Vanit™

[Dexibuprofen]

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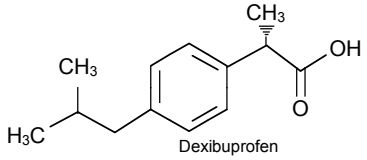
Tablets 200mg, 300mg, 400mg

DESCRIPTION

VANIT (Dexibuprofen), [S(+)-Ibuprofen], is considered as the pharmacologically active enantiomer of ibuprofen. Racemic ibuprofen is a non-steroidal substance that possesses anti-inflammatory and analgesic effects.

Chemically, it is described as S(+)-2-(4-Isobutylphenyl)propionic acid. Its molecular formula is $C_{13}H_{18}O_2$ and the structural formula is:



Dexibuprofen

QUALITATIVE & QUANTITATIVE COMPOSITION

VANIT (Dexibuprofen) is available for oral administration as:

VANIT Tablets 200mg
Each film-coated tablet contains:
Dexibuprofen … 200mg

VANIT Tablets 300mg
Each film-coated tablet contains:
Dexibuprofen … 300mg

VANIT Tablets 400mg
Each film-coated tablet contains:
Dexibuprofen … 400mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Dexibuprofen, a racemic ibuprofen belongs to a family of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). Like other NSAIDs, dexibuprofen acts by inhibiting prostaglandin synthesis. It reduces pain, inflammation and fever and reversibly inhibits ADP and collagen stimulated platelet aggregation.

Pharmacokinetics

Absorption & Distribution

Dexibuprofen is absorbed primarily from the small intestine. Maximum plasma levels are reached about 2 hours after oral administration. The plasma protein binding is about 99%.

The administration of dexibuprofen with a high fat meal delays the time to reach maximum concentrations (from 2.1 hours after fasting conditions to 2.8 hours after a high fat meal) and decreases the maximum plasma concentrations (from 20.6 to 18.1 µg/mL), but has no effect on the extent of absorption.

Metabolism & Excretion

After metabolic transformation in the liver (hydroxylation, carboxylation), the pharmacologically inactive metabolites are completely excreted, mainly by the kidneys (90%), and also in the bile. The elimination half-life is 1.8 - 3.5 hours.

THERAPEUTIC INDICATIONS

VANIT (Dexibuprofen) is indicated for:

- Symptomatic treatment for the relief of pain and inflammation associated with osteoarthritis.
- Acute symptomatic treatment of pain during menstrual bleeding (primary dysmenorrhea).
- Symptomatic treatment of mild to moderate pain, such as muscular skeletal pain or dental pain.
- It may be used as an antipyretic to reduce fever.

DOSAGE AND ADMINISTRATION

VANIT (Dexibuprofen) tablets can be taken with or without a meal. In general NSAIDs (non-steroidal anti-inflammatory drugs) are preferably taken with a meal to reduce gastrointestinal irritation, particularly during chronic use.

The dosage should be adjusted according to the severity of the disorder and the complaints of the patient. The maximum single dose is 400mg, the maximum daily dose is 1200mg dexibuprofen.

Osteoarthritis

The recommended dose is 600mg to 900mg dexibuprofen daily, divided in up to three single doses. The dose may be increased up to 1200mg dexibuprofen per day in patients with acute conditions or exacerbations.

Dysmenorrhea

The recommended dose is 600mg to 900mg dexibuprofen daily, divided in up to three single doses.

Mild to moderate pain

The recommended dose is 600mg dexibuprofen daily, divided in up to three single doses.

If clearly needed in patients with acute pain conditions (e.g. in surgical extraction of teeth) the dose may be transiently increased up to 1200mg dexibuprofen per day.

Children and adolescents

Dexibuprofen is not recommended in children and adolescents (< 18 years).

Elderly

No special dosage modifications are required in the elderly. However, individual dose reduction and assessment has to be considered due to increased susceptibility to GI adverse reactions in the elderly.

