12 May 2023
EMA/HMPC/261330/2022
Committee on Herbal Medicinal Products (HMPC)

Addendum to Assesment report on *Sisymbrium officinale* (L.) Scop., herba

Rapporteurs	A. Assisi
Peer-reviewer	B. Kroes

HMPC decision on review of monograph *Sisymbrium officinale* (L.) Scop., herba adopted on 30 September 2014	26 January 2022
Call for scientific data (start and end date)	From 15 April 2022 to 14 July 2022
Discussion in Committee on Herbal Medicinal Products (HMPC)	July 2022 September 2022 March 2023 May 2023
Adoption by Committee on Herbal Medicinal Products (HMPC)	12 May 2023

Review of new data on *Sisymbrium officinale* (L.) Scop., herba

Periodic review (from 2011 to 2022)

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

- ☒ Scientific/Medical/Toxicological databases (Web of Knowledge, PubMed, Embase)
- ☒ Pharmacovigilance databases (e.g. data from EudraVigilance, VigiBase, national databases)
- ☐ Other

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)

☐ 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 / 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, 56 new references not yet available during the first/previous assessment were identified. The databases Web of Science, PubMed and Embase were searched on 29/12/2022 with the search key »*sisymbrium officinale*« in the time period from the year 2011 onwards. No other restrictions were made. In these databases, 42/21/24 hits were identified, respectively. Out of these new references, 3 references were considered to be relevant for the monograph and 0 references that could trigger revision of the monograph.

The analysis of the abstracts and full texts of the 56 articles revealed that the majority of the papers are not relevant for the EU monograph of *Sisymbrium officinale* (L.) Scop., herba.

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

Assessment of new data

Some articles reported the identification of new or already known compounds, e.g flavonoids,[1] isothiocyanates and glucosinolates.[2,3,4]

New *in vitro* pharmacological data were reported on the antioxidant and anti-inflammatory effect of the methanol extract of the herb,[5] on the antioxidant and antimutagenic (Ames test) effect of the aqueous extract of the herb.[6] The antimutagenicity was evaluated by the Ames test on the *E. coli* WP2uvrAR (trpE65ΔuvrA pKM101) bacterial strain. This assay was not performed and interpreted in conformity with existing OECD and EU guidelines.[7]

The antimutagenic effect might partly be related to glucoputranjivin and isopropyl isothiocyanate, since both compounds (isolated from the aqueous extract) exerted antimutagenic effect in a bacterial reverse mutation assay using E. coli WP2, WP2uvrA, and WP2uvrA/pKM101 strains. In the absence of the exogenous metabolic activation system S9, these compounds exerted antimutagenic activity against the direct-acting mutagen methyl methanesulfonate in all strains. In the presence of S9, both compounds were active against the indirect mutagens 2-aminoanthracene, in WP2uvrA, and 2-aminofluorene, in WP2.[8]

The literature search resulted in the identification of a review paper on *Sisymbrium officinale*.[9] From the references of this paper, a further relevant article was identified.[10] In this paper, a non-controlled clinical trial is reported. 104 patients (8-80 years, mainly artists), claiming vocal tract discomfort were treated with *Sisymbrium*, 90 mg extract/day (not further specified) for 10-20 days and the perceived physical disability was assessed pre and post treatment by VHI (Voice Handicap Index) scores. According to the authors, the VHI scores proof that *Sisymbrium* reduced perceived disability and facilitated voice use, although these findings should be confirmed in further clinical studies including an active control or placebo groups.

Assessor's comment:

None of the references justifies a revision of the monograph. The tests on genotoxicity do not comply with existing OECD and EU guidelines and the clinical trial was not placebo controlled, therefore these data do not trigger the revision of the EU monograph.

Based on the updated market overview, there are no new medicinal products on the market containing Sisymbrium officinale (L.) Scop., herba which trigger the revision of the monograph.

In conclusion, revision cannot be recommended.

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

None.

References

a) References relevant for the assessment:

Alaniya M.D., Kavtaradze N.S., Skhirtladze A.V., Sutiashvili M.G. & Kemertelidze, E.P. Flavonoid glycosides from flowers of *Sisymbrium officinale* and Diplotaxis muralis growing in Georgia. *Chemistry of Natural Compounds.* 2012. 48(2):315–316

Borgonovo G., Zimbaldi N., Guarise M., Bedussi F., Winning M., Vennegeerts T. , *et al.* Glucosinolates in *Sisymbrium officinale* (L.) Scop.: Comparative Analysis in Cultivated and Wild Plants and in Vitro Assays with T2Rs Bitter Taste Receptors. *Molecules* 2019. 24(24):4572

Borgonovo G., Zimbaldi N., Guarise M., De Nisi P., De Petrocellis L., Schiano Moriello A., *et al*. Isothiocyanates and Glucosinolates from *Sisymbrium officinale* (L.) Scop. ('the Singers' Plant'): Isolation and in Vitro Assays on the Somatosensory and Pain Receptor TRPA1 Channel. *Molecules* 2019. 24(5):949

Đulovic A., Popović M., Burčul F., Čikeš Čulić V., Marijan S., Ruščić M., *et al.* Glucosinolates of *Sisymbrium officinale* and *S. orientale*. *Molecules* 2022. 27(23):8431

Amodeo V., Marrelli M., Pontieri V., Cassano R., Trombino S., Conforti F., *et al*. C*henopodium album* L. and *Sisymbrium officinale* (L.) Scop.: Phytochemical Content and *In Vitro* Antioxidant and Anti-Inflammatory Potential. *Plants* 2019. 8(11):505

Di Sotto A., Di Giacomo S., Toniolo C., Nicoletti M. & Mazzanti G. *Sisymbrium Officinale* (L.) Scop. And its Polyphenolic Fractions Inhibit the Mutagenicity of Tert-Butylhydroperoxide in *Escherichia coli* WP2*uvr*AR Strain. *Phytotherapy Res*earch 2016. 30(5):829–834

EMA. Assessment of genotoxicity herbal substances/preparations. European Medicines Agency https://www.ema.europa.eu/en/assessment-genotoxicity-herbal-substancespreparations (2018)

Di Sotto A., Di Giacomo S., Vitalone A., Nicoletti M. & Mazzanti G. Antimutagenic thio compounds from *Sisymbrium officinale*. *Journal of Natural Products* 2012. 75(12):2062-2068

Zorzan M., Zucca P., Collazuol D., Peddio S., Rescigno A., Pezzani R. *Sisymbrium officinale*, the Plant of Singers: A Review of Its Properties and Uses. *Planta Medica* 2020. 86(5):307–311

Calcinoni, O. *Sisymbrium* "Singers' Plant" Efficacy in Reducing Perceived Vocal Tract Disability. *J. Otolaryngol.-ENT Res.* 2017. Volume 8

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 *Sisymbrium officinale* (L.) Scop., herba, by consensus.