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Committee on Herbal Medicinal Products (HMPC)

AESGP hearing at HMPC meeting, November 2019

Report

List of representatives from the Association of the European Self-Medication Industry (AESGP)

Frank Waimer, Catherine Mahony, Mónica Mennet-von Eiff, Barbara Steinhoff, Christelle Anquez-Traxler

1. Pyrrolizidine alkaloids (PAs)

AESGP presented a selection of results of a 2019 data evaluation on PA values found in herbal drugs and extracts as collected by the German herbal industry. From this 2019 evaluation AESGP reported that 44 % of the most important 27 herbal drugs can keep the limit of 0.35 µg PA per day (2018: 37%), whereas 56% can keep the limit of 1.0 µg PA per day (2018: 63%). With regard to the most important 20 herbal extracts, 75 % can keep the limit of 0.35 µg PA per day (2018: 68%), whereas 90% can keep the limit of 1.0 µg PA per day (2018: 82%). AESGP concluded that the 2019 evaluation clearly demonstrates that in many cases the applicable daily limit of 1.0 µg PA per day related to the final product can be kept. However, at the same time, it is evident that a reduction to 0.35 µg PA per day is still not realistic within the next 18 months. Thus, AESGP proposes establishing a permanent limit of 1.0 µg PA per day.

AESGP then gave a short overview on the status of research on PA potencies as regards their toxicity. It was shown that not all PAs are equally potent. Merz and Schrenk had initially demonstrated through their research on PAs the concept of relative potency factors; which is increasingly supported by several data coming from different research streams. A follow-up workshop to the one organised in 2018 is envisaged by the University of Kaiserslautern; this time with a focus on toxicokinetics taking into account that gut permeability rates may differ between various PAs.

HMPC thanked for the information presented and also the data submitted earlier upon the call for data for the revision of the two HMPC Public Statements on PAs. Finalisation is intended before May 2021 with a public consultation planned in 2020.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

2. Estragole

An exchange of views on the current status of the HMPC assessment of estragole and the potential consequences of a limit for estragole for products such as fennel tea and other preparations took place. The HMPC explained that the draft revised Public Statement is close to finalisation. Given the lack of sufficient data the conclusions are particularly challenging and various factors are taken into consideration including appropriate toxicological models for risk assessment, protection of sensitive patients' groups, background intake via food and potential consequences for the market. In case of substantial changes, a second public consultation phase for the revised Public Statement is foreseen. It was reminded that subsequently this may cause delay in finalisation of pending assessments for new or revised monographs on estragole-containing herbal substances.

3. Changes in Ph. Eur. monographs that lead to a change in declaration

AESGP emphasised that in the case of standardised extracts it is important that Ph. Eur. monographs and HMPC monographs are closely and timely aligned. Using the example of Horse chestnut standardised extract, the change from unspecific photometric method to a specific HPLC method requires a change of the declaration of the active marker aescin in products as well as the corresponding HMPC monograph. AESGP expressed the view that if the corresponding HMPC and Ph. Eur. monographs are not aligned, extracts need to be tested according to both methods which results in huge difficulties as the target parameter for standardisation with inert excipients is different depending on the method used. In the light of the upcoming change of the Ph. Eur. monographs for anthrachinone glycoside drugs, AESGP asked the HMPC to consider a fast-tracked partial revision of the corresponding HMPC monograph to align the declaration of the active marker.

HMPC assured that the revision of the specific monograph does take the analytical change at Ph. Eur. into account and will soon be finalized. In general, such a fast track mechanism is not foreseen if not urgently required for safety reasons. The work is usually coordinated along predefined workplans. HMPC also reminded that EU herbal monographs on safety/efficacy are harmonised standards but neither an individual SmPC nor binding. There is practically neither a change of the most important monograph sections (indication, contraindication, etc.) nor of substances/preparations included. The specification/declaration adaptation in line with Ph. Eu. quality requirements should therefore primarily be solved in national procedures for individual products. It was also reassured that regular exchanges are taking place between HMPC and EDQM with EDQM observers at HMPC and QDG and HMPC/QDG members also members of Ph. Eur. expert groups.

Given some difficulties experienced in some MSs, AESGP still proposed a fast track revision of the EU herbal monograph when the Ph. Eur. monograph it refers to is changed and published in English. It was therefore agreed that AESGP may outline the issue in more detail in written form together with a proposed solution for further consideration by HMPC.

4. Publication of HMPC meeting reports and agendas

AESGP emphasised the importance of HMPC public documents for information of the industry on meeting outcomes, upcoming public consultations or progress with guidance documents. AESGP noted with satisfaction that after some delays in publication of HMPC public documents following the move to Amsterdam, the timing seemed to have resumed as before. The HMPC acknowledged some delays in publication of HMPC documents although available internally as usual despite reduced secretariat resources in the context of general staff losses. While the business continuity measures required

prioritisation of several activities, it is anticipated that the situation will improve in 2020 after the move to the final EMA building.

AESGP expressed also an interest in the continuation of the publication of the herbal registrations in Europe (Reports on Uptake of the traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States' based on surveys performed since the end of the transition period in 2011). The HMPC explained that this activity is quite resource intensive and was not given priority recently. Nowadays the check of implementation of more recent legislation may be more important. However, EMA will look into possibilities for another update in the future.

5. AESGP survey on MRP-DCP for herbal medicines

AESGP presented the results of its 2019 survey of MRP-DCP procedures for herbal medicines. These procedures have become more relevant over the last years for herbal MPs. AESGP highlighted the importance of HMPC monographs – both for well-established use authorisations but also traditional use registrations. For 'mono-products' all procedures (except one which was actually a full application) followed a monograph. Procedures not based on monographs were combination products for which monographs were not available.

HMPC appreciated the importance of monographs for harmonisation and their increasing relevance in European procedures as well as the growing number of MRP/DCP for herbal products.

6. AOB

An additional question was raised by the HMPC on the AESGP view on the implications the new Medical Device Regulation may have from May 2020 onwards, in particular for medical devices on the market containing herbal components and how AESGP could see the evolution of the market. AESGP responded that it did not have insights on possible trends but that in any case for a product to be classified as medical device the mechanical mode of action needs to be proven.

The HMPC also asked about the availability of new data on polycyclic aromatic hydrocarbons (PAHs). AESGP explained that data had been submitted at the end of 2018 by the German herbal industry, but based on new evaluations, industry would offer support to the revision of the HMPC Reflection Paper on PAHs. The HMPC thanked for the information provided and referred to the general suspension of guideline activities and subgroups during the move and business continuity provisions. HMPC focused during this period exceptionally on guidance documents for estragole and pyrrolizidine alkaloids. The follow up on the Reflection Paper on PAHs and the valuable discussions during the HMPC Assessors training in 2018 had to be put on hold but will be taken up again.