PACKAGE LEAFLET: Information for the patient

DURILAC

Suppositories – 100 mg

Gel – 1 %

Solution for injection – 75 mg / 3 ml

(Diclofenac sodium)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

What is in this leaflet:

1. WHAT DURILAC IS AND WHAT IT IS USED FOR

Durilac contains the active substance diclofenac sodium, which is a non-steroidal anti-inflammatory drug (NSAID). Its action is based in the inhibition of cyclooxygenases, which participate in the biosynthesis of prostaglandins. Prostaglandins have an important role in the process of pain, inflammation and chills. Non - steroidal anti-inflammatory drugs inhibit cyclooxygenases-1 and-2 (COX-1 and-2). Inhibition of COX-1 is associated with gastrointestinal side effects, while the inhibition of COX-2 is associated with anti-inflammatory action.

Diclofenac is rapidly absorbed when it is given in the form of rectal suppositories or intramuscular injection. Diclofenac is also absorbed percutaneously. Approximately 99 % of the drug is bound with the plasma proteins. Diclofenac passes in the synovial fluid and in the breast milk. Its plasmatic half life is 1 – 2 hours. It is excreted in the form of glucuronides and sulphates, mainly through urine (65 %) and bile (35 %).

Durilac is used:

- in musculo-skeletal disorders such as rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis;
- in peri-articular disorders such as bursitis and tendinitis;
- in soft-tissue disorders such as sprains and strains;
- in painful conditions such as renal colic, acute gout, dysmenorrhoea;
- after some surgical procedures.

2. BEFORE YOU TAKE DURILAC

Do not take Durilac if you:

- are allergic to diclofenac sodium, aspirin, ibuprofen or any other NSAID, or to any of the excipients of Durilac (listed at the end of the leaflet); signs of a hypersensitivity reaction include: swelling of the face and mouth (angioedema), breathing problems, chest pain, runny nose, skin rash or any other allergic type reaction;
- have active or preceding peptic ulcer, a history of gastrointestinal bleeding or perforation;
- have established heart disease and / or cerebrovascular disease e.g. if you have had a heart attack, stroke, mini-stroke (TIA) or blockages to blood vessels of the heart or brain or an operation to clear or bypass blockages;
- have or have had problems with your blood circulation (peripheral arterial disease);
- suffer from severe cardiac failure;
- have serious hepatic or renal impairment;
- suffer from acute porphyria;
- are pregnant or breastfeeding;
- have disturbances of haemopoiesis with an idiopathic nature.

Durilac should not be used in children.

Additional contraindications only for Durilac solution for injection:

Intravenous use of diclofenac is contraindicated if you:

- have hypovolemia or severe or moderate dehydration;
- are taking other non-steroidal anti-inflammatory drugs or anticoagulants;
- have a history of haemorrhagic diathesis, cerebrovascular bleeding or asthma;
- will make a surgical intervention with a high risk of haemorrhage.

Additional contraindication only for Durilac suppositories:

Durilac suppositories should not be used if you suffer from proctitis (ineffectual straining to empty the bowel, diarrhoea or rectal bleeding).

Take special care with Durilac

Ask your doctor or pharmacist before you take this drug.

Non-selective nonsteroidal anti-inflammatory drugs are associated with a small increased risk of thrombosis even when used as a short-term treatment in patients with no cardiovascular risk factors. Diclofenac with a dosage of 150 mg daily is associated with an increased risk of thrombosis.

Nonsteroidal anti-inflammatory drugs should be used with caution in patients with hepatic impairment because there is an increased risk of gastro - intestinal bleeding and fluid retention.
Also, nonsteroidal anti-inflammatory drugs should be used with caution in the elderly (increased risk of serious side effects and fatalities), and in patients with hypertension, in allergic disorders, in coagulation disorders and connective-tissue disorders.

In patients with cardiac impairment, caution is required since nonsteroidal anti-inflammatory drugs may impair renal function.

