Bi-Profenid® 150 mg scored tablets

ketoprofen

SANOFI

1.NAME OF THE MEDICINE
BI-PROFENID 150 mg, scored tablet
2.QUALITATIVE AND QUANTITATIVE COMPOSITION
White Layer(immediate release):
Ketoprofen..... 75, 00 mg
Yellow Layer(modified release):
Ketoprofen..... 75.00 mg
For a scored tablet.
Excipient with a discernable effect: lactose
For a full list of excipients, see section 6.1.
3.PHARMACEUTICAL FORM
Scored tablet.
4.CLINICAL DATA
4.1 Therapeutic indications
They are derived from the analgesic and anti-inflammatory activity of Bi-Profenid, The importance of the manifestations of intolerance to which the medicine gives rise, and its place in the range of anti-inflammatory products currently available.
They are limited, in adults and children from 15 years, to:
•Long-term symptomatic treatment:
o Chronic inflammatory rheumatism conditions including rheumatoid arthritis, ankylosing spondylitis (or related syndromes such as Fiessinger-Leroy-Reiter syndrome and psoriatic arthritis),
o Of certain painful and disabling arthroses.
•short-term symptomatic treatment of acute attacks:
o Abarticular rheumatism such as scapulo-humeral periarthritis, tendonitis, bursitis,
o Microcrystalline arthritis,
o Arthroses,
o Lumbago,
o Radiculalgies,
o Acute benign post-traumatic affections of the musculoskeletal system.
•Treatment of the migraine crisis with or without aura.
4.2 Posology and method of administration
Method of administration: Orally.
The tablets should be swallowed as they are, with a large glass of water.
Dosage
•Rheumatology:
oLong-term symptomatic treatment: 150 mg per day, either one single-dose tablet or two doses of half-tablets.
oShort-term symptomatic treatment of acute attacks: 300 mg per day, ie two tablets of 150 mg in 2 divided doses.
•Treatment of the migraine crisis:
It is recommended to take the treatment as early as possible, from the beginning of the migraine crisis.
Begin the treatment with one half-tablet of BI-PROFENID (75 mg) per crisis.
The efficacy is generally significant within 2 hours after taking the treatment.
If the 75 mg dose is ineffective, a 150 mg dose (ie BI-PROFENID tablet) may be taken during a following crisis.
If a patient is not relieved after the first dose, a second dose (either 75mg or 150mg) should not be taken during the same crisis. However, the crisis can be treated with another treatment that is neither a nonsteroidal anti-inflammatory drug (NSAID) nor aspirin.
If a patient was relieved but the symptoms recur or if a new crisis begins in the same day, the second dose (75 mg or 150 mg) can be taken on the condition of respecting Imperativelyan interval of at least 12 hours between the two doses.
NEVER EXCEED 2 150 mg tablets per 24 hours (300 mg / day).
Frequency of administration: The tablets are to be taken, if possible during a meal or failing with a snack.
The daily dose is to be divided into 1 to 2 times daily.
Populations at Risk
•Renal impairment and elderly:
It is recommended to reduce the initial dose and adjust if necessary to the renal tolerance.
•Hypovolemic Patients: see section 4.4.
4.3 Contraindications
•Beyond 24 weeks of amenorrhea (5 months of age pregnancy) (see section4.61
•Hypersensitivity to Bi-Profenid or to any of the excipients of the product,
•History of asthma triggered by the use of Bi-Profenid or substances of similar activity such as other NSAIDs, aspirin,
•Gastrointestinal haemorrhage, cerebrovascular haemorrhage or another evolving hemorrhage,
•An evolving gastric ulcer or intestinal,
•Severe hepatic impairment,
•Severe renal impairment,
•Severe uncontrolled heart failure.
4.4 Special warnings and precautions for use
Patients with asthma associated with chronic rhinitis, chronic sinusitis and / or nasal polyposis have a risk of allergic manifestation when taking aspirin and / or nonsteroidal anti-inflammatory drugs, higher than the rest of the population. The administration of this product may lead to the onset of asthma or bronchospasm, especially to subjects allergic to aspirin or NSAIDs (see section 4.3V Risk of gastrointestinal bleeding or ulcers / perforations exists and may occur at any time during treatment without necessarily warning signs or history. which can be fatal.
The relative risk increases in the elderly, who are fragil and of low body weight, the patients with platelet function disorders or in patients undergoing anticoagulant or platelet anti aggregating therapy (see section 4.5V In case of gastrointestinal bleeding or ulcer, stop the treatment immediately.
