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Patient Health Protection

Hearing AESGP during May 2013 MLWP meeting

Report

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

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The Chair of the Working Party on Community Monographs and Community List (MLWP) welcomed the AESGP delegation. Dr Cranz thanked the Chairs and the MLWP/HMPC for the opportunity to discuss issues related to the scientific assessment of herbal substances/preparations and the development of Community herbal monographs (M) and Community list entries (LE). The significant size of the AESGP delegation and the inputs received for the agenda clearly attest of the interest in the work of the MLWP/HMPC, added AESGP. However AESGP expressed some concerns with regard to the acceptance of well-established use in monographs and paediatric use, pointing to the interest of all stakeholders to have a system that works properly.

Acceptance of well-established use data

To illustrate the general concern of acceptance of well-established use, two case studies were presented relative to the M on Thyme and Primula and to the M on Pelargonium.

On the first case (M on Primula and Thyme), although many good clinical data were submitted, the well-established use of the combination of plants had been rejected. One study had not been accepted due to the fact that the Bronchitis Severity Score (BSS) was not validated and could not substantiate the indication of acute bronchitis. Another study where the primary endpoint was coughing frequency had been rejected as well. The corresponding medicines which are commercialised in some European countries as well-established medicines were at the end not reflected at all in the monograph as they had been reformulated over the years thus they did not meet the criteria of traditional use.

With regard to the second case study concerning the M on Pelargonium, despite the existence of clinical studies of high quality, the draft M and draft AR released for comments in June 2012 did not reflect the well-established use of the plant. Comments were submitted and then later data on a validated BSS score was provided to the Committee. However the latter submission was not reflected

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in the M nor in the AR. In light of the important changes between the draft and the final M, AESGP regretted that an interim revised draft M had not been published for comments.

The Chairs of the MLWP and of the HMPC understood the concerns and reassured AESGP that each study and data provided are carefully considered and often long discussions are necessary before a M can be finalised. Due to tight timelines, it had not been possible to include the evaluation of the validation data of BSS in time for the Pelargonium monograph. However, an evaluation was subsequently initiated and it was concluded that the BSS can be regarded as validated based on the new data received. It will be reflected if this result will have an impact on related monographs. AESGP expressed its appreciation of this positive sign. The Rapporteurs of the monographs impacted by the decision will review their respective M and provide recommendation to the MLWP and HMPC as to whether the outcome is positive and the M should be revised. Despite constraints on the resources, the Rapporteurs will endeavour that this takes place before the end of the year.

Consultation on draft revised monographs

In case of important new developments in the phase between receipt of comments and final decision on a M that would lead to important changes to the draft M, AESGP would be keen to see a revised draft M being published for comments. The MLWP/HMPC responded that this could be done but should however be limited to exceptional circumstances.

Hearing – bilateral meeting to discuss technical details of key studies

In the case of divergences on the interpretation of a clinical study, AESGP asked whether the offer made by the previous chair of the HMPC, as per the HMPC rules of procedures, was still valid i.e. that a company could come with its experts to discuss technical details with the MLWP (or a subset thereof). The HMPC Chair replied that, although possible in principle, this would be difficult in practice due to limited resources of the Committee which has to re-centre its activities around M and LE. He also referred to the possibility for a company to ask for a scientific advice.

Transparency measures in relation to divergent positions

Knowing countries opposing a monograph (divergent position) being crucial information for companies when preparing their registration strategy, AESGP asked for clarification of the implementation of the provisions of Article 7 of the HMPC rules of procedures as far as the adoption of monographs is concerned. The HMPC secretariat explained that the name of the HMPC member(s) having expressed a divergent position can be obtained upon submission of a request for information via the general EMA Info or the HMPC secretariat e-mails. Further transparency is expected with a cross-committee implementation of a policy to release in the public domain the names of committee members expressing a divergent position (together with the Member State in brackets).

Revision of HMPC scientific guidelines and other guidance documents

With regard to HMPC guidelines, AESGP understood that these would not undergo revision on a fixed frequency but would be modified if deemed necessary (to reflect new legislation, other guidelines, new science, etc.). In that process, the HMPC would follow the principles laid down in the 'Procedure for European Union guidelines and related documents within the pharmaceutical legislative framework' (EMEA/P/24143/2004 Rev. 1 corr. - dated 18 March 2009). The HMPC endorsed AESGP's request to submit proposals including a substantiated justification for modification of a given guideline or reflection paper, for consideration by the committee. In this context, a proposal for adding new Q&A's on stability in the HMPC Quality Q&A had been submitted. This proposal is being discussed in the EMA HMPC Quality Drafting Group.

Revision of Community herbal monographs

With regard to the revision of monographs, the MLWP Chair explained that there is first a call for data on the monograph to which stakeholders can contribute. It also alerts interested parties that a revision will take place. During the revision process, a public consultation takes place in case crucial issues have been changed. Anyhow even after the M is final, interested parties who think that something is wrong or missing can suggest checking if there is a need for correction or reopening of the M.

Revision of public statements

AESGP also asked for confirmation that the submission of new data on a plant covered by a public statement is possible at any time. The MLWP Chair underlined that public statements are not a desired outcome of the Committee. On the contrary, everything is done (AR, list of references published) to incentivise stakeholders to send further appropriate data that may change the original conclusion of the AR and lead to a monograph. The HMPC secretariat will present to the HMPC an amendment of the procedural documents on such public statements to make this option more visible.

Age restriction for children in HMPC monographs

AESGP had analysed monographs of plants indicated for cough and cold and it noted that for all of the monographs on TU the age limit is set at 4 years old for the oral use, although in some instances extensive data exist for the use in younger children. Hence the association wondered what were the criteria to define age restrictions and the expectations in terms of data needed to include the use in children below 4 years in HMPC monographs (especially for TU). AESGP highlighted that clinical trials in children are very costly and recouping the investment later on is extremely difficult.

The MLWP/HMPC reassured AESGP that all paediatric data are carefully considered and validated and paediatric use reflected in the M whenever possible. In some instances (e.g. Tilia) the draft did not include any use in children but the final version did. The HMPC work is a scientific one and conclusions from existing data may be different based on various cultural background of the MSs and the use of herbal medicines in children. The decision to have frequently a threshold at 4 years is seen as an acceptable compromise between older and younger children, taking into account the views of national competent authorities.

A representative of the HMPC added that the lack of data on paediatric use, use in pregnant or breastfeeding women is not necessarily negative but the HMPC is not in the position to extrapolate and recommend the use in M. Clinical trials are not always the norm; pharmacovigilance or observational studies could be done. Studies lasting a reasonable time (2 years) and showing no harm could be considered in AR and M. Obviously the methodology and the number of patients enrolled are important but the HMPC would be more than willing to give its opinion on protocols.

AESGP welcomed this positive mind-set that goes in the right direction. Indeed it should not be forgotten that other legal frameworks are also very attractive and necessitate less investment, have less burdens, etc.

Public statement on the use of medicinal products containing toxic unsaturated pyrrolizidine alkaloids

A brief update was provided on the work status of this public statement. The work is on-going and comments submitted are being reviewed. The finalisation of the M on Symphyti radix is consequently delayed.

Publication of "Uptake of the traditional use directive" based on 2013 figures

AESGP expressed its appreciation of the very recent publication of the latest "Uptake of the traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States". The update of such document is most useful and is also a good political signal as to the use of the Traditional Use Directive and the number of herbal medicinal products put on the market. The Committee clarified that the figures will now be published on a yearly.

The hearing was closed and participants thanked for all contributions.