

# NIMULID MD™

## 1. Introduction

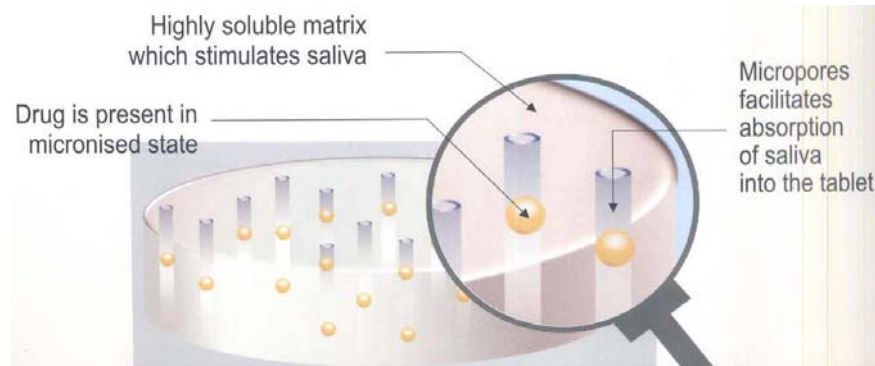
**Nimulid MD™** is a flavoured dispersible Nimesulide tablet with fast mouth dissolving characteristics thereby providing immediate relief. Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) indicated for the **management of a variety of painful and inflammatory conditions** like post operative pain, primary dysmenorrhea and painful osteoarthritis. Nimesulide is currently marketed in more than 50 countries and till date, approximately 346 million treatment courses have been administered during Nimesulide's 19 years of presence in the market. With the recent concerns associated with the safety of selective COX-2 inhibitors, there has been increased interest and preference for Nimesulide due to its unique COX-1 / COX-2 selectivity ratio and established safety and efficacy

Nimesulide appears to exert its therapeutic effects through a variety of mechanisms viz :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

## 2. Nimulid MD™ Drug delivery system

Nimesulide is micronized (particle size less than 5 micron) in **Nimulid MD™** and dispersed in a highly soluble matrix with a unique combination of rapidly soluble polyols. This matrix as also the tablet ingredients like flavours, stimulate saliva secretion. Further, the composition contains the drug in a taste-masked form, along with sweeteners, which are modified with special polymers to have mucoadhesive properties. These sweeteners

provide long lasting sweetness in the mouth, thus preventing the bitter after taste of Nimesulide.



### 3. Clinical Experience

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.

#### 3.1 Study I

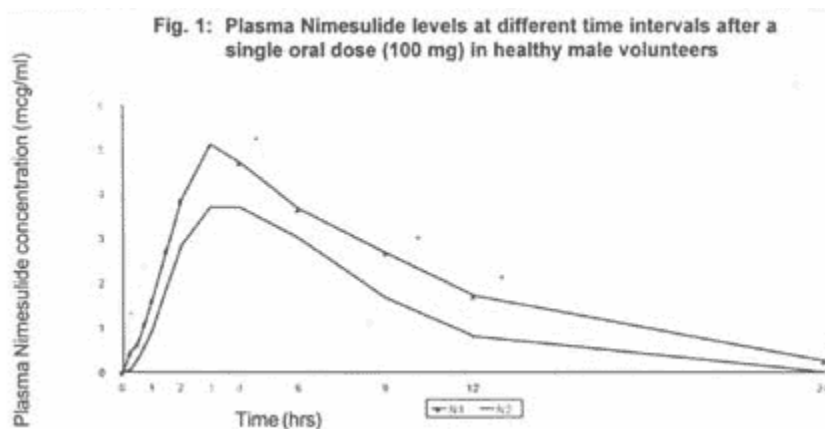
A study in six healthy Indian volunteers was done to evaluate the investigate analgesic activity of single dose treatment of Nimesulide 100 mg. **Nimulid MD™** or **Nimulid™** 100 mg was administered in a two way crossover design and ischemic pain test were repeated at regular intervals till 8 hours after the administration of the drug. Maximum analgesic score (E-max), time for maximum effect (T-emax) and area under the clock time versus time to tolerance (AUC) was calculated for both the groups.

