DESCRIPTION

Nimulid-MD-KID Tablets contain nimesulide which is chemically 4-Nitro-2-phenoxyethane sulphonanilide. Nimulid-MD-KID Tablets are pale yellow coloured, flavoured, round, flat, bevel edged, uncoated tablets, scored on one side and plain on the other.

COMPOSITION

Each uncoated flavoured dispersible tablet contains:

Nimesulide BP ...............50 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 gets into suspension, the quicker is the absorption and ultimate onset of clinical effect. Hence, a mouth dissolving dosage form may be particularly suitable for 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, the mouth dissolving dosage form combines the benefits of liquid formulation with those of a solid oral dosage form.

Panacea Biotec's mouth dissolving formulation of Nimulid-MD-KID tablet 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 ensures an optimal drug suspension which 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 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
Nimesulide 50 mg in children in single oral dose is rapidly absorbed and a mean maximum Nimesulide plasma concentration of 3.5 mg/L is achieved within 2 hours of administration, which subsequently declines in the following 12 hours. Nimesulide is metabolised to a principal metabolite 4-hydroxy-Nimesulide. The mean elimination phase half-life ($t_{1/2}$) is 2.4 hours. Mean hydroxy-Nimesulide concentrations are initially lower than those of the parent drug but are subsequently greater than the parent drug concentration, at the later sampling points ($C_{max} 1.34±0.54$ mg/L, $t_{max} 3.5±1.69$h).

INDICATIONS
Clinical studies have established the analgesic, anti-inflammatory and antipyretic effectiveness of Nimesulide in the treatment of a variety of painful inflammatory conditions,³ including those associated with fractures, soft tissue injury, post operative trauma, sports injuries, ear, nose and throat disorders, dental surgery, thrombophlebitis and upper respiratory inflammations. Nimesulide therapy is characterised by a rapid onset of analgesia and symptomatic relief in pain. Nimesulide is as effective as mfenamic acid or paracetamol in reducing fever and inflammatory symptoms associated with upper respiratory tract infection and in reducing pain of various origins in children. Compared with other NSAIDs and paracetamol, nimesulide generally showed a significantly faster reduction of fever and other sign and symptoms (dyspnoea, cough, asthenia, hyperemia, dysphagia, oedema and pharyngeal pain) of respiratory tract inflammation.

CONTRAINDICATIONS
- Active peptic ulcer disease
- History of allergy to NSAIDs
- History of nasal polyps, angioedema and / or bronchospastic reactivity to any NSAIDs
- Hypovolaemia / dehydration (≥ 10% total body weight)
- Bleeding disorders
- Moderate to severe hepatic impairment
- Renal insufficiency

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.

Caution: Coadministration with other potentially hepatotoxic drugs should be avoided.

ADVERSE REACTIONS
World wide, the majority of adverse reactions recorded affected the digestive system followed by the skin and the nervous system. Of the 17 ADR reports ascribed to Nimesulide as received by the national pharmacovigilance center of the WHO, 5 were of the skin and 4 of the liver. Others were peripheral oedema (2), stomatitis (2), paresthesia (1), thrombocytopenic purpura (1), irritability (1) and headache / reduced visual activity (1). No adverse GI reactions have been reported. Of the hepatic ADR's reported; two cases were compatible with Reye's syndrome. Nimesulide may also cause acute hepatitis and an elevation in liver enzymes.

The adverse effect profile of Nimesulide in Indian population in children was similar to that reported for all age groups. The adverse effects reported in 4097 case report forms were gastrointestinal (3.1%), vomiting (1.34%), burning stomach / irritation in stomach (0.60%), abdominal pain (0.50%), diarrhoea (0.40%), nausea (0.17%), black stools (0.10%), hematemesis (0.02%), skin and mucous membrane (1.7%), itching / rash / urticaria (1.50%), cold and clammy skin (0.10%), stomatitis (0.04%), yellow discolouration (0.04%), dry red lips (0.02%), bleeding gums (0.02%), renal (0.3%), generalised oedema (0.10%), hematuria (0.10%), reduced urine output (0.04%), burning micturition (0.04%), nephritis (0.02%), CNS (0.4%), drowsiness (0.12%), dizziness (0.10%), irritability (0.15%), heavy headedness (0.02%), others (1.3%), puffiness of face / eyelids (0.70%), hypothermia (0.31%), excessive sweating (0.17%), muscle pain (0.07%), chest pain (0.02%), joint swelling (0.02%), peripheral cyanosis (0.02%) and worsening (0.02%). Out of these only patients with hypothermia, hematemesis and muscle pains required hospitalization, but all subsided after stopping the drug.

DRUG INTERACTIONS

Extensively plasma protein bound drugs
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.

Furosemide
Nimesulide reduced the diuretic effect for concomitantly administered furosemide.

Digoxin
Concomitant administration of Nimesulide and Digoxin showed no effect on serum Digoxin concentrations at steady state.

Warfarin
Nimesulide does not appear to interact with Warfarin, in clinical practice; although interaction with oral anticoagulants or other highly protein bound drugs cannot be ruled out.

Theophylline
Nimesulide may cause enzymatic induction of Theophylline when administered concomitantly with it.

Antidiabetic agents
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 overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive therapy, if required.

DOSAGE AND ADMINISTRATION
The usual oral dosage of nimesulide in children is 50 mg twice daily.
STORAGE INSTRUCTIONS
Store in a cool, dry and dark place.

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