

Letter to the Editor

EMA revokes marketing authorization for bufexamac

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To the Editor,

Bufexamac is a non-steroidal anti-inflammatory drug that had been used in topical drug specialties for the treatment of pruritic dermatitis. Medicines containing bufexamac have been authorized in Austria, Bulgaria, the Czech Republic, France, Germany, Hungary, Italy, Latvia, Lithuania, Luxembourg, Portugal, Romania, and Slovakia (EMA/CHMP/239923/2010). On 27 July 2010, the European Commission issued a decision to the member states regarding the revocation of national marketing authorizations for medicinal products containing bufexamac (referring to article 107 of directive 2001/83/EC). This decision was based on an opinion of the European Medicines Agency (EMA; www.ema.eu) of April 2010, which, in turn, was prompted by a review of risk and benefit conducted by the Federal Republic of Germany, namely, the 'Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)', www.bfarm.de/. The BfArM, in turn, relied on epidemiological surveillance data collected and analysed by the Information Network of Departments of Dermatology (IVDK) (www.ivdk.org) (1) and the expertise of the independent Drug Commission of the German Medical Council (2) – see below.

Dermatologists based in (European) countries where bufexamac is not marketed, such as Scandinavian countries or the United Kingdom, will probably not appreciate the above news. Those European dermatologists who have seen unfortunate patients with acute generalized Erythema exsudativum multiforme-like, or severe baboon-like, perianal (3) allergic contact dermatitis caused by bufexamac will certainly be relieved. However, if the above decision is only the favourable end-point of an administrative decision-making process, why is the 'bufexamac story' still worth telling? In our view, two aspects are important: (i) there may be countries outside Europe where bufexamac is still on the market; and (ii) there are lessons to be learnt from the

'bufexamac story'. Regarding the former aspect, national regulatory authorities, supported by dermatologists, are encouraged to consider following the step taken in the EU. Regarding lessons to be learnt, the following aspects seem important:

- Active epidemiological surveillance based on clinical network data (4) is preferable to (voluntary) 'spontaneous' notification systems: between July 1999 and December 2004, 560 of 39 392 patients had a positive patch test reaction to bufexamac in the IVDK alone. The network is estimated to cover about 2–3% of all German patch tests; thus, with extrapolation using the 'Clinical Epidemiology – Drug Utilisation Research' approach, several thousand cases per year must be suspected. During the same 5.5-year period, only 23 suspected cases of bufexamac contact allergy had been registered in the pharmacovigilance system implemented in Germany (1). Thus, extreme under-reporting is apparent, and, along with this, there is a severe underestimation of risk when therapeutic benefit is balanced with the risk of adverse drug reactions.
- The application of standards of 'evidence-based medicine' in the evaluation of both risk and benefit is mandatory: during the formal process of re-evaluating risk and benefit initiated by the German BfArM, first in September 2002, then in April 2006, and finally in November 2009 (the latest step triggering the mechanism at the EU level, see above), data that could substantiate claims of efficacy in the treatment of dermatitis were requested from the companies producing or marketing bufexamac. It became apparent that valid data did not exist, either in published format or on file with the companies, that could be used in the benefit/risk balance. Thus, focusing here on the aspect of potential benefit, it is mandatory to apply current standards for the design of intervention studies even in an area as 'superficial' as the topical treatment of skin conditions.

- European integration has proven to be efficient: the outcome of a review completed by one national agency (in this case, the German BfArM; see above) has triggered a European process that, after just half a year, has resulted in EU-wide regulatory action promoting the safety of drug treatment across Europe.

Sincerely,

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