During the prescription, the physician should take into account the fact that cases of secondary anovulatory infertility by non-rupture of De Graaf follicle, reversible upon discontinuation of treatment, have been described in patients treated by long-term Inhibitors of prostaglandin synthesis.
Like other NSAIDs, Bi-Profenid can mask the signs of progression of an infection.
Bi-Profenid will be administered with caution and special surveillance in patients with a history of gastrointestinal disorders (gastro-duodenal ulcer, ulcerative colitis, Crohn's disease).
Patients with a history of photosensitivity or phototoxicity reactions should be closely monitored.
In patients with impaired hepatic function or with a history of hepatic disease, transaminase monitoring is recommended.
During prolonged treatment, it is recommended to control the CBC, liver and kidney function.
Cardiovascular Risk: NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk • NSAIDs is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.
Renal Function impairment
NSAIDs, by inhibiting the vasodilating action of renal prostaglandins, are likely to cause renal function impairment by decreased glomerular filtration. This adverse effect is depending dose.
In the beginning of treatment or after a dose increase, monitoring of diuresis and renal function is recommended in patients with the following risk factors:
•elderly:
•Associated medicine such as: IEC, sartans, diuretics (see section 4.5).
•Hypovolemia whatever the cause,
•heart failure, •chronic renal failure,
•nephrotic syndrome, •Lupus nephropathy,
•Decompensated hepatic cirrhosis.
Hydro-sodium retention**:**
Hydro-sodium retention with possibility of edema, HTA or increase of HTA, aggravation of heart failure. Clinical monitoring is required from the beginning of treatment in case of HTA or heart failure. A decrease in the effect of antihypertensive drugs is possible (see section 4.51.
Hyperkalaemia
Hyperkalemia favored by diabetes or concomitant treatment with hyperkalaemic medicine (see section 4.5V Regular monitoring of serum potassium should be done in these circumstances.
This drug contains lactose. Its use is not recommended in patients with galactose intolerance, Lapp lactase deficiency, or glucose galactose malabsorption syndrome (rare hereditary disorders).
4.5 Interaction with other medicinal products and other forms of interaction
•Risks related to Hyperkalemia
•Some medications or therapeutic classes are likely to promote the occurrence of hyperkalaemia: potassium salts, hyperkalaemic diuretics, ACE inhibitors, angiotensin II inhibitors, nonsteroidal anti-inflammatory drugs, Heparins (of 3low molecular weight or unfractionated), ciclosporin and tacrolimus, trimethoprim.
The occurrence of hyperkalaemia may depend on the existence of co-associated factors. This risk is increased in the case of association of the medicinal products.
•Risk associated related to antiplatelet agent effect:
Several substances are involved in interactions, due to their antiplatelet medicinal products properties: aspirin and NSAIDs, ticlopidine and clopidogrel, tirofiban, eptifibatide and abciximab, iloprost.
The use of several antiplatelet agents increases the risk of bleeding, as well as their association with heparin or the analogues (hirudins), with oral anticoagulants and with thrombolytics, and should be taken into account by maintaining regular clinical and biological monitoring .
•The simultaneous administration of Bi-Profenid with the following products requires careful monitoring of the clinical and biological condition of the patient.
not recommended Concomitant use
+ Other NSAIDs (including aspirin at high-doses): Increase of ulcerogenic and haemorrhagic digestive risk (additive synergy).
+ Oral anticoagulants : Increase of hemorrhagic risk of oral anticoagulant (inhibition of platelet function and aggression of the gastroduodenal mucosa by NSAIDs).
If the association can not be avoided, close clinical and biological monitoring.
+ Heparin at curative doses or in the elderly : Increase of hemorrhagic risk (inhibition of platelet function and aggression of the gastroduodenal mucosa by NSAIDs).
If the association can not be avoided, close clinical monitoring. Do not exceed a few days of treatment by NSAIDs.
+ Lithium: Increase of lithium levels in blood may reach toxic values (decreased renal excretion of lithium).
If the association can not be avoided, closely monitor the lithium level in blood and adjust the dosage of lithium during the association and after discontinuation of the NSAID.
+ Methotrexate (used at doses above 15 mg / week): Increase of haematological toxicity of methotrexate (decrease of renal clearance of methotrexate by anti-inflammatories in general and displacement of methotrexate from its binding to plasma proteins by NSAIDs).
Respect an interval of at least 12 hours between the end or the start of a treatment with Bi-Profenid and taking methotrexate.
Associations requiring precautions for use
+ Diuretics, ACE inhibitors, angiotensin II inhibitors: Acute renal insufficiency in patients at risk (elderly or dehydrated) by decrease of glomerular filtration (decrease of synthesis of vasodilating prostaglandins by NSAIDs).
