NOTIFICATION OF A REFERRAL UNDER ARTICLE 31 OF DIRECTIVE 2001/83/EC
FAX NUMBER –44 20 75237051

This notification is an official referral under Article 31 of Directive 2001/83/EC made by France, ANSM:

Active Substance	Diacerein for oral administration (Art 50 mg, Zondar capsules and generics)
Marketing Authorisation Holders in the referring Member State	Negma, Actavis, Arrow, Biogaran, Cristers, EG, Evolupharm, Mazal pharmaceutique, Mylan SAS, Qualimed, Ranbaxy, Sanofi-Aventis, Sandoz, Substipharm, Teva Sante, Winthrop, Zydus, Mazal, Niverpharm, Laboratoire Pharma 2000

The above mentioned Member State, considers that it is in the interest of the Union to refer the above mentioned medicinal products to the PRAC.

Diacerein (Art 50 and Zondar) capsules have been nationally approved in France since 1992 in the symptomatic treatment of functional symptoms of osteoarthritis. Following a national procedure of reassessment of marketing authorisation of Symptomatic slow-acting drugs (SYSADOA), the indication of diacerein was modified in 2008 to become "symptomatic treatment through delayed effectiveness of osteoarthritis of the knee and the hip" and adverse reactions have been added in section 4.8 of the French SmPC.

In France, a systematic review of some drugs nationally authorized before 2005 is undertaken since 2011. In some cases, this review could lead to a full benefit / risk reassessment. In that context, Diacerein's national review leads to a national benefit / risk reassessment in 2012.

On one hand, this product was assessed on a pharmacovigilance point of view in 2006 after the report of cases of hepatitis, including one fatal, attributed to diacerein. In the current review, the occurrence of very frequent digestive disorders, cases of hepatitis and serious skin reactions in patients treated with diacerein was underlined.
On the other hand, according to the clinical trials and bibliographical data, the efficacy appears weak in the symptomatic treatment of osteoarthritis with low impact on pain and functional symptoms and with no demonstration of a decrease of NSAIDs intake in patients treated with diacerein.

The safety concerns identified with diacerein (very frequent digestive disorders, including diarrhoea and melanosis, skin reactions sometimes serious, hepatic disorders more often cytolytic with one fatal case and some serious cases reported) were considered unacceptable given the weak benefit of diacerein in the symptomatic treatment of osteoarthritis.

In view of the above and based on available data, the French Health Products Agency (ANSM) considers that the benefit/risk balance of diacerein has become unfavourable in the symptomatic treatment of osteoarthritis of the knee and the hip and that the marketing authorisations should not be maintained. The ANSM requests the PRAC to give a recommendation under Article 31 of Directive 2001/83/EC on whether the balance of benefits and risks is favourable in the authorised indications and whether the marketing authorisation for medicinal products containing diacerein should be maintained varied, suspended or withdrawn.

Signed [redacted]

Pr Dominique MARANINCHI