24 November 2021
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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Levisticum officinale* W.D.J. Koch, radix

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

HMPC decision on review of monograph *Levisticum officinale* W.D.J.Koch, radix, adopted on 20 November 2012	13 January 2021
Call for scientific data (start and end date)	From 01 March 2021 to 31 May 2021
Adoption by Committee on Herbal Medicinal Products (HMPC)	24 November 2021

Review of new data on *Levisticum officinale* W.D.J. Koch, radix

Periodic review (from 2012 to 2021)

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: Medline database through PubMed (NIH).
- ☐ 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)

  There is no information on new single products containing *Levisticum officinale* W.D.J. Koch, radix, preparations, authorised or registered in EU countries between 2012 and 2021.
- ☐ Referral

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☒ Ph. Eur. monograph

New monograph 01/2021:1233 for Lovage root (Levistici radix) was published in the European Pharmacopoeia 10.3 but it does not affect the HMPC 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 / Updated 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 24 new references not yet available during the first/previous assessment were identified.

A search with "*Levisticum* + toxicity" and "lavage + toxicity" resulted in 5 publications. Two of these publications are on hepatoprotective or food preservative properties of extract or essential oil. Other

two publications are covered by the former Assessment report. One recent publication of Michel (2021) concerns the mistaken use of aconite instead of lovage that resulted in aconitine intoxication. Lapeere (2017) reported one case of contact dermatitis caused by lovage oil in Belgium but in the HMPC monograph this is covered by the contraindication: hypersensitivity to the active substance and to other plants of the Apiaceae (Umbelliferae).

Nine references were considered to be relevant for the assessment. However, none of these references justify a revision of the monograph.

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

No revision is considered required because no new information was found, including Eudravigilance and Vigibase data, which may cause change of HMPC view on the content of the monograph.

References

a) References relevant for the assessment:

Afarnegan H, Sharaki A, Sharaki J. The hepatoprotective effects of aquatic extract of *Levisticum officinale* against paraquat hepatocyte toxicity. *Pak. J. Pharm. Sci.* 2017, 30(6 Suppl.):2363-2368

Borges A, Abreu AC, Dias C, Saavedra MJ, Borges F, Simoes M. New perspectives on the use of phytochemicals as an emergent strategy to control bacterial infections including biofilms. *Molecules* 2016, in press, 21:877 doi:10,3390/molecules2170877. Accessed 01/09/2021

Esfahani HM, Farimani MM, Ebrahimi SN, Jung JH, Aliahmadi A, Abbas-Mohammadi M, *et al*. Antibacterial Components of *Levisticum officinale* Koch against Multidrug-resistant *Mycobacterium tuberculosis. Pharmaceutical Sciences (Iran)* 2020, 26(4):441-447

Garvey MI, Rahman M, Gibbons S, Piddock LJV. Medicinal plant extracts with efflux inhibitory activity against Gram-negative bacteria. *International Journal of Antimicrobial Agents* 2011, 37:145-151

Lapeere H, Boone B, Verhaeghe E, Ongenae K, Lambert J. Contact dermatitis caused by lovage (*Levisticum officinalis*) essential oil. *Contact Dermatitis* 2013, 69:181-191

Michel A, Siebe I, Auwarter V, Regul D, Hermanns-Clausen M. Aconitinvergiftung durch eine Verwechslung von Eisenhutblättern mit Liebstöckel. *Anaesthesist* 2021, 70:633-638

Miran M, Esfahani HM, Jung JH, Aliahmadi A, Skropeta D, Abbas-Mohammadi M, *et al*. Characterization and Antibacterial Activity of Phtalides from the Roots of the Medicinal Herb *Levisticum officinale* W.D.J. Koch. *Iranian Journal of Pharmaceutical Research* 2020, 19(2):182-186

Miran M, Feizabadi MM, Kazemian H, Kardan-Yamchi J, Monsef-Esfahani HR, Ebrahimi SN. The activity of *Levisticum officinale* W.D.J. Koch essential oil against multidrug-resistant *Mycobacterium tuberculosis*. *Iranian Journal of Microbiology* 2018, 10(6):394-399

Schinkovitz A, Stavri M, Gibbons S, Bucar F. Antimycobacterial Polyacetylenes from *Levisticum officinale*. *Phytotherapy Research* 2008, 22:681-684

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

☒ 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

The HMPC agreed not to revise the monograph, assessment report and list of references on *Levisticum officinale* W.D.J. Koch, radix, by consensus.