and antiplatelet 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 isolated 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 a high dose can reversibly inhibit platelet aggregation.
Other NSAIDs including cyclooxygenase-2 selective inhibitors and corticosteroids. Co-administration of diclofenac with 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 NSAIDs 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 treatment with methotrexate, since blood concentrations of methotrexate may rise and the toxicity of this substance be increase. Cases of serious toxicity have been reported when methotrexate and NSAIDs including diclofenac are given within 24 hours of each other. This interaction is mediated through accumulation of methotrexate resulting from impairment of renal excretion in the presence of the NSAID.
Cyclosporine. Diclofenac, like other NSAIDs, may increase the nephrotoxicity of cyclosporine 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 cyclosporine.

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 antibacterials. 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 use of a quinolone in patients who are already receiving an NSAID.
Phenytoin. When using phenytoin concomitantly with diclofenac, monitoring of phenytoin plasma concentrations is recommended due to an expected increase in exposure to phenytoin.
Colestipol and cholestyramine. These agents can induce a delay or decrease in absorption of diclofenac. Therefore, it is recommended to administer diclofenac at least one hour before or 4 to 6 hours after administration of colestipol/cholestyramine.
Cardiac glycosides. Concomitant use of cardiac glycosides and NSAIDs in patients may exacerbate cardiac failure, reduce glomerular filtration rate 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 diclofenac with potent CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac due to inhibition of diclofenac metabolism.

Special warnings and precautions for use.
General.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.
The concomitant use of Lekfenac® 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 should be used when the product is administered in the elderly. 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.
Like other NSAIDs, Lekfenac® may mask the signs and symptoms of infection and inflammatory process due to its pharmacodynamic properties.
The sodium metabisulphite present in solution for injection can also lead to isolated severe hypersensitivity reactions and bronchospasm.
Gastrointestinal effects.
Gastrointestinal bleeding (haematemesis, melaena), ulceration or perforation which can be fatal has been reported with all NSAIDs including diclofenac and may occur at any time during treatment, with or without warning symptoms or a previous history of serious GI events. They generally have more serious consequences in the elderly. If gastrointestinal bleeding or ulceration occurs in patients receiving diclofenac, the drug should be withdrawn.
As with all NSAIDs, including diclofenac, close medical surveillance is imperative and particular caution should be exercised when prescribing diclofenac in patients with symptoms indicative of gastrointestinal disorders, or with a history suggestive of gastric or intestinal ulceration, bleeding or perforation. The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses including diclofenac, and in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation.
The elderly have increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.
To reduce the risk of GI toxicity in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation, and in the elderly, the treatment should be initiated and maintained at the lowest effective dose.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant use of medicinal products containing low dose acetylsalicylic acid (ASA) or medicinal products likely to increase gastrointestinal risk.
Patients with a history of GI toxicity, particularly when 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, anti-platelet agents such as acetylsalicylic acid or selective serotonin-reuptake inhibitors.
Hepatic effects.
Close medical surveillance is required when prescribing Lekfenac® 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 Lekfenac®, regular monitoring of hepatic function is indicated as a precautionary measure.
If abnormal liver function tests persist or worsen, if clinical signs or symptoms consistent with liver disease develop, or if other manifestations occur (e.g. eosinophilia, rash), Lekfenac® should be discontinued.
Hepatitis may occur with diclofenac without prodromal symptoms.
Caution is called for when using Lekfenac® in patients with hepatic porphyria, since it may trigger an attack.
Renal effects.
As fluid retention and oedema have been reported in association with NSAIDs 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 those patients with substantial extracellular volume depletion from any cause, e.g. before or after major surgery. Monitoring of renal function is recommended as a precautionary measure when using diclofenac in such cases. Discontinuation therapy is usually followed by recovery to the pre-treatment state.
Skin effects.
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs, including Lekfenac®. Patients appear to be at the highest risk of these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Lekfenac® should be discontinued at the first appearance of skin rash, mucosal lesions or any other signs of hypersensitivity.
Systemic lupus erythematosus (SLE) and mixed connective tissue diseases.
In patients with SLE and mixed connective tissue disorders there may be an increased risk of aseptic meningitis.
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. The patient's need for symptomatic relief and response to therapy should be re-evaluated periodically.
The product is used with caution in patients above 65 years of age.
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy including diclofenac.
Clinical trial and epidemiological data consistently point towards increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150 mg daily) and in long term treatment.
Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with diclofenac after careful risk-benefit assessment only in the dosage up to 100 mg daily. This

