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_3 and the structural formula is:

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  H3C
 /    /
 CH3  CH3
      /    \\
     /     /  \ \\
    /     /   / \\
   /     /   /   \\
  O     H     H   O
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**QUALITATIVE & QUANTITATIVE COMPOSITION**

Vanit (Dexibuprofen) is available for oral administration as:

**Vanit Tablets**
- 200mg
- 300mg
- 400mg

Each film-coated tablet contains:
- Dexibuprofen... 200mg
- Dexibuprofen... 300mg
- 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 AEP 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), 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.

**DOSEAGE 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, melaena, urticaria, pruritus, purpura (including allergic purpura), angioedema, rashes, bronchospasm, nausea, vomiting, visual disturbances and tinnitus.

Rare
Gastrointestinal perforation, swallowing, constipation, esophagitis, esophageal strictures, exacerbation of diverticular disease, unspecified hemorrhagic collits, ulcerative colitis, Crohn’s disease, anaphylactic reactions, psychic 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 polyposis, 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 collits.
- 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.

**VANIT Tablets 200mg**
Store at 25°C (Excursions permitted between 15°C-30°C).

Forced diuresis, hemodialysis or hemoperfusion are unlikely to be of benefit. Emptying of the stomach by emesis may only be considered if the patient is asymptomatic and if the ingestion occurred less than 1 hour previously. In case of ingestion of large quantities of the drug, gastric lavage should not be considered unless a patient has ingested a potentially toxic amount of the drug.

**Special population:**
Hepatic impairment
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.

**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, melaena, urticaria, pruritus, purpura (including allergic purpura), angioedema, rashes, bronchospasm, nausea, vomiting, visual disturbances and tinnitus.

Rare
Gastrointestinal perforation, swallowing, constipation, esophagitis, esophageal strictures, exacerbation of diverticular disease, unspecified hemorrhagic colitis, ulcerative colitis, Crohn’s disease, anaphylactic reactions, psychic 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 anaemia or hemolytic anaemia.

**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 polyposis, 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.
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- 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.
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.

**Chemical Structure**

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:

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\[ \text{Chemical Structure} \]
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**Pharmacodynamics**

Dexibuprofen acts by inhibiting prostaglandin synthesis. It reduces pain, fever, and inflammation. It reversibly inhibits ADP and collagen stimulated platelet aggregation.

**Absorption**

Absorption starts 30 minutes after ingestion and is completed within 2 hours. Maximal plasma levels are reached after 1.8-2.8 hours after a high fat meal. Local inflammation can increase the absorption of dexibuprofen.

**Distribution**

It is highly bound to plasma proteins (99%), mostly to albumin.

**Metabolism & Excretion**

After metabolic transformation in the liver (hydroxylation, carboxylation), the maximum daily dose is 1200mg dexibuprofen.

**Therapeutic Indications**

- Acute symptomatic treatment of pain during menstrual bleeding (primary dysmenorrhea).
- With severely impaired hepatic function.
- With active Crohn's disease or active ulcerative colitis.
- From the beginning of 6th month of pregnancy.
- With cerebrovascular disease or other active bleeding.
- With active bleeding or other active bleeding.
- With severe heart failure.
- With severe hepatic disease.
- In patients with impaired renal function, concomitant use of NSAIDs at high doses should be avoided two days before and two days after the initiation of dexibuprofen treatment and the dosage of the anticoagulant should be adjusted if necessary.
- With severe congestive heart failure.
- 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.
- With coagulopathy.
- With active bleeding or other active bleeding.
- With active bleeding or other active bleeding.

**Possible Side Effects**

Common reactions:
- GI adverse reactions including gastro-intestinal ulceration and hemorrhage. The coadministration of dexibuprofen may also impair inhibition of platelet aggregation by low-dose acetylsalicylic acid.
- Reversible toxic amblyopia, impaired hearing, abnormal liver function, hepatitis, jaundice, blood disorders including thrombocytopenia, leucopenia, visual disturbances and tinnitus.
- Increased susceptibility to GI adverse reactions in the elderly.
- Precipitate attacks of asthma, bronchospasm, acute rhinitis, or cause urticaria.

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 anaphylaxis.

**Interactions**

- **Drugs to be used with caution or avoided**
  - Oral 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.
  - Antithrombotics: 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: Concomitant 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 /Aziidothymidine: 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**

- Cyclosporine, tacrolimus, sirolimus and aminglycoside 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.
- Phenytion, phenobarbital and rifampic: concomitant administration of CYP2C9 and CYP2C19 inducing agents may lower the effects of dexibuprofen.
- Thrombolitics, ticlopidine and antiplatelet agents: increased anti-platelet effect.

**Overdosage**

**Symptoms**

Mild symptoms are most common, including abdominal pain, nausea, vomiting, lethargy, drowsiness, headache, pyrexia, 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 anaphylaxis.

**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.

**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.

**Special Population**

- Keep out of reach of children.

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

**STORAGE**

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