DESCRIPTION

Pale yellow coloured, flavoured, round, biconvex, uncoated tablets, plain on both sides.

COMPOSITION

Each uncoated flavoured dispersible tablet contains:

Nimesulide .......... 100 mg

NIMESULIDE MOUTH DISSOLVING TABLETS

The concept of mouth dissolving tablets emerged from the desire to provide patients with a more convenient means of taking their medication. A mouth dissolving dosage form is designed to release drug rapidly within the oral cavity where it dissolves to form a drug suspension which is then swallowed.

The benefits of this approach are as follows:

- The faster the drug can get into suspension, the quicker the absorption and ultimate onset of clinical effect. Hence a mouth dissolving dosage form may be particularly suitable for those conditions such as fever, pain, inflammation, etc where a fast onset of clinical effect is required.
- The mouth dissolving system rapidly disintegrates in the oral cavity, hence patients do not have to swallow large cumbersome dosage forms which discourages many from taking their medication. In essence, therefore, the mouth dissolving dosage form combines the benefits of liquid formulations with those of a solid oral dosage form.
- Panacea Biotec's mouth dissolving formulation of Nimulid-MD can be described as a highly porous, microfine, matrix tablet. Once placed on the tongue, this matrix rapidly absorbs liquid and disintegrates. The drug, in a stabilized, size-reduced form to ensure an optimal drug suspension, dissolves rapidly in less than 60 seconds.
PHARMACOLOGY

The anti-inflammatory, analgesic and antipyretic activities of Nimesulide, a nonsteroidal anti-inflammatory drug (NSAID) of the sulfonanilide class, have been demonstrated in a number of experimental models and in numerous clinical trials. Nimesulide has exhibited potency similar to or greater than that of Indomethacin, Diclofenac, Piroxicam and Ibuprofen in standard animal models of inflammation such as carrageenan-induced rat paw oedema and inflammation, ultraviolet light-induced erythema in guinea-pigs and adjuvant arthritis in rats.\(^1\) The analgesic efficacy of Nimesulide was similar to that of Ibuprofen and less than that of Indomethacin in an acetic acid writhing test in rats, and acetic acid and acetylcholine writhing tests in mice. Nimesulide has shown superior antipyretic efficacy to Indomethacin, Ibuprofen, Aspirin and Paracetamol (Acetaminophen) in rats with yeast-induced fever.

Nimesulide appears to exert its therapeutic effects through a variety of mechanisms viz:\(^2\)

- Selective cyclooxygenase 2 inhibition.
- Inhibition of generation of superoxide anions from stimulated polymorphonuclear leucocytes.
- Inhibition of platelet activating factor synthesis
- Prevention of Bradykinin/Cytokine induced hyperalgesia of nerves (Inhibiting release of TNF-alpha)
- Scavenging of hypochlorous acid
- Blocking of histamine release
- Prevention of cartilage damage by inhibition of metalloprotease synthesis
- Phosphodiesterase type IV inhibition.

PHARMACOKINETICS

After oral administration of Nimesulide 50 to 200 mg to healthy adult volunteers, peak serum concentrations of 1.98 to 9.85 mg/L are achieved within 1.22 to 3.17 hours. Oral drug absorption is nearly complete and concomitant administration of food may decrease the rate, but not the extent of absorption of Nimesulide. The drug is extensively bound (99%) to plasma proteins and has an estimated apparent volume of distribution of 0.19 to 0.35 L/kg following oral administration.

Nimesulide is extensively metabolised (1 to 3% of a dose is excreted unchanged in the urine) to several metabolites which are excreted mainly in the urine (≈70%) or the faeces (≈20%). The drug is almost completely biotransformed into 4-Hydroxy-Nimesulide in both free and conjugated forms and this metabolite appears to contribute to the anti-inflammatory activity of the compound. Peak concentrations of 4-Hydroxy-Nimesulide ranged from 0.84 to 3.03 mg/L and were attained within 2.61 to 5.33 hours after oral administration of Nimesulide 50 to 200 mg to healthy adult volunteers. The elimination half-life of 4-Hydroxy-Nimesulide ranges from 2.89 to 4.78 hours and is generally similar to or slightly higher than that of the parent compound (1.56 to 4.95 h).