Nonsteroidal anti-inflammatory drugs should be used with caution in patients with renal impairment (the lowest effective doses should be used for the shortest possible duration, and renal function should be monitored).

Patients which suffer of asthma, high temperature, nasal polyps or chronic infections of the respiratory tract and patients with a hipersensitivity to analgesics and to the other nonsteroidal anti-inflammatory drugs are associated with an increased risk of attack of asthma during diclofenac sodium use.

NSAIDs should be used with caution in patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as these conditions may be exacerbated.

Nonsteroidal antiinflammatory drugs should be used with caution in patients with cardiovascular diseases including heart failure history, left ventricular dysfunction or oedema.

Talk to your doctor if you recently had or you are going to have a surgery of the stomach or intestinal tract before taking Durilac, as this product can sometimes worsen wound healing in your gut after surgery.

Make sure your doctor knows, before you are given Durilac:

- if you smoke
- if you have diabetes
- if you have angina, blood clots, high blood pressure, raised cholesterol or raised triglycerides.

Side effects may be minimised by using the lowest effective dose for the shortest duration necessary.

In case of Durilac gel, the preparation should be used in undamaged skin and not in wounds. It should not come in contact with eyes and mucous membranes and also it should not be ingested. Application of large amounts to the skin can result in systemic effects. Durilac gel should not be used under occlusive dressings.

Taking other medicines

Concomitant treatment with other medicines may affect or be affected by Durilac.

Please contact your doctor or pharmacist if you are taking or have recently taken other medicines, including those obtained without a prescription. Do not forget to inform your doctor

for the treatment with Durilac if you have been given any other drug during the treatment.

It is particularly important to inform your doctor that you are being treated with:

- *lithium:* diclofenac sodium increases plasma concentration of lithium by reducing its renal excretion (increases the risk for toxicity);
- *digoxin:* diclofenac sodium increases plasma concentration of digoxin (increases the risk for toxicity);
- *diuretics:* the risk of nephrotoxicity by the nonsteroidal anti-inflammatory drugs is increased by diuretics; NSAIDs can antagonize the effect of the diuretics; the risk to hyperkaliemia is increased if NSAIDs are administered simultaneously with potassium sparing diuretics;
- *methotrexate:* when diclofenac sodium and methotrexate are taken within 24 hours, plasma levels of methotrexate can increase, thereby increasing its toxicity;
- *salicylates:* diclofenac sodium may reduce the salicylates concentration;
- *corticosteroids and other nonsteroidal anti-inflammatory drugs:* simultaneous administration of diclofenac with corticosteroids and other nonsteroidal anti-inflammatory drugs (including aspirin in small doses), increases the risk of gastro - intestinal bleeding;
- *quinolones:* the risk for convulsions can increase if nonsteroidal anti-inflammatory drugs are administered simultaneously with quinolones;
- *anticoagulants:* the anticoagulant effect of coumarins (warfarin) and of phenindions and also the risk for haemorrhage when it is taken with heparins, is increased;
- *antidepressants:* increased risk of bleeding when nonsteroidal anti - inflammatory drugs are taken simultaneously with selective serotonin reuptake inhibitors (SSRI) and venlafaxin;
- *antidiabetics:* nonsteroidal anti-inflammatory drugs may increase the effects of sulfonylureas;
- *ciclosporin:* plasma concentration of diclofenac is increased by cyclosporin;
- *potent CYP2C9 inhibitors (e.g. the antifungal voriconazole):* plasma concentration of diclofenac is increased.

Pregnancy and breastfeeding

Durilac should not be used during pregnancy and breastfeeding.

Ask the pharmacist or the doctor before taking this drug.

Driving and using machinery

Patients who experience vertigo, visual disturbances, somnolence or other central nervous system disturbances after diclofenac use, should not drive and use machines.

Important informations about some of the excipients of Durilac

Durilac gel contains benzyl alcohol, which may cause allergic reactions and mild local irritation.

Durilac solution for injection contains sodium sulphite and metabisulphite, which rarely can cause hypersensitivity reactions and bronchospasm.

