25 September 2019
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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Hamamelis virginiana* L., folium

Rapporteur(s)	Olga Palomino
Peer-reviewer	Ioanna Chinou

HMPC decision on review of monograph *Hamamelis virginiana* L., folium adopted on 12 November 2009	25 September 2019
Call for scientific data	From 01 March 2018 to 31 May 2018
Agreed by Working Party on European Union monographs and list (MLWP) and Committee on Herbal Medicinal Products (HMPC)	September 2018 January 2019 July 2019
Adoption by Committee on Herbal Medicinal Products (HMPC)	25 September 2019

Review of new data on *Hamamelis virginiana* L., *folium*

Periodic review (from 2009 to 2018)

Scientific data (e.g. non-clinical and clinical safety data, clinical efficacy data)

☐ Pharmacovigilance data (e.g. data from EudraVigilance, VigiBase, national databases)

☒ Scientific/Medical/Toxicological databases (PubMed, TOXLINE). Search period was set from January 2006 to January, 2019. The following key words were used Hamameli*, witch hazel. 44 references were found and 18 of them were included in the list of references as relevant.

☐ Other

Regulatory practice

☒ Old market overview in AR (i.e. products fulfilling 30/15 years on the market)

☒ New market overview (including pharmacovigilance actions taken in member states)

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☐ Referral

☒ Ph. Eur. monograph

☐ Other

Consistency (e.g. scientific decisions taken by HMPC)

☐ Public statements or other decisions taken by HMPC

☐ Consistency with other monographs within the therapeutic area

☐ Other

Availability of new information (i.e. likely to lead to a relevant change of the monograph)

Scientific data	Yes	No
New non-clinical safety data likely to lead to a relevant change of the monograph	☐	☒
New clinical safety data likely to lead to a relevant change of the monograph	☐	☒
New data introducing a possibility of a new list entry	☐	☒
New clinical data regarding the paediatric population or the use during pregnancy and lactation likely to lead to a relevant change of the monograph	☐	☒
New clinical studies introducing a possibility for new WEU indication/preparation	☐	☒
Other scientific data likely to lead to a relevant change of the monograph	☐	☒
Regulatory practice	Yes	No
New herbal substances/preparations with 30/15 years of TU	☐	☒
New herbal substances/preparations with 10 years of WEU	☐	☒
Other regulatory practices likely to lead to a relevant change of the monograph	☐	☒
Referrals likely to lead to a relevant change of the monograph	☐	☒
New Ph. Eur. monograph likely to lead to a relevant change of the monograph	☐	☒
Consistency	Yes	No
New or revised public statements or other HMPC decisions likely to lead to a relevant change of the monograph	☐	☒
Relevant inconsistencies with other monographs within the therapeutic area that require a change of the monograph	☐	☒
Other relevant inconsistencies that require a change of the monograph	☐	☒

Summary and conclusions on the review

During the review 44 new references not yet available during the first/previous assessment were identified.

16 references were provided by Interested Parties during the Call for data.

Among them, only 7 were considered to be relevant for the assessment; most of them are reviews summarizing the already known properties of Hammamelis. Results of clinical studies describing the efficacy in dermatitis disease, sensitive scalp, venous insufficiency (in combination) and use in children above 11 years of age have been found. Other references describe new chemical methods for

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qualitative and quantitative analysis of raw material, primary biological properties such as antioxidant ability and new research on other activities (i.e. antitumoral, antimicrobial effects).

The NTP study with Hamamelis water is being developed and all the results published up to the moment about genetic toxicology yielded negative outcomes, so no toxic effects can be foreseen for Hamamelis folium under the conditions of use reflected in the monograph.

Another NTP study was published in 2013 on pyrogallol about its dermal toxicity. The conclusions of these 3 months to 2 years dermal studies showed that there was no evidence of carcinogenic activity of pyrogallol in male or female rats administered 5, 20 or 75mg/kg. There was equivocal evidence of carcinogenic activity in male mice and some evidence of carcinogenic activity in female mice.

Even the lowest tested dose is much higher than the recommended posology for the different Hamamelis preparatios and also the duration of use is much shorter (no more than two weeks).

As a consequence of this, no references were considered to be relevant to justify a revision of the monograph.

No revision is considered to be required because no clinical studies or new safety concerns related to the use of *Hamamelis virginiana* L., folium were found. There are no new products in the EU market containing *Hamamelis virginiana* L., folium as the single active substance. Thus, no new relevant data have been found which could affect the existing monograph, and no changes in the regulatory practice have been introduced.

References

a) References relevant for the assessment:

Cesarone MR, Belcaro G, Grossi MG, Pellegrini L, Ledda A, Vinciguerra G, *et al*. LINFAVENIX: improvement of signs and symptoms of chronic venous insufficiency and microangiopathy. Minerva Cardioangiol 2008, 56(5):55-61

Gangemi S, Minciullo PL, Miroddi M, Chinou I, Calapai G, Schmidt RJ. Contact dermatitis as an adverse reaction to some topically used European herbal medicinal products – Part 2: Echinacea purpurea–Lavandula angustifolia* Contact Dermatitis 2015, 72:193–205

NTP Hamamelis water (witch hazel) 10183-P (https://ntp.niehs.nih.gov/go/ts-10183-p)

NTP technical report on the toxicology and carcinogenesis studies of pyrogallol (CAS NO. 87-66-1), February 20 13. Pyrogallol, NTP TR 574. NIH Publication No. 13-5916

Paulsen E, Chistensen LP, Andersen KE. Cosmetics and herbal remedies with Compositae plant extracts - are they tolerated by Compositae-allergic patients? Contact Dermatitis 2008, 58(1):15-23

Qinna NA. Safety profile of suppository Hamamelis virginiana leaf extract. JMPR 2013, 7(36):2669-2679

Trüeb RM. North American Virginian Witch Hazel (Hamamelis virginiana): Based Scalp Care and Protection for Sensitive Scalp, Red Scalp, and Scalp Burn-Out. Int J Trichology 2014, 6(3):100-103

b) References that justify the need for the revision of the monograph:

None

Rapporteur's proposal on revision

☐ Revision needed, i.e. new data/findings of relevance for the content of the monograph

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☒ No revision needed, i.e. no new data/findings of relevance for the content of the monograph

HMPC decision on revision

☐ Revision needed, i.e. new data/findings of relevance for the content of the monograph

☒ No revision needed, i.e. no new data/findings of relevance for the content of the monograph

HMPC agreed with Rapporteurs position that no monograph revision is needed because no new data of relevance were detected that would change the content of the monograph.

The HMPC decided by majority not to revise the monograph, assessment report and list of references on *Hamamelis virginiana* L., folium.

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