EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Cucurbita pepo* L., semen

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HMPC decision on review of monograph *Cucurbita pepo* L., semen adopted on 20 November 2012	13 January 2021
Call for scientific data (start and end date)	From 01 February 2021 to 30 April 2021
Adoption by Committee on Herbal Medicinal Products (HMPC)	24 November 2021

Review of new data on *Cucurbita pepo* L., semen

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 (PubMed, TOXLINE). Search period was set from December 2012 until June 2021. The following key words were used *Cucurbita* + efficacy and *Cucurbita* + safety. 27 and 19 references were found, respectively.
- ☐ 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)
- ☐ Referral
- ☐ Ph. Eur. monograph
- ☐ Other

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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

Other

☒ Original AR and MO adopted 9 years ago

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 27 new references not yet available during the first/previous assessment were identified for the search terms *Cucurbita* + efficacy and 19 new references for the search terms *Cucurbita* + safety, although most of the references were the same in both results.

No new references were provided by Interested Parties during the Call for data. Moreover, no Pharmacovigilance alerts referring to the use of *Cucurbita* seeds have been found.

Six references were considered to be relevant for the assessment.

In their guidelines (2020, 2021) for the management of non-neurogenic male lower urinary tract symptoms (LUTS), the European Association of Urology (EAU) noted the traditional use of *Cucurbita pepo* L. semen and the HMPC therapeutic indication for the relief of lower urinary tract symptoms related to benign prostate hypertrophy or related to an overactive bladder, after serious conditions have been excluded by a medical doctor.

Several of the new references were reviews summarising the already described properties of *Cucurbita* seeds. Some clinical trials have been performed and published during the last years to evaluate the efficacy and safety of pumpkin seed oil alone or in combination in the management of symptoms of medically diagnosed BPH.

Hong *et al.* (2009) carried out a long-term study (12 months) to evaluate the effectiveness and potential side effects of pumpkin seed oil and/or saw palmetto oil in Korean men with symptomatic BPH; treatment with 320 mg per day of pumpkin seed oil significantly reduced the International Prostate Symptom Score (IPSS) when compared to placebo group; the reduction of IPSS in the group treated with pumpkin seed oil (320 mg per day) plus saw palmetto oil (320 mg per day) was higher, but with no statistically significant differences when compared to the treatment with pumpkin seed oil alone. Nevertheless, this reference is not considered to be relevant to justify a revision of the monograph due to the limited data including small number of patients.

There are no new products in the EU market containing *Cucurbita pepo* L. as the single active substance different from those included in the current EU monograph. In fact, some of the products which were already in the market during the first Assessment have been withdrawn from the market by the responsible companies.

No references justify a revision of the monograph.

References

a) References relevant for the assessment:

Cicero AFG, Allkanjari O, Busetto GM, Cai T, Larganà G, Magri V, *et al*. Nutraceutical treatment and prevention of benign prostatic hyperplasia and prostate cancer. *Arch Ital Urol Androl* 02 October 2019, 91(3), in press, doi 10.4081/aiua.2019.3.139

Coulson S, Rao A, Beck SL, Steels E, Gramotnev H, Vitetta L. A phase II randomised double-blind placebo-controlled clinical trial investigating the efficacy and safety of ProstateEZE Max: a herbal medicine preparation for the management of symptoms of benign prostatic hypertrophy. *Complement Ther Med* June 2013, 21(3):172-9, in press, doi 10.1016/j.ctim.2013.01.007. Electronic publication 23 February 2013

Gravas S, Cornu JN, Gacci M, Gratzke C, Herrmann TRW, Mamoulakis C, *et al.* EAU Guidelines on Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). *European Association of Urology,* update March 2020. Available at: http://www.uroweb.org/guidelines

Gravas S, Cornu JN, Gacci M, Gratzke C, Herrmann TRW, Mamoulakis C, *et al.* Management of Non-Neurogenic Male Lower Urinary Tract Symptoms (LUTS), incl. Benign Prostatic Obstruction (BPO). *European Association of Urology*, update March 2021. Available at: http://www.uroweb.org/guidelines

Hong H, Kim CS, Maeng S. Effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia. *Nutrition Research and Practice* 2009, 3(4):323-327, in press, doi 10.4162/nrp.2009.3.4.323

Pagano E, Laudato M, Griffo M, Capasso R. Phytotherapy of benign prostatic hyperplasia. A minireview. *Phytother Res* July 2014, 28(7):949-55, in press, doi 10.1002/ptr.5084

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 *Cucurbita pepo* L., semen, by consensus.