



16 January 2019
EMA/HMPC/638288/2018
Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Capsella bursa-pastoris* (L.) Medikus, herba

Rapporteur	A Assisi
Peer-reviewer	L Anderson

HMPC decision on review of monograph <i>Capsella bursa-pastoris</i> (L.) Medikus, herba adopted on 12 July 2011	30 January 2018
Call for scientific data (start and end date)	From 30 April 2018 to 31 July 2018
Agreed by Working Party on European Union monographs and list (MLWP)	September 2018
Adoption by Committee on Herbal Medicinal Products (HMPC)	16 January 2019

Review of new data on *Capsella bursa-pastoris* (L.) Medikus, herba

Periodic review (from 2011 to 2018)

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

- Pharmacovigilance data (e.g. data from EudraVigilance, VigiBase, national databases): The EudraVigilance database was searched on 2018-08-22 with terms "*Capsella*" and "Shepherd's purse" and no adverse reaction was reported.
- Scientific/Medical/Toxicological databases: PubMed (Using the Mesh term "*Capsella*", from 2011 to present, Search date: 2018-09-03, 249 hits), Embase (Using the search terms "*Capsella*" and "*Capsella bursa-pastoris*" (including Shepherd's purse) from 2011 to present, Search date: 2018-09-03, 325 hits and 194 hits, respectively), ToxNet (Using the



search terms "*Capsella*" and "Shepherd's purse" excluding PubMed records, Search date: 2018-09-03, 4 hits)

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 (no monograph in Ph. Eur.)
- Other: British Pharmacopoeia monograph

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)

<i>Scientific data</i>	Yes	No
New non-clinical safety data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical safety data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New data introducing a possibility of a new list entry	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical data regarding the paediatric population or the use during pregnancy and lactation likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New clinical studies introducing a possibility for new WEU indication/preparation	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other scientific data likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<i>Regulatory practice</i>	Yes	No
New herbal substances/preparations with 30/15 years of TU	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New herbal substances/preparations with 10 years of WEU	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other regulatory practices likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Referrals likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
New / Updated Ph.Eur. monograph likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
<i>Consistency</i>	Yes	No
New or revised public statements or other HMPC decisions likely to lead to a relevant change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Relevant inconsistencies with other monographs within the therapeutic area that require a change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Other relevant inconsistencies that require a change of the monograph	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Summary and conclusions on the review

Scientific data

The anti-inflammatory and the anti-microbial properties of *Capsella Bursa-pastoris* herba have been confirmed by *in vitro* studies on single constituents, such as the lignin glycoside (+)-pinortessinol- β -D-glucoside, the phenolic glycoside β -hydroxy-propiovanillone-3-O- β -D-glucopyranoside and sulforaphane.

An *in vitro* study showed that methanolic extracts of *Capsella bursa-pastoris* herba decrease cell growth and induce apoptosis. Another *in vitro/in vivo* study suggested that an ethanolic extract of *Capsella bursa-pastoris* herba could attenuate the lipid accumulation. Details on the preparation of the methanol and ethanolic extracts used in these studies are missing.

The effect of a hydroalcoholic extract of *Capsella bursa-pastoris* herba on heavy menstrual bleeding was investigated in a triple-blinded, randomized clinical trial conducted in 100 women, who referred to gynecology clinics affiliated to Shahid Beheshti University of Medical Sciences, Teheran, Iran. The experimental group received two capsules of mefenamic acid (500 mg) every 8 hours and two *Capsella bursa-pastoris* capsules, containing 320 mg of the shepherd’s purse extract (equal to 2.5 g of the herb), every 12 hours. There was no significant difference between the experimental and control group regarding to pictorial blood loss assessment chart score in first ($p=0.678$) and second month ($p=0.242$); the mean duration of menstrual bleeding was reduced in both the groups, following the intervention based on repeated measurement test ($p<0.001$). Nevertheless, no significant difference was observed between the two groups at the end of treatment courses. The reduction rate in the treatment group was higher than the control group ($p=0.032$).

