Technical Alert

TGA Safety Reports and Potential Future Changes – Vitex agnus-castus and Fallopia multiflora

Vitex agnus-castus – potential for interaction with oral contraceptives

The TGA have reported an unintended pregnancy following concurrent use of *Vitex agnus-castus* (Chaste Tree, Chaste berry, or Monk's Pepper) and norethisterone, a progesterone-only oral contraceptive pill. One other similar case has also been reported internationally.

The progesterone-only oral contraceptive pill (or "mini-pill") has a higher failure rate than oestrogen based contraceptives and is especially sensitive to how users take it, including timing. In this respect it may also be particularly sensitive to the influence of interactions with other medicines.

Vitex agnus-castus is traditionally used for symptoms related to female hormonal balance, and there is some scientific information to suggest that an interaction upon hormone receptors.

The herb currently does not have any requirements against its use (such as warning statements) in the Permissible Ingredients Determination (No 1. of 2019).

Both Health Canada and the European Medicines Agency (EMA) advise consumers to consult a health practitioner prior to using *Vitex agnus-castus*-containing products if they are taking hormone-containing medications such as progesterone preparations, oral contraceptives or hormone replacement therapy.

TGA Review of Vitex agnus-castus

The TGA are currently reviewing this ingredient, and have advised that sponsors should consider appropriate risk communication strategies to inform consumers of any possible interaction.

In relation to the above safety alert, the TGA are:

1) advising consumers that taking an oral contraceptive to prevent pregnancy should be aware that *Vitex agnus-castus* may interfere with how well the contraceptive works, and that consumers taking medicines with contraceptive, hormonal and/or dopaminergic actions should consult their health professional prior to combined use with *Vitex agnus-castus*.

2) Advising health professionals that should be aware that some studies indicate *Vitex agnus-castus* may bind estrogen[1] and dopamine receptors[2], which suggests the potential for interaction with medications that have estrogenic and/or dopaminergic actions; and that combined use of the herb with certain medicines, including oral contraceptives and other medicines with hormonal and/or dopaminergic actions, may result in decreased efficacy or additive effects, although there is limited evidence to verify the extent of these effects.

Possible Future Outcomes of the TGA review into Vitex agnus-castus

It is likely that the outcome of the above will be that there will be a warning statement for medicines containing *Vitex agnus-castus* and taking oral contraceptives or other medications. CMA will be working with TGA on the outcome of the above.

Fallopia multiflora – potential for liver damage

The TGA is conducting safety investigation of the ingredient and is monitoring products on the ARTG that contain the herb ***Fallopia multiflora*** due to reports of adverse liver events.

Nine cases of liver damage have been reported in the last 10 years linked with the herb, which is also known by:-

- **'he shou wu'** (Chinese name);
- ***Polygonum multiflorum***
- ***Fo ti***
- ***Reynoutria multiflora***
- **Chinese fleeceflower root.**

The following label warning statement is already required for listed medicines containing Fallopia multiflora:

> Warning: *Fallopia multiflora* may harm the liver in some people. Use under the supervision of a healthcare professional.'

The TGA have identified that some products available through practitioners that contain the ingredient were not carrying the required warning statement. Four medicines were subject of a Class II consumer level recall.

Sponsors should remain aware that listed medicine containing the ingredient, irrespective of the intended use (retail or practitioner), must contain the required safety label warning statement and remain visible after any practitioner labelling.

More information about the investigation is published in English and Chinese on the TGA website.

Possible Future Outcomes of the TGA review into Fallopia multiflora

Possible future outcomes of the TGA include cancellation or recall of products if they are considered unsafe or are missing advisory statements.

Other possible outcomes are changes to the availability of the ingredient, or the requirements for the ingredient such as new or additional warning statements.

Pharmacovigilance requirements - Reporting of adverse reactions

In 2018 the TGA updated the information on its website regarding pharmacovigilance requirements of sponsors. Reporting of known safety issues, including adverse reactions is a legal responsibility of all sponsors under their pharmacovigilance reporting requirements. Other obligations also include informing the TGA of the pharmacovigilance contact person in the company, as well as keeping records pertaining to the reporting requirements and safety for the medicine (under Subsection 28(5)(ca) of the *Therapeutic Goods Act 1989*.)

Pharmacovigilance resources for sponsors:

- **Pharmacovigilance responsibilities of medicine sponsors – Australian recommendations and requirements**
    - Guidance on website
    - Guidance by PDF
- **Pharmacovigilance Inspection Program (Sponsor audit)**
    - Background
    - Guidance on website
    - Guidance by PDF

ENDS