Bern, December 2024

Important safety-related information regarding the prescription of preparations containing betahistine.

Dear Ladies and Gentlemen,

Swissmedic would like to inform you of the following:

Summary
- The nitrosamine impurity N-nitroso-betahistine, shown to be highly mutagenic, has been found in batches of medicines/products containing betahistine
- A safety level has been established internationally to ensure a sufficient quality of batches released for the Swiss market based on the authorised maximum daily dose.
- When prescribing betahistine products, the indications authorised by Swissmedic, corresponding dosages and expiry dates must be strictly adhered to.

Background
Preparations containing betahistine are indicated for the first-line treatment of dizziness due to circulatory disorders of the inner ear, as well as Ménière's syndrome and Ménière-like syndrome (dizziness, ringing in the ears, hearing loss).

N-nitroso-betahistine was recently shown to be mutagenic *in vitro* and in animals and measures have been taken to mitigate a potential carcinogenicity risk for humans. Based on the maximum authorised daily dose of betahistine products (48 mg), an internationally harmonised acceptable intake level has been defined that should not be exceeded in the finished product. In this regard, Swissmedic has imposed requirements to ensure that any potentially existing traces of N-nitroso-betahistine in Swiss batches of betahistine products do not exceed this safety level.

Betahistine-containing products have a reputation for being drugs with a very favourable safety profile for their approved indications. There are some literature reports recommending off-label use even at very high dosages over long periods of time. So far, there has been no evidence for major safety concerns in the context of such off-label use. However, the safety profile of such off-label use with respect to N-nitroso-betahistine exposure is not known. In the light of the highly mutagenic properties of N-nitroso-betahistine, betahistine-containing products should not be prescribed outside the use authorised by Swissmedic (referring to, but not limited to respective indications, and their corresponding dosages). Expiry dates indicated on the folding boxes must be strictly adhered to.

Intensive work is ongoing to improve the manufacturing process to further reduce the levels of N-nitroso-betahistine in betahistine-containing products.

Adverse Drug Reaction Reporting
Swissmedic recommends the use of its dedicated portal Electronic Vigilance System (ElViS) for reporting adverse drug reactions (ADRs). All the necessary information about this system can be found under www.swissmedic.ch.

Contact details
If you have any further questions or require additional information, please contact the respective market authorisation holder of the product.

Supplements
For further information, in particular the approved indications, corresponding dosages and storage conditions of products we also refer to the respective Information for healthcare professionals under www.swissmedicinfo.ch.

Swissmedic
Hallerstrasse 7
3012 Bern