The effect of a hydroalcoholic extract of *Capsella bursa pastoris* herba on early postpartum haemorrhage was investigated in a single-blinded, randomised clinical trial in women at the maternity ward of Afzalipour Hospital in Kerman, Iran. This study was carried out on 100 women who had given vaginal birth. The intervention group ($n=50$) was given 10 sublingual drops of the hydroalcoholic extract of *Capsella bursa pastoris* herba (each drop contained 50 mg of the extract) plus an infusion of 20 U of oxytocin in 1 l of Ringer’s solution. The control group ($n=50$) was given 10 sublingual drops of the placebo plus an infusion of 20 U of oxytocin in 1 l of Ringer’s solution. There was significant decrease in the amount of postpartum bleeding in both groups in terms of the amount of blood loss ($p<0.001$). However, the mean decrease in the amount of bleeding was significantly more in the *Capsella bursa pastoris* group ($p<0.001$).

Both randomised clinical studies are not relevant for the monograph as information on the nature of the extract is missing (i.e. the strength of alcohol used for the extraction and the DER).

Regulatory practice

The only new herbal medicinal product containing Bursa pastoris herba as dry extract (DER 5-9:1, extraction solvent ethanol 25% V/V) has been marketed in Austria since April 2018 based on a traditional registration scheme. The indication approved is similar with the one from the current monograph. As the extract is comparable to the liquid extract already included in the current monograph, there is no need to revise the EU herbal monograph.

Active substance	Indication	Pharmaceutical form Strength Posology Duration of use	Regulatory Status
Dry extract (DER 5-9:1, extraction solvent ethanol 25% V/V)	Traditional herbal medicinal product for the reduction of heavy menstrual bleeding in women with regular menstrual cycles, after serious conditions have been excluded by a medical doctor.	Coated tablet 400 mg dry extract per tablet 3 times daily 1 tablet	TU registration 04/2018

References

a) References relevant for the assessment:

Cha JM, Suh WS, Lee TH, Subedi L, Kim SY, Lee KR. Phenolic Glycosides from *Capsella bursa-pastoris* (L.) Medik and Their Anti-Inflammatory Activity. *Molecules* 2017, 22; 1023.

doi: 10.3390/molecules22061023.

Choi WJ, Kim SK, Park HK, Sohn UD, Kim W. Anti-Inflammatory and Anti-Superbacterial Properties of Sulforaphane from Shepherd's Purse. *Korean J PhysiolPharmacol.* 2014 Feb; 18:33-39.

Choi HK, Shin EJ, Park SJ, Hur HJ, Park JH *et al.* Ethanol Extract of *Capsella bursa-pastoris* Improves Hepatic Steatosis Through Inhibition of Histone Acetyltransferase Activity. *J Med Food.* 2017; 20(3):251-257.

Ghalandari S, Kariman N, Sheikhan Z, Mojab F, Mirzaei M, Shahrahmani H. Effect of Hydroalcoholic Extract of *Capsella bursa pastoris* on Early Postpartum Hemorrhage: A Clinical Trial study. *The Journal of Alternative and Complementary Medicine.* 2017; 23(10):794-799.

Lee KE, Shin JA, Hong IS, Cho NP, Cho SD. Effect of methanol extracts of *Cnidiumofficinale* Makino and *Capsella bursa-pastoris* on the apoptosis of HSC-2 human oral cancer cells. *Experimental and Therapeutic Medicine.* 2013; 5:789-792.

Naafe M, Kariman N, Keshavarz Z, Khademi N, Mojab F, Mohammadbeigi A. The Effect of Hydroalcoholic Extracts of *Capsella Bursa-Pastoris* on Heavy Menstrual Bleeding: A Randomized Clinical Trial. *JAltern ComplementMed.* 2018; 24(7):694-700.

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

HMPC agreed with Rapporteurs position and that no monograph revision is needed because no new data of relevance were detected that would change the content of the monograph.

The HMPC decided by consensus not to revise the monograph, assessment report and list of references on *Bursae pastoris herba*.