20 September 2023
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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Rosa centifolia* L.; *Rosa gallica* L.; *Rosa damascena* Mill., flos

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HMPC decision on review of monograph *Rosa centifolia* L.; *Rosa gallica* L.; *Rosa damascena* Mill., flos adopted on 1 July 2014	26 January 2022
Call for scientific data (start and end date)	From 13 April 2022 to 14 July 2022
Discussion in Committee on Herbal Medicinal Products (HMPC)	May 2023 July 2023 September 2023
Adoption by Committee on Herbal Medicinal Products (HMPC)	20 September 2023

Review of new data

Periodic review (from 2014 to 2023)

Sources checked for new information:

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

☒ Scientific/Medical/Toxicological databases

Scientific data of the period 2014 - 2023 was reviewed using Google Scholar browsing machine and sources available in library of PubMed, Reaxys, SciFinder, Scopus, The Cochrane Library,

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ScienceDirect. Search terms "Rosa + flos", "Rose flower", "Rosa + gallica L.", "Rosa + damascena Mill", "Rosa + centifolia L."

☒ Pharmacovigilance databases

☒ data from EudraVigilance (accessed 18.07.23)

☒ from other sources (data from VigiBase; accessed 18.07.23)

☐ 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)

☐ 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 358 references were found.

For *Rosa gallica* L. 40 references, mostly on essential oils analyses (>90%) and further uses in cosmetics, were found. Existing data could not trigger any potential change to the existing monograph.

Related to *Rosa centifolia* L. 45 references were detected, also mostly on essential oil analyses, but also uses in combinations, in body lotions & other cosmetics, on antioxidant activities. Existing data could not trigger any potential change to the existing monograph.

Concerning *Rosa damascena* Mill.*,* 273 references were found, mostly on essential oil analyses, in products from industrial uses, b-cyclodextrin nanoparticles loaded extracts, phenolic compositions, antioxidant activities, *in vitro* cytotoxicities, extensive uses in aromatherapy (the essential oils), anti-dandruff activity, repellency against mosquitos and against polycystic ovaries syndrome (PCOS) (essential oil). In combinations against constipation, asthma, sexual dysfunction as well as in a hyaluronic based gum gel, branded product, for babies against symptoms of teething. Out of these new references, three references were considered to be relevant for the monograph and that 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

Nili *et al*. (2020) evaluated the effect of *Rosa damascena* Mill. products on constipation during pregnancy, in a clinical trial. This was a single-arm clinical trial study on pregnant women with constipation diagnosed based on Rome IV criteria in Tehran and Qom, Iran (2018-2019), where the consumption of *Rosa damascena* Mill. products was recommended daily for four weeks. The severity of constipation and the quality of life were assessed via the Rome IV criteria and the World Health Organization (WHO) quality of life questionnaires (WHOQOL-BREF), respectively. The study was performed on 35 pregnant women (pregnancy between week 14-34). The consumption of *Rosa damascena* Mill. products decreased the score of Rome IV criteria (mean 9.4 to 1.1) while increasing the frequency of bowel movements and improving the overall quality of life (p<0.001). The product used was *Rosa damascena*'s petals separated, dried, and powdered and 750 mg of the powder packaged with 1250 mg white rock candy. Thirty minutes after breakfast, the product was consumed with 25 cc of rose water. The predominant constipation signs, including straining, lumpy and hard stools, a sensation of incomplete evacuation, a sensation of anorectal obstruction, manual facilitation manoeuvres, and less than three spontaneous bowel movements per week significantly improved after the consumption of *Rosa damascena* Mill. products (p<0.001). The authors concluded that *Rosa damascena* Mill. products could be consumed with a potential positive outcome.

