

PROFENID CAPS 50mg

DATA SHEET

NAME OF THE MEDICINAL PRODUCT

PROFENID 50mg, capsules

COMPOSITION

Each capsule contains 50mg ketoprofen.
Each capsule contains also 93mg Lactose.

PHARMACEUTICAL FORM

Capsule

DRUGS-ABOUT.COM

CLINICAL DATA

Therapeutic indications

Anti inflammatory (for non-infectious conditions) and analgesic for rheumatic diseases.

Dosage and administration

Method of administration:

Oral route.

Capsules are to be swallowed as they are, with a large glass of water.

Dosage:

- long-term symptomatic treatment: 3 X 50mg capsules daily, i.e. 150 mg daily.
- Short-term symptomatic treatment of acute exacerbation: 6 x 50 capsules daily, i.e. 300 mg daily.

Frequency of administration

The capsules are to be taken with meals.

The daily dosage is to be divided into 2 to 3 intakes daily.

Populations at risk:

Patients with renal insufficiency and elderly patients: the initial should be reduced then adjusted, if necessary, depending on renal safety.

- hypovolemic patients: see section "Warning and specific precautions for use"

CONTRA-INDICATIONS

This drug is contra-indicated in the following cases:

- After 24 weeks of amenorrhea (5 complete months of pregnancy) (see Pregnancy and Lactation).
- Hypersensitivity to ketoprofen or one of the excipients,
- History of asthma triggered by taking ketoprofen or substances with a similar activity such as other NSAIDs or aspirin,
- Gastrointestinal hemorrhage, cerebrovascular hemorrhage or any other active hemorrhage,
- Active gastric or peptic ulcer,
- Severe hepatic impairment,
- Severe renal impairment,
- Severe uncontrolled cardiac insufficiency.

WARNING AND SPECIFIC PRECAUTIONS FOR USE

- patients with asthma associated with chronic rhinitis, chronic sinusitis and/or nasal polyposis are at higher risk of allergic reactions than the general population when taking aspirin and/or non-steroidal anti-inflammatory drugs. Administration of this medicine may result in an asthma attack, or bronchospasm, particularly in patients who are allergic to NSAIDs or aspirin.

- Risk of gastrointestinal hemorrhage or ulcers/perforations exists and may occur at any moment during treatment without prior warning signs or history. The relative risk increases with age, weakness, low body weight, patients who presents with platelet dysfunction or in patients undergoing anticoagulant or antiplatelet treatment (see Interactions with other drugs and other forms of interaction). In the event of gastrointestinal bleeding or ulcer, treatment must be stopped immediately.
- When prescribing this medicinal product, the doctors must take into account that cases of secondary anovulatory infertility due to non rupture of the Graafian follicle (reversible after treatment discontinuation) have been described in patients after long-term treatment with certain prostaglandin synthesis inhibitors.
- As with other NSAIDs, ketoprofen may mask signs of progression of an infection.
- Ketoprofen should be administered with care and closely monitored in patients with history of gastrointestinal disorders (peptic ulcer, ulcerative colitis, Crohn's disease).
- Patients with history of photosensitivity or phototoxicity reactions must be closely monitored.
- At the start of the treatment, the urine volume and renal function should be carefully monitored in patients with chronic cardiac, hepatic and renal insufficiency, in patients taking diuretics, after major surgery that induced hypovolemia, and particularly in elderly patients. Administration of ketoprofen to these patients may induce a decrease in renal blood flow related to prostaglandin inhibition, and may result in acute renal insufficiency. In the event of severe cardiac insufficiency, the patient's condition may deteriorate.

- Transaminases should be monitored in patients with impaired hepatic function or with history of liver disease.
- Monitoring of complete blood count and hepatic and renal function is recommended during long-term treatment.
- Because of the presence of lactose, this product is contraindicated in the event of congenital galactosemia, glucose or galactose malabsorption syndrome, or lactase deficiency .

INTERACTIONS WITH OTHER DRUGS AND OTHER FORMS OF INTERACTION

- **Risk related to hyperkalemia:**

Certain medicines or therapeutic classes are likely to favor the onset of hyperkalemia: potassium salts, potassium-containing diuretics, angiotensin-converting enzyme inhibitors, angiotensin II inhibitors, non-steroidal anti-inflammatory drugs, low molecular weight or unfractionated heparin, cyclosporin, tacrolimus and trimethoprim.

Onset of hyperkalemia may depend on the presence of associated factors.

This risk is increased in combination with the above-mentioned medicines.

- **Risk related to antiplatelet activity:**

Due to their antiplatelet properties several substances are involved in interactions: aspirin and NSAIDs, ticlopidine, clopidogrel, tirofiban, eptifibatid and abciximab, iloprost.

The use of several antiplatelet agents exacerbates the risk of hemorrhage, as does their association with heparin, oral anticoagulants and thrombolytic agents. Regular clinical and biological monitoring should be carried out in patients taking these drugs.

