Pyrrolizidine alkaloids

Risk assessment and analysis of pyrrolizidine alkaloids in phytopharmaceuticals and homoeopathic products

Background

On 1st March 2023, the Federal Institute for Medicinal Products and Medical Devices (BfArM) released its updated statement on testing pyrrolizidine alkaloid levels in order to ensure the quality and safety of medicinal products containing homoeopathic preparations derived from herbal source materials as active pharmaceutical ingredients. Information on all relevant developments can be found below.

Strategic evaluation

The statement released on 1st March 2023 supersedes the statement dated 1st March 2016 and now only contains measures that are dedicated to ensuring the quality of medicinal products containing homoeopathic preparations derived from herbal source materials. It also makes reference to the HMPC Public Statement on pyrrolizidine alkaloids (EMA/HMPC/893108/2011 Rev. 1).
According to this, there is no need to submit a risk assessment for finished homoeopathic or anthroposophic medicinal products containing active pharmaceutical ingredients of herbal origin where the dilution levels in the finished medicinal product are D4 or higher. If the dilution levels are lower than D4, a risk assessment must be submitted, giving details of the final concentrations of active pharmaceutical ingredients present in the medicinal product along with justification for dispensing with a PA quantitation procedure (safe potency level).
Unlike the statement published in 2016, the new one explicitly refers to children as being a vulnerable group of patients. Product-specific limit values and test concepts based on the 2016 BfArM statement will need to be revised and adapted where necessary.

Analysis

PhytoLab offers carefully targeted analytical procedures for source drugs containing PAs (e.g. Eupatorium, Petasites, Borago) for the analysis of herbal source materials, homoeopathic mother tinctures, active herbal ingredients and medicinal products derived from these, as well as for products which must be examined for the presence of PA contamination attributable to weeds.

Need for action

The risk assessment is based on the maximum tolerable PA intake of 0.0237 µg/kg body weight per day, according to the HMPC Public Statement.
This calculation basis applies to the same extent to both herbal medicinal products and homoeopathic products derived from herbal source materials. The maximum dosage for the youngest age group is not only authoritative for the risk assessment, but also for determination of a product-specific limit value for the medicinal product. The reference dosage values for the toxicological assessment of registered homoeopathic medicinal products are given in the statement.

We can advise you with respect to the determination of safe potency levels and prepare risk assessments for herbal medicines and homoeopathic preparations.
We also provide support when it comes to such regulatory matters as compiling the necessary dossier documentation and responding to official statements from authorities.

Any questions? Your contacts at PhytoLab

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