DR.REDDY'S

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.

Nise™

(Nimesulide Tablets100 mg)

COMPOSITION:
Each uncoated tablet contains:
Nimesulide BP 100 mg

CLINICAL INFORMATION

INDICATIONS

In the short-term treatment of inflammatory conditions including joint disorders such as rheumatoid arthritis, post-traumatic and post-operative painful conditions and fever.

DOSAGE AND ADMINISTRATION

The usual adult dose is 100 mg twice daily, orally.

CONTRAINDICATIONS

- Known hypersensitivity to nimesulide.
- History of hypersensitivity reactions (bronchospasm, rhinitis, urticaria) to aspirin or other NSAIDs.
- Patients with active peptic ulcer disease.
- Patients with hepatic or renal impairment.
- Pregnancy and lactation.

WARNINGS AND PRECAUTIONS

Caution is advised when administering warfarin and nimesulide concurrently (see DRUG INTERACTIONS).

Use in Patients with Impaired Liver Function

Nimesulide is extensively metabolised in the liver to 4-hydroxy-nimesulide, a metabolite that contributes to the anti-inflammatory activity of nimesulide. In patients with moderate to severe hepatic impairment, metabolism of nimesulide to 4-hydroxy- nimesulide is impaired leading to decreased clearance and increased plasma concentrations of nimesulide resulting in drug accumulation. Therefore, nimesulide should not be administered in such patients.

Use in Patients with Impaired Kidney Function

There are reports about renal failure in patients on nimesulide therapy. In most such cases the casualty with nimesulide could not be established with certainty. It is, therefore, advised that patients with renal impairment should use nimesulide with caution. Patients with severe renal impairment should preferably avoid using nimesulide.

Patients with compromised renal function, congestive heart failure, cirrhosis, underlying metabolic disorders and those who are volume-or salt-depleted or dehydrated are more sensitive to the renal effects of NSAIDs; hence nimesulide should be used with caution in such patients.

Use in Asthmatic Patients

As with other NSAIDs, caution should be exercised while using nimesulide in patients with bronchial asthma.

INTERACTIONS

With Other Drugs

No clinically significant interactions involving interference with drug metabolism have been reported with nimesulide. Nimesulide is extensively bound to plasma proteins and may be displaced from binding sites by concurrently administered drugs such as fenofibrate, salicylic acid, valproic acid and tolbutamide. In addition, nimesulide may displace salicylic acid, methotrexate and furosemide, but not warfarin from plasma proteins.

Nimesulide has been used in clinical studies concomitantly with digoxin, gliclazide, glipizide, glyburide, metformin and warfarin without evidence of clinically significant adverse interactions. However, increased anticoagulant activity was observed in some patients with the concurrent administration of nimesulide and warfarin. Therefore, monitoring of coagulation tests is recommended with concomitant administration of these two drugs.

With Food

Food has limited effect on the rate and extent of nimesulide absorption. It may therefore be taken preferably after food to reduce gastric irritation.

With laboratory tests

When screening for occult fecal blood loss, nonsteroidal antiinflammatory drugs (NSAIDs) may need to be withheld for two to four days prior to testing, as a positive fecal hemoccult test may be attributable to NSAID-induced gastrointestinal bleeding. When a histamine skin prick-test evaluation is needed, nimesulide may need to be withheld for three to seven days prior to testing as nimesulide reduces the release of histamine by basophils and mast cells.

EFFECT IN PREGNANT OR IN LACTATING WOMEN

Safety and efficacy of nimesulide in pregnant and lactating women have not been established. Therefore, nimesulide is not indicated for use in pregnant and lactating women.

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ADVERSE REACTIONS

In general, treatment with nimesulide is well tolerated. Among the adverse events reported with nimesulide, the common ones are gastrointestinal disturbances (epigastric pain, heartburn, nausea, diarrhea, vomiting), skin reactions (rash, pruritus) and CNS effects (dizziness, somnolence, headache). No serious anaphylactoid or gastrointestinal complications such as ulceration and/or bleeding were observed following nimesulide therapy. Occasionally excessive perspiration, flushing, hyperexcitability and sleep disorders have been reported.

Isolated cases of mild renal toxicity, acute hepatitis, acute, irreversible liver failure and Reye's syndrome or Reye-like illness have been reported following nimesulide therapy.

Thrombocytopenic purpura was reported in a male patient with human immunodeficiency virus infection following 3 days of nimesulide therapy. Antiplatelet antibodies were not detected in plasma in the presence of nimesulide, suggesting a non-immunologic mechanism.

Laboratory abnormalities include transient increase in liver enzyme values (aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase), serum creatinine values, and serum uric acid values.

Nimesulide has been reported to cause hepatic adverse events, ranging from mild abnormal liver function to severe liver injuries including fatal hepatic failure in a few cases. Most of these patients were elderly women. It is reported that this adverse event appears to be idiosyncratic or immunologic in nature.

OVERDOSAGE AND TREATMENT

No information is available on overdosage with nimesulide.

PHARMACOLOGICAL INFORMATION

Nimesulide is a nonsteroidal anti-inflammatory drug (NSAID) of the sulphonanilide class that also has analgesic and antipyretic properties.

Mechanism of Action

Nimesulide is a selective cyclooxygenase-2 inhibitor and appears to exert its therapeutic effects through a variety of other mechanisms, which include:

- Reduced generation of superoxide anion by stimulated polymorphonuclear leucocytes through inhibition of protein kinase C translocation and phosphodiesterase type IV.
- Inhibition of platelet-activating factor (PAF) synthesis.
- Prevention of bradykinin-and cytokine-induced hyperalgesia by inhibition of tumour necrosis factor-α (TNF-α) release.
- Scavenging of hypochlorous acid.
- Inhibition of the signal transduction sequence leading to activation of the integrin CD11b/CD118.
- Prevention of inactivation of α_1-proteinase inhibitor.
- Inhibition of proteases (eg. elastase, collagenase).
- Inhibition of histamine release from human basophils and mast cells.
- Reduced degradation of cartilage matrix through inhibition of metalloprotease synthesis.

Pharmacokinetic Profile

After oral administration of 100 mg to healthy fasting volunteers, peak nimesulide plasma concentrations are achieved in 1-3 hours after administration. Nimesulide is extensively bound to (99%) plasma proteins. Nimesulide is extensively metabolised (<0.1% of a dose is excreted unchanged in the urine) to metabolites, which are excreted mainly in the urine with minor quantities excreted in the faeces.

The drug is mostly biotransformed into active 4-hydroxy-nimesulide, which possibly contributes to the anti-inflammatory activity of the compound. Peak concentrations of 4-hydroxy-nimesulide are attained within 3 to 5 hours after oral administration of nimesulide 50 to 200mg to healthy adult volunteers. The elimination half-life of nimesulide is1.5 - 5 hours.

PHARMACEUTICAL INFORMATION

STORAGE: Store in a cool place, protected from light & moisture.

PRESENTATION: Blister of 15 tablets in a new metallised pack.

For further Information, please write to
Medical Information cell,
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Dr. REDDY'S LABORATORIES LTD.,
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