assessment should be performed before long-term treatment of patients with risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).
Patients should be informed of the possible severe cases (chest pain, shortness of breath, weakness, speech impairment) that may occur at any time. In these cases immediate medical help should be sought.
Haematological effects.
During prolonged treatment with Lekfenac®, as with other NSAIDs, monitoring of the blood count is recommended.
Like other NSAIDs, Lekfenac® may temporarily 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), angioedema 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 Lekfenac® 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 Lekfenac® should be considered.

Use during pregnancy and in nursing women.
Pregnancy.
Lekfenac® can be used during in the first and second trimesters of pregnancy only if the expected benefit to the mother outweighs the potential risk to the foetus and only the minimum effective dose. The duration of treatment should be as short as possible. In late pregnancy, as with other NSAIDs, the drug is contraindicated because it may inhibit uterine contractions and cause premature closure of the ductus arteriosus).
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/or 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 shown to result in increased pre-and post-implantation loss and embryo-foetal lethality.
In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during organogenetic period. If Lekfenac® is used by a woman attempting to conceive, or during the 1st 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 the pregnancy, to:
– possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
– inhibition of uterine contractions resulting in delayed or prolonged labour.

Consequently, Lekfenac® is contra-indicated during the third trimester of pregnancy.
Lactation.
Like other NSAIDs, diclofenac passes into breast milk in small amounts. Therefore, Lekfenac® should not be administered during breast feeding in order to avoid undesirable effects in the infant.
Fertility.
As with other NSAIDs, the use of Lekfenac® 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 Lekfenac® should be considered.

Effects on ability to drive and use machines.
Patients who experience visual disturbances, dizziness, vertigo, somnolence, central nervous system disturbances, drowsiness or fatigue while taking Lekfenac® should refrain from driving or operating machinery.

Dosage and administration.
The lowest effective dose for the shortest duration should be used, considering the problem of treatment for each individual patient.
Adults.
Lekfenac® solution for injections should not be given for more than two days. If necessary, treatment can be continued with Lekfenac® tablets or suppositories.
Intramuscular injection.
The following directions for intramuscular injection must be adhered to in order to avoid damage to a nerve or other tissue at the injection site.
The usual dose of 75 mg (one ampoule) is administered intramuscularly by deep intragluteal injection into the upper outer quadrant. In severe cases (e.g. cramps) the daily dose may be increased to two injections of 75 mg with an interval of several hours (one injection in each buttock). Alternatively, 75 mg of solution for injections can be combined with other dosage forms of Lekfenac® (tablets or suppositories) up to the maximum daily dosage of 150 mg.
In migraine attacks, clinical experience is limited to initial use of one ampoule of 75 mg administered as soon as possible, followed by suppositories up to 100 mg on the same day if required. The total dose should not exceed 175 mg on the first day.
There are no available data on the use of Lekfenac® for the treatment of migraine attacks for more than one day.
Intravenous infusions.
Immediately before initiating an intravenous infusion, Lekfenac® must be diluted with 100-500 ml of either sodium chloride solution (0.9%) or glucose solution (5%). Both solutions should be buffered with sodium bicarbonate solution (0.5 ml 8.4% or 1 ml 4.2%). Only clear solutions should be used.
Lekfenac® solution for injections should not be administered as intravenous bolus injection.
The following alternative regimens of Lekfenac® solution for injections are recommended:
– for the treatment of moderate to severe post-operative pain, 75 mg should be infused continuously over a period of 30 minutes to 2 hours. If necessary, treatment may be repeated after 4-6 hours, not exceeding 150 mg within any period of 24 hours;
– for the prevention of post-operative pain, a loading dose of 25 mg to 50 mg should be infused after surgery over 15 minutes to 1 hour, followed by a continuous infusion of approx. 5 mg per hour up to a maximum daily dosage of 150 mg.
Elderly.
Although the pharmacokinetics of Lekfenac® are not impaired to any clinically relevant extent in elderly patients, nonsteroidal anti-inflammatory drugs should be used with particular caution in such patients who generally are more prone to adverse reactions. In particular it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low body weight (see also Precautions) and the patient should be monitored for GI bleeding during NSAID therapy.