- Concomitant administration of ketoprofen with the following medicinal products requires close clinical and laboratory monitoring.

Inadvisable associations

- **other NSAIDs (including aspirin at high doses):** increased risk of ulcers and gastrointestinal bleeding (additive synergy).
- **Oral anticoagulants:** increased risk of bleeding due to the oral anticoagulant (inhibition of platelet function and damage to gastroduodenal mucosa by NSAIDs).
If the combination cannot be avoided: careful clinical and laboratory monitoring.
- **heparins at curative doses or in elderly patients:** increased risk of bleeding (inhibition of platelet function and damage to gastroduodenal mucosa by NSAIDs).
If the combination cannot be avoided: careful clinical monitoring. Do not prolong treatment with NSAIDs beyond a few days.
- **lithium:** increased plasma lithium, potentially reaching toxic levels (decreased renal excretion of lithium).
If the combination cannot be avoided, lithium serum levels should be monitored closely and the lithium dosage adjusted during and after therapy with the NSAID.

- **methotrexate (used at doses >15mg/week):** increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatories in general and displacement from plasma protein binding by NSAIDs).
Allow an interval of at least 12 hours between stopping or starting treatment with ketoprofen and giving methotrexate.

Associations requiring precautions for use:

- **diuretics, angiotensin converting enzyme (ACE) inhibitors and angiotensin II inhibitors:**
Acute renal insufficiency in risk patients (elderly patient and/or dehydrated patient) due to decreased glomerular filtration (inhibition of vasodilator prostaglandins by NSAIDs).
Hydrate the patient and monitor renal function at the start of treatment.
- **methotrexate used at low doses (less than 15mg/week):** increased haematological toxicity of methotrexate (decreased renal clearance of methotrexate by anti-inflammatories in general and displacement from plasma protein binding by NSAIDs).
Weekly blood counts during the first weeks of the combination.
Enhanced monitoring in the presence of even mildly impaired renal function, as well as in the elderly.

Associations to be taken into consideration:

- other antiplatelet agents** (ticlopidine, clopidogrel, tirofiban, eptifibatide and abciximab, iloprost), heparin at prophylactic doses: increased risk of hemorrhage.
- other drugs inducing hyperkalemia:** potassium salts, potassium-containing diuretics, angiotensin-converting enzyme inhibitors, angiotensin II inhibitors, other non-steroidal anti-inflammatory drugs, low molecular weight or unfractionated heparin, cyclosporin, tacrolimus and trimethoprim: risk of hyperkalemia.
- beta-blockers:** (by extrapolation, from indomethacin): reduced antihypertensive effect (inhibition of vasodilator prostaglandins by NSAIDs).
- cyclosporin:** risk of cumulative nephrotoxic effects, especially in the elderly.
- intra-uterine device:** possibility of decreased efficacy, which remains controversial.

PREGNANCY AND LACTATION:

Pregnancy

Malformation: 1st trimester

Animals studies have evidenced no teratogenic effects.

In the absence of teratogenic effects in animal, malformative effects are not expected in man.

To the present date, substances responsible for malformation in man have been teratogenic in animals during well-conducted studies in two species.

In humans, there have been no reports of specific malformation related to administration

during the first trimester of pregnancy. However, further epidemiological studies are necessary to confirm the absence of risk.

Fetal and neonatal toxicity: 2nd and 3rd trimesters

This toxicity concerns all drugs in the class of prostaglandin synthesis inhibitors.

Administration during the 2nd and 3rd trimesters exposes to:

- renal functional impairment:

**in utero* that may be observed from 12 weeks of amenorrhea (implement fetal diuresis): oligoamnios (generally reversible after treatment discontinuation), or even amniotic fluid deficiency, particularly after prolonged exposure.

*at birth, renal insufficiency (reversible or not) may persist, particularly after late and prolonged exposure (with risk of severe, late onset hyperkalemia).

- risk of cardiopulmonary impairment:

Partial or complete closure of the ductus arteriosus *in utero*. This may occur from 5 months and may result in fetal or neonatal right cardiac insufficiency, or even fetal death *in utero*. The closer the drug is taken to delivery time, the greater the risk (less reversibility). This effect is present even after an occasional administration.

- risk of lengthening of bleeding time in mother and child.

Consequently:

- Up to 12 weeks of amenorrhea: Profenid 50mg should only be administered if necessary.
- Between 12 and 24 weeks of amenorrhea (between the start of fetal diuresis and 5 complete months): short-term treatment should only be prescribed if necessary. Long-term treatment is definitely not recommended.
- After 24 weeks of amenorrhea (5 complete months): any occasional intake is contraindicated (see Contraindications). Any erroneous administration after 24 weeks of amenorrhea (5 complete months) requires fetal and/or neonatal renal and cardiac monitoring, depending on exposure time. Monitoring time will depend on half-life elimination.

