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EU Bitter Fennel Oil Monograph May Be Withdrawn Due To Estragole Safety Concerns

by [David Ridley](#)

The European Medicines Agency's Committee on Herbal Medicinal Products (HMPC) says the EU herbal monograph for bitter fennel oil "cannot be supported anymore" because of new data on the genotoxicity and carcinogenicity of estragole.

The European Medicines Agency's Committee on Herbal Medicinal Products (HMPC) is considering withdrawing the monograph for *Foeniculi amari fructus aetheroleum* (bitter fennel oil) based on concerns about one of its minor constituents, estragole.

As a result of new information on the genotoxicity and carcinogenicity of estragole (see box), and taking into account the "high intake 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," the HMPC said it is now of the opinion that the European Union herbal monograph for *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, *aetheroleum* "cannot be supported anymore."

[In the revised draft assessment report](#) (pdf) for bitter fennel oil – which was out for consultation until 30 November – the HMPC concluded that such an intake would "expose patients to safety concerns, which are not balanced by the beneficial effects in the therapeutic indication supported by the evidence of traditional use."

Estragole Concerns

A major or minor component of many plants or plant parts used for herbal medicinal products, botanicals and flavorings, volatile phenylpropanoid estragole has been

Bitter fennel oil is currently approved as a traditional herbal medicinal product for the symptomatic treatment of mild, spasmodic gastro-intestinal complaints including bloating and flatulence and minor spasm associated with menstrual periods.

It is also approved for use as a traditional herbal medicinal product as an expectorant in cough associated with cold.

However, “other safer therapeutic options, including herbal preparations from several plants, are available on the European market,” the HMPC noted.

The HMPC next meets on 23-25 January 2023.

Bitter Fennel Fruit

In its “[public statement on the use of herbal medicinal products containing estragole](#)” (pdf) the HMPC noted that the fruit of bitter fennel as well as the oil, and also *Pimpinella anisum* L. (anise oil), were the “most interesting plants” from a European regulatory perspective.

However, as regulatory expert Mihai Inceu points out, these ingredients are, so far, not subject to the same level of concern as bitter fennel oil.

The monograph for bitter fennel fruit – which has the same indications as bitter fennel oil – has been reviewed and is set to be renewed, Inceu, who is senior regulatory affair officer at Jenson R+.

“This ingredient can be used provided that estragole content in the final product is kept under certain limits,” he told HBW Insight.

In its [draft assessment report on bitter fennel fruit](#) (pdf), the HMPC recommends that for adults and adolescents, only the lower dose of 1.5g of (fresh) fruits with 0.25l of boiling water three times daily as a herbal tea should be included in the monograph.

“However, each action from selection of cultivars and cultivation of the plant to the manufacture

increasingly identified with cancer risk.

Since 2005, a large number of significant publications on estragole and various alkenylbenzenes have appeared in the scientific literature and prompted the HMPC to reassess the toxicology of estragole and of preparations containing these constituents.

As a result of its analysis, the HMPC earlier this year issued a warning that the use of estragole-containing excipients should be avoided as much as possible in (traditional) herbal medicinal products and exposure to estragole should be kept as low as practically achievable. (Also see “[EU Regulatory News Round Up: NSAIDs During Pregnancy, Estragole Excipients, ePIs](#)” - HBW Insight, 4 May, 2022.)

of herbal medicinal product containing fennel fruits, which could minimize the exposure of humans to estragole, should be recommended,” the HMPC added.

Anise Oil

Approved as a traditional herbal medicinal product for symptomatic treatment of mild, spasmodic gastrointestinal complaints including bloating and flatulence, and as a traditional herbal medicinal product used as an expectorant in cough associated with cold, the EU monograph for anise oil was subject to a systematic review in 2012.

[*The final monograph was published in 2014*](#) (pdf) with a contraindication for children and adolescents under 18 due to a lack of data and presence of estragole.

However, the estragole contents were not assessed as a risk for adults and elderly due to low exposure, Inceu explained.

“A new periodic revision would normally take place every five years unless the HMPC decides that it’s not needed,” Inceu added. “However, unscheduled revisions can take place if new relevant data is brought to their attention.”