Durilac solution for injection contains 120 mg benzyl alcohol in each ampoule of 3 ml, which may cause allergic reactions. Ask your doctor or pharmacist for advice if you are pregnant or breast-feeding, or if you suffer from liver or kidney disease because large amounts of benzyl alcohol can build-up in your body and may cause side effects ("metabolic acidosis").

Durilac solution for injection contains 900 mg propylene glycol in each ampoule of 3 ml.

3. HOW TO TAKE DURILAC

Always take Durilac exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Durilac 100 mg suppositories:

Adults:

One 100 mg suppository may be given as a once daily treatment, usually at night.

When it is necessary, therapy may be combined with tablets up to a total maximal dose of 150 mg daily of diclofenac in divided doses.

Children:

Durilac 100 mg suppositories should not be used in children.

Durilac 1% gel

Depending on the size of the affected site, apply the gel in a quantity of 2 - 4 g (a quantity between a cherry and a walnut) 3 - 4 times daily and massage it carefully. The duration of the treatment depends on the indication and patient response. It is recommended to review the

treatment after 14 days or after 28 days if the gel is used for osteoarthritis. The gel can be used also with other pharmaceutical forms of diclofenac sodium.
Durilac gel should not be used in children.

Durilac 75 mg / 3 ml solution for injection

The dose is generally one ampoule daily (75 mg), which is injected deeply into the gluteal muscle in the upper and external side. In rare cases, in serious conditions (e.g. colics), two injections may be used, with an interval of a few hours (one on each side). It is possible to combine one ampoule with other pharmaceutical forms of diclofenac (tablets or suppositories) up to a maximum daily dose of 150 mg. Durilac in the form of ampoules should not be used more than two days; if it is necessary, the treatment can continue with diclofenac tablets or suppositories. Durilac solution for injection is not recommended to be used in children.

Intravenous dose: Diclofenac is given as a continuous intravenous infusion or intermittent, diluted with glucose 5% or sodium chloride 0.9% (buffered previously with sodium bicarbonate 8.4%). For the treatment of postoperative pain, a dose of 75 mg may be given over 30 to 120 minutes. The dose can be repeated if necessary after 4 or 6 hours.
To prevent postoperative pain, it is used as an initial dose of 25 to 50 mg over 15 to 60 minutes after surgery followed by 5 mg/hour to a maximal dose of 150 mg / day. The maximum period recommended for parenteral use of diclofenac ampoules is 2 days.

As a rule, Durilac should be used with particular caution in elderly patients as well as the recommended maximum daily dose should be reduced in patients with low body weight (less than 60 kg).

If you take more Durilac than you should

If you take more Durilac than you should, or if the children have taken this medicine incorrectly, please contact your doctor or call the hospital or emergency to get an opinion for the risk and an advice for the actions to be taken.

If you forget to take Durilac

If you forget a dose (or more doses), take the following dose when it is time to take it usually. Do not take a double dose (or higher) to make up for the forgotten dose (doses).

If you have further questions on the use of this medicinal product, ask your doctor or pharmacist.

The above advices are valid in the case of Durilac suppositories and solution for injection.

4. POSSIBLE SIDE EFFECTS

Like all other medicines, Durilac can cause side effects, although not everybody manifests them. Sometimes they are serious, sometimes not. Do not get alarmed by this list of possible side effects. You may get none of them.

Tell your doctor immediately if you notice the following:

chest pain, which can be a sign of a potentially serious allergic reaction called Kounis syndrome.

For the evaluation of side effects, the following frequencies are used:

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	(frequency cannot be estimated from the available data).

Potential side effects

Common or very common

- epigastric pain, nausea, vomiting, diarrhoea, gastrointestinal discomfort and disorders, appetite decreased, irritation where the suppository is inserted; diclofenac suppositories may cause local reactions such as itching, burning, or exacerbation of haemorrhoids;
- headache and dizziness, vertigo;
- elevations of serum aminotransferase activity;
- skin reactions, rash, dermatitis.