Hydrate the patient and monitor renal function at the beginning of treatment.
+ Methotrexate, used at low doses (less than 15 mg / week): Increase of haematological toxicity of methotrexate (decrease of renal clearance of methotrexate by anti-inflammatories in general and displacement of methotrexate from its binding to plasma proteins).
Weekly control of the hemogram during the first weeks of the association.
Increased monitoring in case of alteration (even mild) of renal function, as well as in the elderly.
Associations to be taken into account
+ Other antiplatelet agents (abciximab, eptifibatide, clopidogrel, iloprost, ticlopidine and tirofiban), heparins at **prophylactic doses:**
Increase of the hemorrhagic risk.
+ Other hyperkalaemic (potassium salts, hyperkalaemic diuretics, ACE inhibitors, angiotensin II inhibitors, other nonsteroidal anti-inflammatory drugs, heparins (low molecular weight or unfractionated), ciclosporin and tacrolimus, trimethoprim).
Risk of hyperkalaemia.
+ Beta-blockers (by extrapolation from indomethacin)
Reduction of the antihypertensive effect (inhibition of vasodilating prostaglandins by NSAIDs).
+ Cyclosporine Risk of addition of nephrotoxic effects, especially in the elderly.
+ Intrauterine device Controversial risk of decreased efficacy of the intrauterine device**.**
4.6 Pregnancy and breast feeding
Pregnancy
Malformative aspect: 1st trimester.
In the human, no specific malformative effects associated with administration during the first trimester of pregnancy have been indicated. However, additional epidemiological studies are needed to confirm the absence of risk.
fetotoxic and neonatal Appearance: 2nd and 3rd trimester
This is a class of toxicity concerning all prostaglandin synthesis inhibitors.
The administration during the 2nd and 3rd trimester exposes in
•impaired renal function:
oIn utero can be observed since 12 weeks of amenorrhoea (initiation of fetal diuresis): oligoamnios (most often reversible at the end of treatment), or even anamnios especially during prolonged exposure;
oAt birth, a renal insufficiency (reversible or not) may persist especially in cases of delayed and prolonged exposure (with a risk of delayed severe hyperkalaemia).
•A risk of cardiopulmonary involvement:
Partial or complete construction in utero of the ductus arteriosus. The construction of the ductus arteriosus can occur after 5 months and may lead to fetal or neonatal right cardiac insufficiency or even fetal death in utero. This risk is all the more important as the dose is close to the term (less reversibility). This effect exists even for a limited dose;
•A risk of prolonged bleeding duration for mother and child.
Consequently:
•Up to 12 weeks of amenorrhea: the use of BI-PROFENID 150 mg should only be considered if necessary.
•Between 12 and 24 weeks of amenorrhea (between the beginning of fetal diuresis and after 5 months): a brief intake should only be prescribed if necessary. A prolonged use is strongly discouraged.
•After 24 weeks of amenorrhea (after 5 months): any one-time use is contraindicated (see section 4.3Y Inadvertent intake after 24 weeks of amenorrhea (after 5 months Justifies fetal and / or neonatal, cardiac and renal monitoring according to the term exposure. The duration of this monitoring will be adapted to the elimination half-life of the molecule.
Breastfeeding
NSAIDs. Passing into breast milk, as a safety precaution, it is advisable to avoid administering them in nursing woman**.**
4.7Effects on ability to drive and use machines
Prevent patients from the possible appearance of vertigo drowsiness, convulsions or visual disturbances. It is advisable not to drive or use machines if any of these symptoms appear.
4.8 Side effects
Gastrointestinal effects Gastrointestinal disorders have been reported that include nausea, vomiting, diarrhea, constipation, gastrointestinal discomfort and gastric pain, gastritis, stomatitis, and more rarely colitis. At the dose of 200 mg per day, oral Bi-Profenid causes an increase in occult digestive blood losses: these are all the more frequent when the dosage used is raised.
The most serious side effects are peptic ulcer, digestive hemorrhage and intestinal perforations.
Hypersensitivity reactions •Very rare cases of angioedema an anaphylactic shock;
•Dermatological: eruption, rash, pruritus, urticaria, aggravation of chronic urticaria,
•Respiratory: possibility of asthma attack or bronchospasm, especially in subjects allergic to aspirin and to other NSAIDs.
Neuro-psychiatric disorders •Can be observed headache, vertigo, somnolence, unusually, convulsions and mood disorders.