The recommended maximum daily dose of Lekfenac® is 150 mg.

Paediatric patients.

Lekfenac® solution for injections is not recommended for use in children.

Overdose.

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 bleeding, diarrhoea, dizziness, disorientation, excitation, coma, drowsiness, tinnitus, fainting or convulsions. In case of significant poisoning acute renal failure and liver damage are possible.
Treatment. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of potentially toxic amounts. Frequent or prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition. Treatment is symptomatic.

Undesirable effects.

Adverse reactions are described based on its frequency, the most frequent first, using the following convention: 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 available data).
The following undesirable effects of Lekfenac® include those reported with other short-term or long-term use.
Blood and lymphatic system disorders: very rare – thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.
Immune system disorders: rare – hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock); very rare – angioneurotic oedema (including face oedema).
Psychiatric disorders: very rare – disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders: common – headache, dizziness; rare – somnolence, tiredness; very rare – paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident; unknown – confusion, hallucinations, disturbances of sensation, malaise.
Eye disorders: very rare – visual disturbance, vision blurred, diplopia; unknown – optic neuritis.
Ear and labyrinth disorders: common – vertigo; very rare – tinnitus, hearing impaired.
Cardiac disorders: very rare – palpitations, chest pain, cardiac failure, myocardial infarction.
Vascular disorders: very rare – hypertension, hypotension, vasculitis.
Respiratory, thoracic and mediastinal disorders: rare – asthma (including dyspnoea), bronchospasm; very rarely – pneumonitis.
Gastrointestinal system disorders: common – nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia; rare – gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly); very rare – 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.
Hepatobiliary disorders: common – transaminases increased; rare – hepatitis, jaundice, liver disorder; very rare – fulminant hepatitis, hepatic necrosis, hepatic failure.
Skin and subcutaneous tissue disorders: common – rash; rare – urticarial; very rare – dermatitis bullous, eczema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, alopecia, photosensitivity reactions, purpura including allergic purpura, pruritus.
Renal and urinary disorders: very rare – acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, papillary necrosis.

General disorders and administration site conditions: common – injection site reaction, injection site pain, injection site induration; rare – oedema, injection site necrosis, very rarely - an abscess at the injection site.
Reproductive system and breast disorders: very rare – impotence.
Clinical trial and epidemiological data consistently point towards increased risk of arterial thrombotic events (for example myocardial infarction or stroke) associated with the use of diclofenac, particularly at high dose (150 mg daily) and in long term treatment.

Pharmaceutical particulars.
Basic physical and chemical properties: colorless to pale yellow solution.

Incompatibilities. Lekfenac®, solution for injection, should not be mixed with other injection solutions.

Shelf life. 2 years.

Storage. Store in original package at temperature not exceeding 25 °C. Keep away from children.

Nature and contents of container. 3 ml ampoules, 5 ampoules in a carton box with inner dividers or 5 ampoules in a one-sided blister, 1 blister in a carton box or 100 ampoules in a carton box with inner dividers.

Prescription status. By prescription.

Manufacturer. Joint Stock Company «Lekhim-Kharkiv».

Location. Ukraine, 61115, Kharkiv region, Kharkiv, Severyna Pototskoho street, building 36.

Date of the last revision.