Assessor's comment:
*No revision of the EU herbal monograph is required since medicinal products corresponding to the indication (*constipation during pregnancy) *described in the above mentioned clinical study are not reported from the EU market. Furthermore, the design of the study is not considered adequate to support the indication and is out of the ones in the existing monograph.*

Among other reviews, two by Koohpayeh *et al*. (2021, 2022) evaluated clinical existing data regarding therapeutic effects of *Rosa damascena* on pain.
In the first study by Koohpayeh *et al*. (2021), clinical data have been evaluated regarding the effects of *Rosa damascena* Mill. on primary dysmenorrhea (PD) and premenstrual syndrome (PMS), summarising the findings of randomized controlled trials (RCTs) regarding the effects of this therapeutic approach on menstruation-related pain as the primary outcome and menstruation-related headache, fatigue, anxiety, and bloating as the secondary outcomes. This study evaluated parallel-group and cross-over RCTs on aromatherapy, topical treatment, or oral intake of *Rosa damascena* Mill. products for the treatment groups versus placebo, nontreated, or conventional treatment groups. Seven electronic databases (Web of Science Core Collection, Scopus, Embase, CENTRAL, CINAHL, SID, and MagIran) and one search engine (PubMed) were searched from inception to January 15, 2021. After examining the full text of 13 studies for compliance with the inclusion criteria, seven studies were considered eligible for the review. A random-effects model was used to pool the data; otherwise, a narrative summary was presented. The retrieved studies were conducted on females with PD or PMS, aged 18-35 years. The total sample size of the intervention and comparator arms was 276 and 272. The results showed that *Rosa damascena* Mill. had a non-significant alleviating effect on the menstruation-related pain. The authors concluded that further studies with improved methodological quality are suggested to evaluate the effects of the treatment on these symptoms, probably using different dosages and durations.
In the second study by Koohpayeh *et al*. (2022), the effects of topical application and oral intake of *Rosa damascena* Mill. on acute pain in adults has been tested in a systematic review and meta-analysis. It has been referred that from a total of 11 studies that met the inclusion criteria, four studies administered *Rosa damascena* Mill. through topical application and seven by oral intake (almost in all cases referred in essential oils' use). Nine studies recruited only females. Ten studies had parallel-group design, while one adopted cross-over design. The oral intake of *Rosa damascena* Mill. reduced pain severity non-significantly. However, the topical application of this treatment had no pain-alleviating effect. The authors concluded that more robust RCTs are needed for accurate estimation of the effects of oral and topical use of *Rosa damascena* Mill. on the severity of different types of acute pain in adults.

Assessor's comment:
The effects of Rosa damascena Mill. products (including essential oils) have been evaluated in several clinical studies in pain associated with primary dysmenorrhea (PD) and premenstrual syndrome (PMS) and in acute pain. None of the reviews is considered to be relevant for the monograph on Rosae flos since medicinal products corresponding to the indications described in the above mentioned clinical studies are not reported from the EU market. Furthermore, if any, only non-significant effects were seen.

Moreover, no records appeared during the search on Eudravigilance and VigiBase (July 2023).

New regulatory practice that could trigger a revision of the monograph

There are no new herbal substances/preparations with 30/15 years of TU or 10 years of WEU.

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

Koohpayeh SA, Hosseini M, Nasiri M, Rezaei M. Effects of *Rosa damascena* (Damask rose) on menstruation-related pain, headache, fatigue, anxiety, and bloating: A systematic review and meta-analysis of randomized controlled trials. *Journal of Education and Health Promotion* 10, 2021

Koohpayeh SA, Hosseini M, Nasiri M, Rezaei M. Effects of topical application and oral intake of *Rosa damascena* on acute pain in adults: A systematic review and meta-analysis. *Oman Medical Journal* 37(5), 2022

Nili N, Hadavand S, Emadi F, Gholami-Fesharaki M, Emaratkar E. Evaluation of the effect of *Rosa damascena* Mill. product on constipation during pregnancy: A single-arm clinical trial. *International Journal of Women's and Reproduction Sciences* 9(1), 2020, 11-16

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