Skin Reactions •Photosensitivity, alopecia and exceptionally, bullous dermatosis (Stevens-Johnson and Lyell's syndrome).
Ocular disorders •Visual blur.
Hearing problems•Tinnitus.
Kidney disorders•Hydrosodic retention with possibility of edema, hyperkalaemia (see sections 4.4 and 4.5).
•Acute renal Insufficiency (ARI) in patients with risk factors (see section 4A).
•Organic kidney damage that may result by ARI: isolated cases of interstitial nephritis, acute tubular necrosis, nephrotic syndrome, papillary necrosis have been reported.
Hematologic disorders •Thrombocytopenia, anemia due to chronic hemorrhage, rare cases of leucopenia with possibility of agranulocytosis.
Hepatic disorders
•Increased transaminase levels, exceptional cases of hepatitis.
Cardiac disorders •Hypertension, aggravation of cardiac insufficiency.
4.9Overdose
In adults, the main signs of overdose are headache, vertigo, drowsiness, nausea, vomiting, diarrhea and abdominal pain.
In case of severe poisoning, hypotension, respiratory depression and gastrointestinal haemorrhage have been observed.
The patient should be transferred immediately to a specialized hospital where symptomatic treatment will be initiated.
Gastric lavage or administration of activated charcoal may be practiced to limit the absorption of Bi-Profenid.
There is no specific antidote. .
5.PHARMACOLOGICAL PROPERTIES
5.1Pharmacodynamic properties
ANTI-INFLAMMATORY, ANTI-RHUMATISMAL, NON-STEROIDAL, (M: Muscle and Skeleton), ATC Code: **M01AE03).**

Bi-Profenid is a nonsteroidal anti-inflammatory drug derived from aryl carboxylic acid, from the group of propionics. It has the following properties:
•Peripheral and central analgesic property,
•Antipyretic property,
•Anti-inflammatory properties,
•Property of short-term inhibition of platelet function.
All of these properties are related to the inhibition of prostaglandin synthesis. On several experimental models, it has been observed for Bi-Profenid like other NSAIDs central analgesic component.
5.2 Pharmacokinetic properties
Absorption
It is also fast for the upper layer than that observed with Ketoprofen , capsule.
The time for appearance the serum level is 1.21 ± 0.88 h and the plasma concentration is 7.72 ± 1.6 mg.
The release from the lower layer is superimposed on the release from the upper layer.
Plasma concentrations show a plateau from the 45th to the 90th minute and then are greater than those observed with the capsules from the 3rd hour.
When Bi-Profenid is administered with food, the absorption rate is slowed down, causing a delay and decreased plasmatlque peak (Cmax). However, its total bioavailability is not modified.
Distribution
The mean plasma half-life is 3.6 hours.
Bi-Profenid is 99 % bound to plasma proteins.
It diffuses into the synovial liquid and persists at serum concentrations after the 4th hour following an oral dose.
It crosses the placental barrier and the blood-brain barrier.
The volume of distribution is about 7 I.
Metabolism
The biotransformation of Bi-Profenid is carried out according to two processes: one very minor (hydroxylation), the other largely predominant (conjugation with glucuronic acid).
Less than 1 % of the administered dose of Bi-Profenid is found unchanged in the urine, while glucuronide is approximately 65-75%..
Excretion
The excretion, mainly urinary, is rapid, with 50 %. of the administered dose being eliminated within 6 hours after the administration, whatever the way of administration.
In 5 days following the oral administration, 75 - 90 % of the dose is excreted by the kidney and1-8 % in feces.
Physiopathological variations
Elderly: In the elderly, the absorption of Bi-Profenid is not modified, against the half-life of elimination is lengthened.
Renal insufficiency: In these patients, the total clearance is lengthened in proportion to the degree of renal insufficiency.
5.3. Preclinical safety data
Not applicable.
6.PHARMACEUTICAL PARTICULARS
6.1 List of excipients
•White Layer.
•Lactose monohydrate, Wheat starch, hydrated colloidal silica, magnesium stearate,Gelatin powder.
•Yellow Layer:
Hydroxyethylcellulose, calcium hydrogen phosphate, Riboflavin Sodium Phosphate magnesium stearate.
6.2 Incompatibilities
Not applicable.
Storage
Do not exceed the expiry date listed on the outer packaging.
Store at a temperature not exceeding 30° C in dry place
Shelf life: 3 years
Nature and contents of the outer packaging
Boxes containing 2 or 100 (orange PVC/AL) strips each of 10 scored tablets and inner leaflet each.

Manufactured by Sanofi Egypt S.A.E
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KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

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