

## Nimesulide: A double-edged sword must be banned

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Dear Editor, My purpose in writing this letter is to draw your attention to a very susceptible situation of possible adverse reactions like hepatotoxicity caused by Nimesulide. It is being prescribed as an over-the-counter drug and is available even online for home delivery without any prescription in Pakistan.

Nimesulide is an atypical selective COX-2 inhibitor that is similar in anti-inflammatory effects as compared to other classical NSAIDs and selective COX-2 (celecoxib & rofecoxib) inhibitors but different as it has a protective effect on NSAID-induced ulcers as compared to other more selective COX-2 inhibitors, which do prevent but do not protect NSAID induced ulcers.<sup>1</sup>

But, does this only benefit of being gastroprotective justify its use as a relatively common drug with or without a prescription?

I have serious reservations regarding using this drug even with a prescription, as its easy access and dispatch on the same medicine can lead to many serious adverse effects. I am here to persuade the doctor community involved in policymaking to take serious notice of this drug.

Although the Union Ministry of Health and Family Welfare in India suspended the pediatric use of this drug in March 2011, the concern arises from its unrestricted availability to adults without requiring a prescription.<sup>2</sup> Donati M et al. reported in a multicenter study in BJCP that nimesulide is associated with a higher risk of hepatotoxicity as compared to ibuprofen and high doses of ketoprofen, with an adjusted OR for serious liver injury of 2.10, at 95 % CI 1.28 - 3.47 with the risk increasing according to the length of exposure<sup>3</sup>. Besson F. et al., in an international collaborative study done in 2021, showed that with a median time of onset of 40 days, 81 % were jaundiced.<sup>4</sup> There was a hepatocellular pattern of Drug-induced Liver Injury ( DILI ). Overall, 21% of patients developed acute liver failure, 8.8% died, and 5% underwent liver transplantation. Latency was  $\leq$  15 days in 12 patients

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(21%), and one patient developed ALF within 7 days from treatment initiation. DILI latency was < 15 days among those who developed liver failure, and one had DILI within 7 days of administration. A meta-analysis done by Kwon, J., et al. in 2019 clearly showed that nimesulide was significantly associated with hepatotoxicity [RR 2.21, 95% CI 1.72-2.83]<sup>5</sup>. Even less than 15 days of consumption of this drug was associated with hepatotoxicity, which can lead to mortality and the need for a Liver transplant. It is hereby suggested based on the above evidence that risking a side effect of hepatotoxicity for a class of drug whose many alternatives are easily available with good efficacy is not a sane choice, and things must be kept in check to avoid such drug-induced side effects whose results can be really worrisome.

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