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SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Public statement on *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum

Final

Initial assessment	
Discussion in Working Party on European Union Monographs and European Union List (MLWP)	25 October 2006
Adoption by Committee on Herbal Medicinal Products (HMPC) for release for consultation	26 October 2006
End of consultation (deadline for comments)	28 February 2007
Re-discussion in MLWP	May 2007 July 2007
Adoption by HMPC: Monograph (EMA/HMPC/263292/2006) Assessment Report (EMA/HMPC/137426/2006) List of References (EMA/HMPC/456740/2006) Overview of comments received during the public consultation (EMA/HMPC/200857/2007) HMPC Opinion (EMA/HMPC/280059/2007)	5 July 2007
First systematic review	
Discussion in MLWP and HMPC	April 2016 May/June 2016 January 2021 March 2021 July 2021 September 2021

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	January 2022 March 2022 May 2022 July 2022
Adopted by HMPC for release for consultation	20 July 2022
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Keywords	Herbal medicinal products; HMPC; Public statements; *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum; Foeniculi amari fructus aetheroleum; Bitter fennel fruit oil

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PROBLEM STATEMENT

The HMPC/MLWP had first assessed *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum in 2006-2007 and published a European Union herbal monograph on 5th of July 2007.

The HMPC/MLWP decided to review all new data and revise the published European Union herbal monograph on *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum as announced in the January 2013 HMPC meeting report.

A comprehensive literature search was conducted and available data, including information on products on the market in the European Union, were assessed in relation to the requirements laid down in Directive 2001/83/EC and its Annex I, in particular Article 1, Article 10a and Chapter 2a.

The European Pharmacopoeia monograph sets a maximum content of estragole in the bitter fennel oil of 6.0%.

Due to new data available from literature on the genotoxicity and carcinogenicity of estragole, HMPC has recently revised the "Public statement on the use of herbal medicinal products containing estragole" (EMA/HMPC/137212/2005). The HMPC concluded that:

1. "…the intake of estragole from (T)HMPs in the general population should be as low as possible, which includes a short-time duration of use (maximum 14 days) and a discussion about the single / daily doses necessary according to the risk assessment relevant for the concerned (T)HMP".

2. "The usage of estragole containing (T)HMPs in children is not recommended if the daily intake of estragole exceeds the guidance value of 1.0 µg/kg bw, unless otherwise justified by a risk assessment based on adequate safety data."

The data on the content of estragole in the bitter fennel fruit oil raised concerns of the HMPC regarding its relevance for the safe human use and safe metabolisation of estragole, contained in the essential oil or of the oil containing medicinal products. Carcinogenicity studies with fennel oil have not been carried out. There is some risk with daily intakes of estragole when bitter fennel oil is taken as an expectorant in cough associated with cold according to the posologies supported by evidence of traditional use. Therefore, there are safety concerns with this use of bitter fennel fruit oil, which contains estragole, due to risks of genotoxicity and carcinogenicity in humans (see "Public statement on the use of herbal medicinal products containing estragole" (EMA/HMPC/137212/2005).

The HMPC concluded that the following requirements for the establishment of a European Union herbal monograph on traditional or well-established herbal medicinal products containing *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum are not fulfilled:

- the requirement laid down in Article 16a(1)(e) of Directive 2001/83/EC that "the data on the traditional use of the medicinal product are sufficient; in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience";

- the requirement laid down in Article 10a of Directive 2001/83/EC that the active substance has a recognised efficacy and an acceptable level of safety and that the period of well-established medicinal use has elapsed.

The daily intake of estragole with bitter fennel fruit oil would expose patients to risks, which are not balanced by the beneficial effects in the therapeutic indications as supported by the evidence of traditional use only, taking into account that other safer therapeutic options, including herbal preparations from several plants, are available on the European market. Therefore, the benefit-risk balance on *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum is now considered unfavourable with respect to a European Union herbal monograph.

CONCLUSIONS

Due to new data available from literature on the genotoxicity and carcinogenicity of estragole and taking into account the high intake of estragole when bitter fennel fruit oil is taken as an expectorant in cough associated with cold according to the posologies supported by evidence of traditional use, the HMPC is of the opinion that a European Union herbal monograph on *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum cannot be supported anymore. The HMPC reconsiders therefore its opinion EMA/HMPC/280059/2007 and proposes the withdrawal of monograph EMA/HMPC/263292/2006.

To read more about the assessment carried out, a link is provided to the page where to access the assessment report on *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, aetheroleum and its list of references. The HMPC will welcome the provision of the safety data to allow maintaining an EU herbal monograph.

https://www.ema.europa.eu/en/medicines/herbal/foeniculi-amari-fructus-aetheroleum