Uncommon

- myocardial infarction, palpitations, chest pain, heart failure, ventricular premature complexes, vasodilation, flushing and tachycardia.

Rare or Very rare

- peptic ulcer, gastrointestinal bleeding, colonic ulceration, small bowel perforation, pseudomembranous colitis, constipation, taste altered, Crohn's disease, pancreatitis, gastritis, vomiting blood, diarrhoea with blood in it or bleeding from the back passage, black, tarry faeces or stools, inflammation of the tongue, mouth ulcers, iflammation of the inside of the mouth or lips;
- tremor, drowsiness, depression, insomnia, anxiety, irritability, asthenia, somnolence, tingling sensation, dreams, myoclonus, migraine, paraesthesia, seizures, memory disturbances, nightmares, disorientation, psychotic reactions and abnormal coordination, confusion, meningitis aseptic (patients with connective-tissue disorders such as systemic lupus erythematosus may be especially susceptible);
- blood formation disorders including agranulocytosis, anaemia (including aplastic anaemia and haemolytic anaemia), thrombocytopenia, neutropenia;
- hypertension, thrombophlebitis, decreased systolic and diastolic blood pressure, angina-like attack or distress, vasculitis, angioedema, stroke;
- acute kidney injury, tubulointerstitial nephritis, nephrotic syndrome, renal papillary necrosis, proteinuria;
- clinical hepatitis, including fatal fulminant hepatitis, hepato-renal damage, hepatotoxicity;
- alopecia, photosensitivity reaction, facial swelling, bullous eruption, serious skin rashes including Stevens-Johnson syndrome, pruritis, erythema multiforme, allergic purpura, urticaria, eczema;
- pneumonitis, asthma, dyspnea;
- hypersensitivity, anaphylactic and anaphylactoid reactions, shock;
- vision disorders (blurred vision, diplopia);
- hearing impairment, tinnitus (ringing in the ears);
- erectile dysfunction.

Not known

- burning sensation at the application site (referring to the gel);
- dry skin (referring to the gel);
- hallucinations, malaise;
- inhibition of platelet aggregation;
- Kounis syndrome, fluid retention (edema);
- optic neuritis.

Other adverse effects

- A syndrome resembling the syndrome of inappropriate antidiuretic hormone secretion, hyponatremia.

When the gel is used for a long period of time and in a large skin area, it can not be ruled out completely the possibility of the occurrence of systemic adverse effects; in such cases, you should consult your doctor immediately.
If any of the side effects worsens, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE DURILAC

Keep this medicine out of the sight and reach of children.
Do not use Durilac after the expiry date which is stated on the carton box.
Do not store in a temperature above 25°C.
Keep in the original packaging to protect it from light.

6. OTHER INFORMATION

What Durilac 100 mg suppositories contain:

The **active substance** is diclofenac sodium.
1 suppository contains 100 mg diclofenac sodium.
The **excipients** are: colloidal anhydrous silica and hard fat.

What Durilac 1% gel contains:

The **active substance** is diclofenac sodium.

1 g of gel contains 10 mg of diclofenac sodium.

The **excipients** are: ethanol 96%, menthol, benzyl alcohol, caprylocaproyl macrogolglycerides, hydroxypropyl cellulose, purified water.

What Durilac 75 mg / 3 ml solution for injection contains:

The **active substance** is diclofenac sodium.

1 ampoule with 3 ml of solution for injection contains 75 mg diclofenac sodium.

The **excipients** are: mannitol, benzyl alcohol for injection, propylene glycol, sodium metabisulphite, sodium hydroxide may be added for pH adjustment, anhydrous sodium sulphite, water for injection.

Contents of the pack:

Durilac 100 mg suppositories:

Carton box with 10 suppositories.

Durilac 1% gel:

Carton box with 1 tube of 30 g.

Durilac 75 mg / 3 ml solution for injection:

Carton box with 10 ampoules 3 ml.

Marketing Authorisation Holder (MAH) and Manufacturer:

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