The pharmacokinetic profile of Nimesulide is not significantly altered in children, elderly volunteers and patients with moderately impaired renal function [creatinine clearance 1.8 to 4.8 L/h (30 to 80 ml/min)]. Slight accumulation of 4-Hydroxy-Nimesulide was noted in patients with moderate renal impairment; however, the clinical significance of this finding is unknown.
INDICATIONS

Clinical studies have established the analgesic, anti-inflammatory and antipyretic effectiveness of orally (mostly 200 mg/day) administered Nimesulide in the treatment of a variety of painful inflammatory conditions, including those associated with osteoarthritis, rheumatoid arthritis, oncology, post operative trauma, sports injuries, ear, nose and throat disorders, dental surgery, bursitis/tendinitis, thrombophlebitis, upper airways inflammation and gynaecological disorders. Nimesulide therapy was characterised by a rapid onset of analgesia and symptomatic relief in pain in clinical trials where a significant difference in clinical efficacy between active treatments was observed. Also Nimesulide has shown to be well tolerated even by aspirin sensitive asthmatic patients.

CONTRAINDICATIONS

Active peptic ulcer disease.

Moderate to severe hepatic impairment.

Severe renal failure.

PRECAUTIONS

Like other NSAIDs, Nimesulide should be used with great caution in patients with compromised renal function, cirrhosis of liver, congestive heart failure, renovascular disease or those who are volume or salt depleted. It is important to monitor hepatic injury parameters when using NSAIDs. Therefore, it is recommended that the serum levels of liver function tests be assayed periodically when starting Nimesulide for chronic use. Discontinue the drug immediately in cases with worsening liver tests.

Warning

Usage in pregnancy and nursing mothers: No well controlled studies are available regarding the use of Nimesulide in pregnancy and lactation. Avoid the use of Nimesulide in such cases.

Usage in children: Safety and efficacy of Nimesulide in children is well established.

ADVERSE REACTIONS

The most common adverse reactions are gastrointestinal disturbances (epigastralgia, heart burns, nausea, diarrhoea and vomiting). Dermatological reactions include rash and pruritus; central nervous system associated side effects are dizziness, somnolence and headache. Occasionally, excessive perspiration, flushing, hyperexcitability and sleep disorders have been reported. Rarely, a rise in liver enzyme levels have also been reported.
DRUG INTERACTIONS

Due to the extensive plasma protein binding Nimesulide may be displaced from the binding site by concurrent administration of fenofibrate, salicylic acid, valproic acid and tolbutamide. Moreover, Nimesulide may displace salicylic acid, methotrexate and furosemide from binding sites. Nimesulide reduced the diuretic effect for concomitantly administered furosemide. Concomitant administration of Nimesulide and digoxin showed no effect on serum digoxin concentrations at steady state. Although Nimesulide does not appear to interact with Warfarin, in clinical practice, interaction with oral anticoagulants or other highly protein bound drugs cannot be ruled out. Nimesulide may cause enzymatic induction of theophylline when administered concomitantly with it. Nimesulide had no significant effect on fasting blood and glucose tolerance in patients treated with antidiabetic agents.

OVERDOSAGE AND TREATMENT

No data is available on overdosage toxicity. In the event of an overdosage the stomach may be emptied and symptomatic treatment should be given.

DOSAGE AND ADMINISTRATION

The usual oral dosage of Nimesulide in adults is 100 to 200 mg twice daily.

STORAGE INSTRUCTIONS

Store in a cool, dry and dark place.

PRESENTATION

10 X 1 X 10 tablets.
REFERENCES