



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Addendum to Assessment report on *Cetraria islandica* (L.) Acharius s.l., thallus

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HMPC decision on review of monograph on <i>Cetraria islandica</i> (L.) Acharius s.l., thallus adopted on 24 November 2014	13 January 2021
Call for scientific data (start and end date)	From 01 April 2021 to 30 June 2021
Adoption by Committee on Herbal Medicinal Products (HMPC)	24 November 2021

Review of new data on *Cetraria islandica* (L.) Acharius s.l., thallus

Periodic review (from 2013 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, search date November 2013 – July 2021, key words: *Cetraria islandica*, Lichen islandicus, Island moss.
- ☐ Other

Regulatory practice

- ☒ Old market overview in AR (i.e. products fulfilling 30/15 years on the market)
- ☒ New market overview – information from Member States
- ☐ Referral
- ☒ Ph. Eur. monograph
- ☒ Other:

New data from the German market with slightly different posology than the approved one.

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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

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 checked="" type="checkbox"/>	<input 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

PubMed was searched on 18th August 2021 for a period of time, from the year 2013 to 2021, with the use of the search terms "Cetraria islandica", "Lichen islandicus", and "Iceland moss". 207 results have been revealed. No new data regarding clinical efficacy and safety has been published.

During the review 33 new references not yet available during the first assessment were identified.

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

16 references were considered to be relevant for the assessment.

No references justify a revision of the monograph.

The overall review of pharmacovigilance data obtained from EudraVigilance showed 92 case reports concerning Iceland moss. Out of these cases, only 4 could be related particularly to the Iceland moss where the adverse events (AEs) refer to hypersensitivity reaction, vomiting, cough and diarrhoea. The AEs were resolved after discontinuation of the treatment except the hypersensitivity reaction. To be concluded, the causality between any AE and Iceland moss cannot be established based on limited number of provided cases.

From the market overview (Germany), slight difference in posology for comminuted herbal substance (herbal tea) had been identified when compared with the approved monograph.

Although the single doses are a bit lower (1.3 g 3-4 times daily) when compared with the dose in the approved monograph (1.5 g 3-4 times daily), the daily doses are considered comparable.

Therefore, no change in monograph is proposed.

References

a) References relevant for the assessment:

Bakır TÖ, Geyikoglu F, Çolak S, Türkez H, Aslan A, Bakır M. The effects of *Cetraria islandica* and *Pseudevernia furfuracea* extracts in normal and diabetic rats. *Toxicol Ind Health* 2015, 31(12):1304-17

Bessadóttir M, Skúladóttir EÁ, Gowan S, Eccles S, Ögmundsdóttir S, Ögmundsdóttir HM. Effects of anti-proliferative lichen metabolite, protolichesterinic acid on fatty acid synthase, cell signalling and drug response in breast cancer cells. *Phytomedicine* 2014, 21(12):1717-24

Borisova KL, Pelageev DN, Kochergina TY, Pokhilo ND, Pushilin MA, Denisenko VA, *et al.* Concerning the structure of islandoquinone isolated from the lichen *Cetraria islandica*. *Nat Prod Commun* 2014, 9(6):837-40

Çolak S, Geyikoglu F, Türkez H, Bakır TÖ, Aslan A. The ameliorative effect of *Cetraria islandica* against diabetes-induced genetic and oxidative damage in human blood. *Pharm Biol* 2013, 51(12):1531-7

Çolak S, Geyikoğlu F, Aslan A, Deniz GY. Effects of lichen extracts on haematological parameters of rats with experimental insulin-dependent diabetes mellitus. *Toxicol Ind Health* 2014, 30(10):878-87

Çolak S, Geyikoğlu F, Bakır TÖ, Türkez H, Aslan A. Evaluating the toxic and beneficial effects of lichen extracts in normal and diabetic rats. *Toxicol Ind Health* 2016, 32(8):1495-1504

Deniz GY, Geyikoğlu F, Türkez H, Bakır TÖ, Çolak S, Aslan A. The biochemical and histological effects of lichens in normal and diabetic rats. *Toxicol Ind Health* 2016, 32(4):601-13

Fernández-Moriano C, Divakar PK, Crespo A, Gómez-Serranillos MP. Neuroprotective activity and cytotoxic potential of two Parmeliaceae lichens: Identification of active compounds. *Phytomedicine* 2015, 22(9):847-55

Fernández-Moriano C, Divakar PK, Crespo A, Gómez-Serranillos MP. In vitro neuroprotective potential of lichen metabolite fumarprotocetraric acid via intracellular redox modulation. *Toxicol Appl Pharmacol* 2017, 316:83-94

Grujičić D, Stošić I, Kosanić M, Stanojković T, Ranković B, Milošević-Djordjević O. Evaluation of in vitro antioxidant, antimicrobial, genotoxic and anticancer activities of lichen *Cetraria islandica*. *Cytotechnology* 2014, 66(5):803-13

Igoli JO, Gray AI, Clements CJ, Kantheti P, Singla RK. Antitrypanosomal activity & docking studies of isolated constituents from the lichen *Cetraria islandica*: possibly multifunctional scaffolds. *Curr Top Med Chem* 2014, 14(8):1014-21

Malaspina P, Catellani E, Burlando B, Brignole D, Cornara L, Bazzicalupo M, *et al.* Depigmenting potential of lichen extracts evaluated by in vitro and in vivo tests. *PeerJ* 2020, 8:e9150

Rassabina AE, Gurjanov OP, Beckett RP, Minibayeva FV. Melanin from the Lichens *Cetraria islandica* and *Pseudevernia furfuracea*: Structural Features and Physicochemical Properties. *Biochemistry (Mosc)* 2020, 85(5):623-628

Thorsteinsdottir UA, Thorsteinsdottir M, Lambert IH. Protolichesterinic Acid, Isolated from the Lichen *Cetraria islandica*, Reduces LRRC8A Expression and Volume-Sensitive Release of Organic Osmolytes in Human Lung Epithelial Cancer Cells. *Phytother Res* 2016, 30(1):97-104. Available at: <https://onlinelibrary.wiley.com/doi/10.1002/ptr.5507>
<https://pubmed.ncbi.nlm.nih.gov/26549524/>

Xu M, Heidmarsson S, Olafsdottir ES, Buonfiglio R, Kogej T, Omarsdottir S. Secondary metabolites from cetrarioid lichens: Chemotaxonomy, biological activities and pharmaceutical potential. *Phytomedicine* 2016, 23(5):441-59

Zacharski DM, Esch S, König S, Mormann M, Brandt S, Ulrich-Merzenich G, *et al.* β -1,3/1,4-Glucan Lichenan from *Cetraria islandica* (L.) ACH. induces cellular differentiation of human keratinocytes. *Fitoterapia* 2018, 129:226-236

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 *Cetraria islandica* (L.) Acharius s.l., thallus, by consensus.