EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Humulus lupulus* L., flos

Rapporteur(s)	W. Dymowski
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HMPC decision on review of monograph *Humulus lupulus* L., flos adopted on 06 May 2014	31 January 2024
Call for scientific data (start and end date)	From 01 March 2024 to 31 May 2024
Discussion in Committee on Herbal Medicinal Products (HMPC)	January 2025 March 2025
Adoption by HMPC	19 March 2025

Review of new data

Periodic review (from 2014 to 2024)

Sources checked for new information:

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

☒ Scientific/Medical/Toxicological databases

Warsaw Medical University Library with access to resources: Access Medicine, Nature Pubishing group, ACS Publications, Oxford University Press, British Medical Journal, Polska Bibliogarafia Lekarska, ProQuest, PubMed, Reaxys, ScienceDirect, EBSCOhost, SciFinder, Scopus, Embase, TheCochrane Library, Taylor & Fransis Online, UptoDate, Karger, Web of Science, Wiley Online Library, Medline Ultimate in October 2024. PubMed supplied, in period 2006-2025, for "Hop+strobile" 8 hits, for Lupuli flos 2 hits (both on quality). Google Scholar, for term "Hop strobile", in period 2006-2025, supplied 99 hits.

☒ Pharmacovigilance databases

☒ data from EudraVigilance

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☒ from other sources (e.g. data from VigiBase, national databases)

☒ Other: Polish national vigilance base (no reports)

Regulatory practice

☒ Old market overview in AR (i.e. check products fulfilling 30/15 years of TU or 10 years of WEU on the market)

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

☒ PSUSA

☒ Feedback from experiences with the monograph during MRP/DCP procedures

☒ 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

Other

☒ Published study

Availability of new information that could trigger a revision of the monograph

Scientific data	Yes	No
New non-clinical safety data that could trigger a revision of the monograph	☐	☒
New clinical safety data that could trigger a revision 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 that could trigger a revision of the monograph	☐	☒
New clinical studies introducing a possibility for new WEU indication/preparation	☐	☒
Other scientific data that could trigger a revision 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	☐	☒
New recommendations from a finalised PSUSA	☐	☒
Feedback from experiences with the monograph during MRP/DCP procedures that could trigger a revision of the monograph	☐	☒
New/Updated Ph. Eur. monograph that could trigger a revision of the monograph	☐	☒
Other regulatory practices that could trigger a revision of the monograph	☐	☒
Consistency	Yes	No

New or revised public statements or other HMPC decisions that could trigger a revision of the monograph	☐	☒
Relevant inconsistencies with other monographs within the therapeutic area that could trigger a revision of the monograph	☐	☒
Other relevant inconsistencies that could trigger a revision of the monograph	☐	☒
Other	Yes	No
Study on young adults using hop strobile preparations was published over the review period	☒	☐

Summary of new references

During the review, new publications with the terms "Lupuli flos" were found (6 publications) and "Hop strobile" (22 publications). PubMed Natural 10 publications. Google Scholar "Hop strobile sleep" 50 hits. Nineteen references considered to possibly be relevant for the monograph and two references that could trigger revision of the monograph.

No references were provided by Interested Parties during the Call for data.

The only mono-component herbal medicinal product containing hop strobile extract, that was available on the market, it is no longer registered since 2022.

Assessment of new data

Pharmacovigilance data

Search for the term "Lupuli flos" and "Hop strobile" in EudraVigilance database supplied only data on combination products, combined food supplements and homeopathic products.

Search for term "dry extract from hop strobile" supplied five reports on one product, containing hop strobile methanol (50% V/V) extract (4-5:1): dizziness in one patient who also took bisoprolol (where the effect is known); diarrhoea in one patient with irritable colon who used the product taking also metoprolol and L-thyroxin; nausea (lasting up to two hours) in one patient using valsartan and candesartan and took three dragees of the hop strobile for asleeping; one telephone call of one patient complaining for unavailability of the product on the market, which was reported as possible a dependency reaction; one dry eyes symptom after using the product was reported to the BfArM. The reports were not consistent, repeatable to start any further action as signal detection.

New scientific data that could trigger a revision of the monograph

Over the review period (2014-2024) one study was identified:

The aim of the work by Kyrou *et al.* (2017) was to study the effects of a hop strobile dry extract at a single dose of two 0.2 g capsules (with the extract of unknown DER and extraction solvent) taken once daily on depression, anxiety and stress levels in young adults, which were self-reported. The study included 42 "apparently healthy young adults" from the University of Athens who reported self-assessment of their symptoms of at least mild depression, anxiety and stress according to the Depression Anxiety Stress Scale-21 (DASS-21). The study was software randomized (1:1), placebo-controlled, double-blind, according to crossover design with two 4-week intervention periods separated by a 2-week wash-out periods. Anthropometric measurements, DASS-21 assessments and

measurements of cortisol plasma levels in the morning were performed at the beginning and the end of the 4-week treatment periods. 36 participants (females/males: 31/5; age: 24.7±0.5 years) completed the study intervention (attrition bias: 6/42). No significant changes in body weight and in level of morning circulating cortisol were noted in groups taking hop strobile or placebo. DASS-21 anxiety, depression and stress scores were decreased with hop strobile (9.2±7.3 vs. 5.1±5.9, 11.9±7.9 vs. 9.2±7.4, and 19.1±8.1 vs. 11.6±8.1), which were greater compared to those in placebo (all p values <0.05). The authors concluded that "in otherwise healthy young adults" reporting at least mild depression, anxiety and stress symptoms, daily supplementation with a hop strobile dry extract can significantly improve all these symptoms over a 4-week period.

Assessor's comments

The strength of the tested product was not given. The term "apparently healthy young adults" was used while the volunteers reported depression. DASS-21 multifactorial scale is a screening tool for primary assessment if the patient should visit a doctor. Although the tested group is small the result is consistent with the area of traditional use of hop strobile preparations.

New regulatory practice that could trigger a revision of the monograph

Not applicable.

Inconsistency that could trigger a revision of the monograph

Not applicable.

Other issues that could trigger a revision of the monograph

Not applicable,

New information not considered to trigger a revision at present but that could be relevant for the next review

Not applicable.

References

Kyrou I, Christou A, Panagiotakos D, Stefanaki C, Skenderi K, Katsana K, Tsigos C. Effects of a hops (Humulus lupulus L.) dry extract supplement on self-reported depression, anxiety and stress levels in apparently healthy young adults: a randomized, placebo-controlled, double-blind, crossover pilot study. *Hormones* 2017, 16(2):171-180.

Rapporteur's proposal on revision

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

☐ Revision likely to have an impact on the corresponding list entry (if applicable)

☒ 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