19 July 2023
EMA/HMPC/765801/2022
Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment Report on *Origanum majorana* L., herba

Rapporteur(s)	O Palomino
Peer-reviewer(s)	I Chinou

HMPC decision on review of monograph *Origanum majorana* L., herba adopted on 20 September 2016	26 January 2022
Call for scientific data (start and end date)	From 14 March 2022 to 14 June 2022
Discussion in Committee on Herbal Medicinal Products (HMPC)	September 2022 March 2023 May 2023 July 2023
Adoption by Committee on Herbal Medicinal Products (HMPC)	19 July 2023

Review of new data

Periodic review (from 2016 to 2023)

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 on November 2022 and January 2023; period covered: 2016 until January 2023; search terms: '*Origanum majorana* marjoram' or 'wild marjoram efficacy and/or safety'

☒ 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 98 new references not yet available during the first/previous assessment were identified. None out of these new references were considered to be relevant for the monograph or could trigger a revision of the monograph.

The search in pharmacovigilance databases revealed only 1 case report.

From regulatory praxis no new indications, herbal preparations and dosages were identified.

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

Not applicable

New regulatory practice that could trigger a revision of the monograph

Not reported

Inconsistency that could trigger a revision of the monograph
Not applicable

Other that could trigger a revision of the monograph
Not applicable

There are no new products in the market containing *Origanum majorana* herba which could trigger a revision of the monograph.

No new publications regarding Ames test or animal reproductive and developmental toxicity studies are available.

Most of the new references referred to chemical studies; several references reviewed or include new pre-clinical studies to previously reported properties such as antibacterial, antifungal and anti-acne ones, mainly on the cutaneous use of the essential from *Origanum majorana* (Mohamad *et al.,* 2021; Taleb *et al*., 2018).

Some of them referred to new pre-clinical studies such as benign prostatic hyperplasia (Elsherbini *et al*., 2022). Among them, 82 references were related to safety and revealed no new signs of toxicity (Esmaeilizadeh and Moradi, 2017; Jurowski and Krośniak, 2033).

The majority of new references referred to phytochemical studies (mostly quantitative and qualitative analyses on phenolic compounds and flavonoids)(Méabed *et al*., 2018)or genomic profils of the plant species. Moreover, several references referred to known pre-clinical pharmacological activities (antioxidative properties, influence on cell cycle, cardiac hemostatis etc.).

Adverse event(s) or other safety data: A search was performed in EVDAS (EudraVigilance) data base. Key words were »Spontaneous, Other, Not available to sender (unknown), Report from Studies, suspect interacting,« in EEA.

The search revealed 1 case, including the referred case report. This single case was related to the use of a combination product containing *Levisticum officinale, Melissa officinalis, Origanum majorana, Phosphorus, Pulsatilla vulgaris a*nd *Vitex agnus-castus*. It was considered as a non-serious adverse

event (AE) (diarrhoea, abdominal cramps) which dissappeared after withdrawal the use. The casual relationship was assessed as possible.

Assessore's comment:

This AE is related to a combination product in which Origanum majorana is not the main component. Thus, it is not possible to relate the observed GI disorders with only one component of the product. Moreover, this AE has not been found reported elsewhere, nor in the literature nor in the Pharmacovigilance system of the marketed products.

No revision is considered required because there are no new products in the market and no new scientific data related to non-clinical and clinical safety or clinical efficacy which could trigger a revision.

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

Not applicable

References

a) References relevant for the assessment

Elsherbini DMA, Almohaimeed HM, El-Sherbiny M, Mohammedsaleh ZM, Elsherbiny NM, Gabr SA, *et al*. *Origanum majorana* L. Extract Attenuated Benign Prostatic Hyperplasia in Rat Model: Effect on Oxidative Stress, Apoptosis and Proliferation. *Antioxidants* 11(6), 2022 Art No 1149

Esmaeilizadeh M, Moradi B. Medicinal herbs with adverse effects in pregnancy - an evidence-based review study. *Iranian Journal of Obstetrics, Gynecology and Infertility* 20, 2017, pp. 9-25

Jurowski K**,** Kroś**ś**niak M**.** The Toxicological Risk Assessment of Dermal Exposure of Patients Exposed to Lead and Cadmium Due to Application of Ointments with Marjoram Herb Extract **(**Majoranae herbae extractum**).** *Int J Env Res Publ Health* 20(3) 2023 ArtNo 2701

Méabed EMH, El-Sayed NM, Abou-Sreea AIB, Roby MHH. Chemical analysis of aqueous extracts of *Origanum majorana* and *Foeniculum vulgare* and their efficacy on Blastocystis spp. cysts. *Phytomedicine* 2018, 43:158-163. doi:10.1016/j.phymed.2018.04.017. Epub 2018 Apr 10

Mohamad R, Mussa R, Suslina SN. Prospects for using *Origanum syriacum* (L.) as a source of antimicrobial agents. *J Adv Pharm Technol Res* 2021, 12(4):340-344. doi:10.4103/japtr.japtr_106_21. Epub 2021 Oct 20

Taleb MH, Abdeltawab NF, Shamma RN, Abdelgayed SS, Mohamed SS, Farag MA, *et al*. *Origanum vulgare* L. Essential Oil as a Potential Anti-Acne Topical Nanoemulsion-In vitro and In vivo Study. *Molecules* 2018, 23(9):2164. doi: 10.3390/molecules23092164

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