EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 March 2025
EMA/HMPC/419121/2024
Committee on Herbal Medicinal Products (HMPC)

Addendum to assessment report on *Melilotus officinalis* (L.) Lam., herba

Rapporteur(s)	W. Dymowski
Peer-reviewer(s)	B. Kroes

HMPC decision on review of monograph *Melilotus officinalis* (L.) Lam., herba adopted on 21 November 2017	31 January 2024
Call for scientific data (start and end date)	From 01 April to 30 June 2024
Discussion in Committee on Herbal Medicinal Products (HMPC)	September 2024 November 2024 January 2025 March 2025
Adoption by HMPC	19 March 2025

Review of new data

Periodic review (from 2017 to 2024)

Sources checked for new information:

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

☒ Scientific/Medical/Toxicological databases
PubMed was searched in July and August 2024 using the following search terms and filters: "Melilotus" AND "officinalis" in years 2016-2024 with 170 results and "Melilot" term in years 2016-2024 with 432 results.

☒ Pharmacovigilance databases

☒ data from EudraVigilance

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

☐ Other

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

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

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	☐	☒

Summary of new references

During the review 170 new references not yet available during the first/previous assessment were identified. Out of these new references 2 reference were considered to be possibly relevant for the monograph and none of reference could trigger revision of the monograph.

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

Assessment of new data

New scientific data that could trigger a revision of the monograph

New clinical assessment of the former data

In a pilot trial Stafanini (1996) compared the treatment of venous insufficiency in 55 patients (51 woman, 4 men), randomly separated in three groups: 20 treated with a Melilotus officinalis extract (not characterised) in a dose 200 mg/patient per day, 15 treated with ozone therapy and 20 treated with combination therapy with the melilot preparation and ozone therapy. The treatment with the extract presented strong antiedematous effect in "edema malleolar"(ankle swelling) (p=0.0005) and significant in symptoms of "night cramps" (p=0.01) and in the "feeling of leg heaviness" (p=0.0037) after 15 days of therapy. The combined therapy provided overall better results although at the level of ankle swelling and nocturnal cramps uncomparable to those of Melilot extract alone.

De Morales Silva et al. (2023) by the occasion of analyse a data on the effectiveness of belneotherapy in chronic venous insufficiency, took some data of the Stefanini (only the data from patients treated with melilot extract or treated with balneotherapy, 35 of 55 patients) and used it for another comparison with an odd ratio criterion from the perspective of the influence on subjective symptoms of pain and hyperthermia, disease severity and quality of life obtaining. From the point of view of influence on subjective reception of pain symptoms there was very low or no difference between pharmacotheraphy with melilot extract and ozone balneotheraphy and in the feeling of the edema very low evidence.

Assessor's comment

Feeling of inflammatory states symptoms during the use of melilot preparations is not an indication in the EU herbal monograph. The publication does not change the former HMPC assessment.

EudraVigilance data

The EudraVigilance database was searched in July 2024 with the active substance contains: Melilotus officinalis, Melilot, Melilot extract, Melilotus officinalis extract. No new safety issues could be identified that would trigger revision of the monograph.

There were no reports on single component products containing *Melilotus officinalis*. L., herba, or its extracts.

VigiLyze reports for "Melilot" and "Melilotus officinalis"

In the WHO VigiBase were reported only adverse events on combination products containing melilot extract, in most cases hypersensitivity reactions for combination of rutoside and melilot extracts, for combination products containing Melilotus officinalis extract, heparini sodium and troxerutin and products containing Melilotus extract and Ruscus extract.

Assessor's comment *The reports do not change the safety profile of the single melilot preparations.*

New regulatory practice that could trigger a revision of the monograph

No new herbal substances/preparations with 30/15 years of TU or 10 years of WEU was declared from the UE member countries in the review period.

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

Over a review period were published studies which cannot immediately influence the content of the herbal monograph established within the EU. In China Liu et al. (2018) continued works on the anti-inflammatory activity of compounds isolated from *Melilotus officinalis* ethanol extract. In Iran Derakhshan et al. (2022) continued works on the product of *Melilotus officinalis* herb by testing new forms for administration of the extract in diabetic food ulcers.

References

De Morales Silva MA, Nakano LCU, Cisneros LL, Miranda JrF. Balneotherapy for chronic insufficiency (Review). *Cochrane Database of Systematic Reviews* 2023, issue 1. Art. No.: CDO13085; DOI 10.1002/14651858.CD013085.pub3

Derakhshan MA, Nazeri N, Khoshnevisan K, Heshmat R, Omidfar K. Three-layered PCL-collagen nanofibers containing melilotus officinalis extract for diabetic ulcer healing in a rat model. *Journal of Diabetes & Metabolic Disorders* 2022, 21:313–321; https://doi.org/10.1007/s40200-022-00976-7

Liu Y-T, Gong PH, Xiao FQ, Shao S, Zhao DQ, Yan MM, Yang XW. Chemical Constituents and Antioxidant, Anti-Inflammatory and Anti-Tumor Activities of *Melilotus officinalis* (Linn.) Pall. *Molecules* 2018, 23, 271; doi:10.3390/molecules23020271

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