Special population:

Hepatic impairment

Patients with mild to moderate hepatic impairment should start therapy at reduced doses and be closely monitored.

Renal impairment

The initial dose should be reduced in patients with mild to moderate impaired renal function.

ADVERSE REACTIONS

Common

Dyspepsia, diarrhea, nausea, vomiting, abdominal pain, rash, fatigue or drowsiness, headache, dizziness, vertigo, edema and hypertension.

Uncommon

Gastrointestinal ulcers and bleeding, ulcerative stomatitis, gastritis, malaena, urticaria, pruritus, purpura (including allergic purpura), angioedema, rhinitis, bronchospasm, insomnia, anxiety, restlessness, visual disturbances and tinnitus.

Rare

Gastrointestinal perforation, flatulence, constipation, esophagitis, esophageal strictures, exacerbation of diverticular disease, unspecific hemorrhagic colitis, ulcerative colitis, Crohn's disease, anaphylactic reactions, psychotic reactions, depression, irritability, disorientation, confusion, agitation, reversible toxic amblyopia, impaired hearing, abnormal liver function, hepatitis, jaundice, blood disorders including thrombocytopenia, leucopenia, granulocytopenia, pancytopenia, agranulocytosis, aplastic anemia or hemolytic anemia.

CONTRAINDICATIONS

Dexibuprofen is contraindicated in patients:

- Previously sensitive to dexibuprofen, to any other NSAID, or to any of the excipients of the product.
- In whom substances with a similar action (e.g., aspirin or other NSAIDs) precipitate attacks of asthma, bronchospasm, acute rhinitis, or cause nasal polyps, urticaria or angioneurotic edema.
- With a history of gastrointestinal bleeding or perforation, related to previous NSAID therapy.
- With active, or a history of recurrent peptic ulcer/hemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- With cerebrovascular bleeding or other active bleedings.
- With active Crohn's disease or active ulcerative colitis.
- With severe heart failure.
- With severe renal dysfunction (GFR < 30 ml/min).
- With severely impaired hepatic function.
- From the beginning of 6th month of pregnancy

Pregnancy

During the first and second trimester of pregnancy NSAIDs should not be given unless clearly necessary. If NSAIDs are used during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible.

NSAIDs may impair fertility reversibly and are not recommended in women attempting to conceive.

Nursing mothers

Dexibuprofen is slightly excreted in human milk. Breast-feeding is possible with dexibuprofen if dosage is low and the treatment period is short.

PRECAUTIONS

- The use of dexibuprofen with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided. Care is recommended in conditions that predispose patients to the gastrointestinal adverse effects of NSAIDs. These patients should be closely monitored for digestive disturbances, especially gastrointestinal bleeding, perforation & ulceration.
- 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 edema have been reported in association with NSAID therapy. Patients with uncontrolled hypertension, congestive heart failure, established ischemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with dexibuprofen after careful consideration.

- If used in the patients with renal or hepatic disease, the dose of dexibuprofen should be kept as low as possible and renal function should be regularly monitored.
- Dexibuprofen should only be given with care to patients with systemic lupus erythematosus and mixed connective tissue disease because such patients may be predisposed to NSAID-induced renal and CNS side effects, including aseptic meningitis.
- Dexibuprofen should be used with particular caution in patients with bronchial asthma or other chronic diseases of the pulmonary tract as well as in persons prone to allergy as NSAIDs can cause bronchospasm in such patients.
- It is advisable to avoid use of dexibuprofen in case of varicella.
- Patients receiving long-term treatment with dexibuprofen should be monitored as a precautionary measure.

Drug Interactions
Anticoagulants:
NSAIDs may enhance the effect of anti-coagulants, such as warfarin. Blood coagulation tests (INR, bleeding time) should be performed during the initiation of dexibuprofen treatment and the dosage of the anticoagulant should be adjusted if necessary.