Lactation

NSAIDs are secreted into breast milk, so as a precautionary measure they should not be given to nursing mothers.

EFFECTS ON THE ABILITY TO DRIVE OR OPERATE MACHINES

Patients should be warned of the risk of dizziness, drowsiness, convulsions or vision disorders. It is recommended not to drive or use machines if any of these symptoms appear.

ADVERSE EVENTS

- Gastrointestinal reactions: gastrointestinal disorders including nausea, vomiting, diarrhea, constipation, gastrointestinal discomfort and gastric pains, gastritis, stomatitis and more rarely, colitis, have been reported.
At the dose of 200 mg/day, oral ketoprofen increases occult bleeding in the gastrointestinal tract: the higher the dosage, the more frequent the bleeding.

The most serious side effects are peptic ulcer, gastrointestinal hemorrhage and intestinal perforation.

- Hypersensitivity reactions:
-very rare cases of Quincke's edema and anaphylactic shock,
dermatological: eruption, rash, pruritus, urticaria, exacerbation of chronic urticaria,
respiratory: possible onset of asthma or bronchospasm, particularly in patients who are allergic to aspirin and other NSAIDs.
- Central nervous system reactions: headaches, dizziness and drowsiness may be observed. Exceptionally, convulsions and mood disturbance.
- Skin reactions: photosensitivity, alopecia and exceptionally bullous dermatosis (Stevens-Johnson syndrome and Lyell's syndrome).
- Ocular disorders: blurred vision.
- Hearing disorders: tinnitus.
- Renal disorders: acute renal insufficiency, especially in the event of history of renal impairment and/or hypovolemia, exceptionally, interstitial nephritis, nephrotic syndrome.
- Hematological disorders: thrombocytopenia, anemia due to chronic hemorrhage, rare cases of leukopenia and possible agranulocytosis.
- Hepatic disorders: increased transaminases, rare cases of hepatitis.
- Cardiac disorders: hypertension.
- Other disorders: edema.

OVERDOSAGE

In adults, the principal signs of overdose are headache, dizziness, drowsiness, nausea, vomiting, diarrhea and abdominal pain.

In the event of serious poisoning, hypotension, respiratory depression and gastrointestinal hemorrhage have been observed.

The patient must be transferred immediately to a specialized unit and symptomatic treatment instituted.

Gastric lavage may be performed or active charcoal administered to limit ketoprofen absorption. There is no specific antidote.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

NON-STEROIDAL, ANTI-RHEUMATISMAL, ANTI-INFLAMMATORY DRUG

Code ATC : MO1AE03

(M: muscle and skeleton)

Ketoprofen is a non-steroidal anti-inflammatory drug. It is an arylcarboxylic acid derivative, belonging to the propionic acid group. It has the following properties:

- peripheral and central analgesic activity.
- Antipyretic activity.
- Anti-inflammatory activity.
- Inhibitory activity of short duration on platelet function.

All these properties are linked to inhibition of prostaglandin synthesis.

In several experimental models, ketoprofen, like other NSAIDs, has been seen to possess central analgesic activity.

PHARMACOKINETIC PROPERTIES

Absorption:

Successive measurements of serum levels after administration of a therapeutic show that ketoprofen is very rapidly absorbed. Plasma peak is reached 60 to 90 minutes after the oral dose.

When ketoprofen is administered with food, the absorption rate is slowed down resulting in a delay and decrease in plasma peaks (C_{max}). Total bioavailability however, is not modified.

Distribution:

Plasma elimination half-life is 1.5 to 2 hours for the oral route.

Ketoprofen is 99% bound to plasma proteins.

Ketoprofen enters the synovial fluid and remains at levels above serum concentrations after the 4th hour following oral intake.

It crosses the placental and blood brain barriers.

Distribution volume is approximately 7 l.

Metabolism:

Ketoprofen is biotransformed according to two processes: one minor (hydroxylation), and one major pathway (glucuronic acid conjugation).

Less than 1% of the Ketoprofen dose administered is found in unchanged form in urine, whereas the glucuroconjugated metabolite represents around 65 to 75% of the dose administered.

Excretion:

In the 5 days following oral intake, 75 to 90% of the dose is excreted via the kidney and 1 to 8% in the feces.

Excretion, mainly urinary, is very rapid, since 50% of the administered dose is eliminated within 6 hours after dosing, whatever the route of administration.

Physiopathological variations

-Elderly subjects: absorption of ketoprofen is not modified in the elderly. However, elimination half-life is increased (3h).

-Renal insufficiency: in these patients, total clearance is prolonged proportionally to the extent of renal insufficiency.

Pre-clinical safety data

Not applicable.

SPECIAL PRECAUTIONS FOR STORAGE

To be stored at not more than 25⁰ in dry place.

MANUFACTURER

HAUPT PHARMA , FRANCE

MARKETING AUTHORIZATION HOLDER

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