

1985 - Nimesulide is first marketed in Europe.

1985 - Reports of serious adverse reactions to nimesulide begin to surface from across Europe.^{i ii}

2002 - Finland and Spain withdraw the medicine from the market following cases of liver injury caused by nimesulide.ⁱⁱⁱ Shortly afterwards, Finland alerted the EMA, which mandated representatives from Italy, the country with the highest consumption of nimesulide, and Finland to report on the safety profile of the medicine.^{iv}

2003 - Patients taking nimesulide have double the chance of suffering severe liver damage compared to the risk posed by other non-steroidal anti-inflammatory, according to a recently published Italian study conducted on 397 500 patients between 1997 and 2001.^v

2004 - Nimesulide retains its licence for the European market, following the EMA's re-evaluation of the medicine. Certain limitations are also imposed, such as a lower maximum dose.^{vi}

2007 - Ireland suspends the sale of nimesulide after six cases of liver failure requiring liver transplants are reported in association with the medicine.^{vii}

2007 - This prompted the EMA to re-evaluate the safety profile of nimesulide, this time appointing Ireland as the rapporteur. The EMA ruled that the data did not support a move to suspend the marketing of nimesulide across Europe. However, the use of nimesulide is further restricted to a second-line treatment at the lowest effective dose.^{viii}

2008 - Over 570 cases of hepatic disorders associated with nimesulide are reported from across Europe since 1985.^{ix}

2010 - Patients have 2.5 times higher risk of hospitalisation for acute liver damage with nimesulide than with other non-steroidal anti-inflammatories,^x according to a case-control study conducted between 2001 and 2004 but not published until this year.^{xi}

2011 - The EMA affirms that the benefits of nimesulide-containing medicines continue to outweigh the risks, while its use is restricted to treat only acute pain and menstrual pain.^{xii xiii}

ⁱⁱ La revue prescrire. Nimesulide: patients still exposed to a risk of severe hepatitis (2011) URL:

<http://english.prescrire.org/en/D888466637A59AC42A489AA0BE9B2235/Download.aspx>

ⁱⁱⁱ EMA post-authorisation evaluation of nimesulide (2004) URL:

http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Nimesulide_31/WC500013818.pdf

^{iv} See EMA post-authorisation evaluation of nimesulide (2004)

^v Traversa G et al. "Cohort study of hepatotoxicity associated with nimesulide and other non-steroidal anti-inflammatory drugs".

^{vi} See EMA post-authorisation evaluation of nimesulide (2004)

^{vii} EMA Press Release - European Medicines Agency recommends restricted use of nimesulide-containing medicinal products (2009) URL:

http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500011199.pdf

^{viii} See EMA Press Release (2009)

^{ix} See La revue prescrire (2011)

^x Except with celecoxib, rofecoxib, diclofenac and ibuprofen

^{xi} Lee CH et al. "Increased risk of hospitalization for acute hepatitis in patients with previous exposure to NSAIDs" *Pharmacoepidemiol Drug Saf* 2010;

^{xii} The review of nimesulide was conducted in the context of a formal review under Article 31 of Directive 2001/83/EC, initiated in January 2010 at the request of the European Commission

^{xiii} EMA Press Release - European Medicines Agency concludes review of systemic

nimesulide-containing medicines (2011) URL:

www.ema.europa.eu/docs/en_GB/document_library/Press_release/2011/06/WC500107903.pdf