

**NOTIFICATION OF A REFERRAL UNDER ARTICLE 107i OF
DIRECTIVE 2001/83/EC
FAX NUMBER -44 20 75237051**

This notification is an official referral under Article 107i of Directive 2001/83/EC as amended, to the PRAC made by France -ANSM

Active substance	Tetrazepam for oral use (Myolastan 50 mg, tablets and generics)
Marketing Authorisation Holders in the referring Member State	Arrow, Biogaran, Cristers, Daiichi Sankyo France, EG Labo, Mylan SAS, Qualimed, Ratiopharm GMBH, Ranbaxy, Sandoz, Sanofi, Teva Santé, Zydus.

Myolastan (tetrazepam) was authorized in France in 1967. This medicinal product marketed by Sanofi-Aventis and the generics are registered in France through a national procedure. Tetrazepam is indicated in France for the treatment of painful muscle spasm in rheumatological diseases (in association with specific treatments).

Following the reporting of new serious cutaneous cases and of an occupational contact dermatitis (in a nurse working in a nursing home, crushing tetrazepam tablets for patients who cannot swallow tablets) a national pharmacovigilance survey was initiated. This French review of pharmacovigilance data concerned all adverse drug reactions, especially cutaneous reactions, recorded in the French National Pharmacovigilance Database, since the marketing of tetrazepam in France.

This review highlighted a cutaneous toxicity of tetrazepam, in addition of the pharmacological expected adverse drugs reactions (ADRs) of a benzodiazepine. Half of ADRs reported with tetrazepam were cutaneous; among the 648 serious cases reported, 305 cases belonged to the SOC "Skin and subcutaneous disorders". This safety profile was unusual compared to the safety profile known for other benzodiazepines.

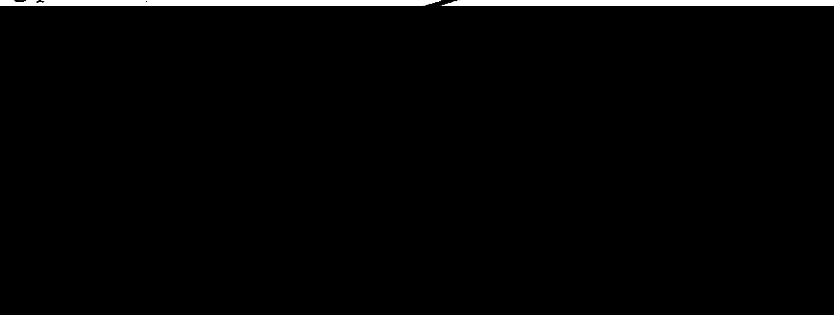
Moreover the seriousness of some reported cases was of concern: 33 Stevens-Johnson syndrome (SJS), 33 toxic epidermal necrolysis (TEN), 59 erythema multiforme and 15 DRESS syndrome cases have been reported; 11 of them had a fatal outcome (1 SJS, 9 TEN, 1 erythema multiforme).

Among the cutaneous cases reported, an allergic work-up with tetrazepam was done in 105 reports and in 64% of the cases, tetrazepam was the only drug suspected.

Due to this major safety concern with an unusual and serious cutaneous risk for a benzodiazepine, and taking into account the symptomatic indication of tetrazepam, the French Health Products Agency (ANSM) considers that the risk is unacceptable and that an urgent action should be taken. ANSM considers revoking the marketing authorisation of tetrazepam containing products.

In view of the above ANSM requests the PRAC to give a recommendation under the urgent union procedure, article 107i of the Directive 2001/83/EC as amended for tetrazepam containing products for all their indications.

Signed



Date 20 DEC. 2012