Parameters	Nimulid MD™ 100 mg	Nimulid™ 100 mg
<b>E<sub>max</sub> (secs)</b>	44.33 ± 12.84	35.66 ± 11.63
<b>T-emax (hours)</b>	02.41 ± 00.49	02.58 ± 00.66
<b>AUC 0-8 hr (sec x hours)</b>	150.37 ± 51.83	136.45 ± 35.48

**Table 1: Mean Pharmacodynamic Parameters**

### 3.2 Study II

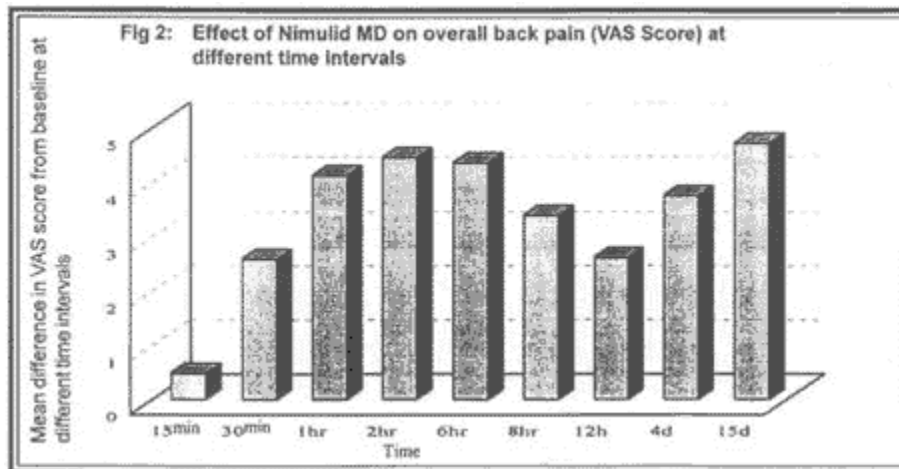
A randomized, two-treatment, two-sequence, single dose, crossover bio-availability study on Nimesulide mouth dissolving tablets 100 mg (**Nimulid MD™ 100mg**) comparing with conventional Nimesulide formulation (Nise 100 mg) in 12 healthy, adult, male human subjects under fasting conditions. The various pharmacokinetic parameters for both the drugs were calculated and the results reflected significantly greater rate and extent of N<sup>1</sup>s as compared to that of N<sup>2</sup> since C<sub>max</sub> and AUC were significantly increased with N<sup>1</sup> as compared to N<sup>2</sup>. (Fig. 1)



### 3.3 Study III

An open labelled non-comparative trial was conducted to evaluate the efficacy and safety of mouth dissolving formulation of Nimesulide in acute low back pain. Fifty-six patients with acute low back pain (LBP) were enrolled and were given Nimesulide mouth

dissolving tablets (**Nimulid MD**™ 100mg) in morning and evening for 14 days. Pain intensity was measured on visual analogue scale at various points of time on day 1, then on day 4, day 8 and day 15. Forty-nine patients completed the trial and various parameters of pain were reduced significantly as measured on VAS scoring (Fig. 2). Adverse effects were seen in 8.16% of patients in the form of epigastric pain, nausea and heartburn.



### 3.4 Study IV

A single blind comparative evaluation of efficacy and safety of **Nimulid MD**™ (Nimesulide Mouth Dissolving Tablets - 100mg) with Piroxicam and Diclofenac was done in patients of acute low back pain. **Nimulid MD**™ showed a rapid relief from pain as seen with reduction in VAS score in all the parameters which were measured. The pain reduction was significant as compared to Piroxicam and Diclofenac. **Nimulid MD**™ was well tolerated with no side effects and good acceptability by the patients.

## 4. IPR Status

Products patents have been filed in all major countries across the globe and already granted in some of the countries

## 5. Development Stage

- Commercialized in the Indian market
- CTD compilation under process for regulated markets

## 6. Product Presentation

### **Nimulid MD™**

Flavoured dispersible tablet

#### **Each tablet contains**

Nimesulide BP                      100mg



### **Nimulid MD™ Kid**

Flavoured dispersible tablet

#### **Each tablet contains**

Nimesulide BP                      50mg