Methotrexate used at doses of 15 mg/week or more:
The concomitant use of dexibuprofen and high dose treatment with methotrexate within 24 hours of each other is not recommended because it may increase the potential for methotrexate toxicity.

Lithium:
NSAIDs can increase the plasma levels of lithium, by reducing its renal clearance so this combination is not recommended.

Other NSAIDs:
The concomitant use with other NSAIDs and salicylates (approximately 100 mg/day) should be avoided, since it can increase the risk of gastrointestinal ulceration and hemorrhage. The coadministration of dexibuprofen may also impair inhibition of platelet aggregation by low-dose acetylsalicylic acid.

Antihypertensives:
NSAIDs may reduce the efficacy of beta-blockers, possibly due to inhibition of the formation of vasodilatory prostaglandins. The concomitant use of NSAIDs and ACE inhibitors or angiotensin-II receptor antagonists may be associated with an increased risk of acute renal failure, especially in patients with pre-existing impairment of renal function.

Diuretics:
Concurrent use of an NSAID and a diuretic may increase the risk of renal failure secondary to a reduction in renal blood flow.

Oral anti-diabetic drugs:
Concomitant use of an NSAID and sulphonylurea may cause fluctuations in blood glucose level. Therefore, appropriate monitoring may be required.

Zidovudine (Azidothymidine):
Concomitant use of NSAIDs and zidovudine has been reported to increase the risk of hemarthrosis and hematoma in patients with hemophilia.

Pemetrexed:
High doses of NSAIDs may increase the concentration of pemetrexed. In patients with impaired renal function, concomitant use of NSAIDs at high doses should be avoided two days before and two days after pemetrexed administration.

Alcohol:
Excessive alcohol consumption during NSAID-therapy may increase gastro-intestinal adverse effects.

Caution should be taken with the concomitant administration of the following drugs:
- Cyclosporine, tacrolimus, sirolimus and aminoglycoside antibiotics: there is an increased risk of nephrotoxicity.
- Corticosteroids: may lead to increased risk of gastrointestinal ulceration or bleeding.
- Digoxin: may lead to digoxin toxicity.
- Phenytoin, phenobarbital and rifampicin: concomitant administration of CYP2C8 and CYP2C9 inducing agents may lower the effects of dexibuprofen.
- Thrombolytics, ticlopidine and antiplatelet agents: increased anti-platelet effect.

OVERDOSAGE
Symptoms:
Mild symptoms are most common, including abdominal pain, nausea, vomiting, lethargy, drowsiness, headache, nystagmus, tinnitus and ataxia. Rarely, moderate or severe symptoms include gastrointestinal bleeding, hypotension, hypothermia, metabolic acidosis, seizures, impaired kidney function, coma, adult respiratory distress syndrome and transient episodes of apnea.

Treatment:
Treatment is symptomatic, and there is no specific antidote. Amounts not likely to produce symptoms (less than 50 mg/kg dexibuprofen) may be diluted with water to minimize gastrointestinal upset. In case of ingestion of a significant amount, activated charcoal should be administered. Emptying of the stomach by emesis may only be considered if the procedure can be undertaken within 60 minutes of ingestion. Gastric lavage should not be considered unless a patient has ingested a potentially life-threatening amount of the drug and the procedure can be undertaken within 60 minutes of ingestion.
Forced diuresis, hemodialysis or hemoperfusion are unlikely to be of assistance because dexibuprofen is strongly bound to plasma proteins.

STORAGE
Store at 25°C (Excursions permitted between 15°C-30°C).
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
VANIT (Dexibuprofen) Tablets 200mg is available in blister pack of 30's.
VANIT (Dexibuprofen) Tablets 300mg is available in blister pack of 30's.
VANIT (Dexibuprofen) Tablets 400mg is available in blister pack of 30's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
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www.getzpharma.com
29-30/27, K.I.A., Karachi, Pakistan
L-200008119