EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee on Herbal Medicinal Products (HMPC)

Opinion of the HMPC on a European Union herbal monograph on *Melaleuca alternifolia* (Maiden and Betch) Cheel, *M. linariifolia* Smith, *M. dissitiflora* F. Mueller and/or other species of *Melaleuca*, aetheroleum

Opinion

The HMPC, in accordance with Article 16h(3) of Directive 2001/83/EC, as amended, and as set out in the appended assessment report, establishes by a majority of 24 out of 29 votes a European Union herbal monograph on *Melaleuca alternifolia* (Maiden and Betch) Cheel, *M. linariifolia* Smith, *M. dissitiflora* F. Mueller and/or other species of *Melaleuca*, aetheroleum which is set out in Annex I.

The divergent positions are appended to this opinion.

The Norwegian HMPC member agrees with the above-mentioned recommendation of the HMPC.

This opinion is forwarded to Member States, to Iceland and Norway, together with its Annex I and appendices.

The European Union herbal monograph and assessment report will be published on the European Medicines Agency website.

London, 24 November 2014

On behalf of the HMPC

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Annex I: European Union herbal monograph (EMA/HMPC/320930/2012)

Appendix I: Assessment report (EMA/320932/2012)

Appendix II: Divergent positions

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

As representative of the Finnish Medicines Agency in the HMPC, I hereby express a divergent opinion on the community herbal monograph on Melaleuca oil, as the substance does not fulfil the safety requirements of Directive 2004/24/EC, i.e. cannot be "considered not to be harmful under normal conditions of use."

Tea tree oil is a common contact allergen (the most common allergen in the Antimicrobials/Preservatives Series in Finland in 2011-2012 based on Helsinki University Central Hospital records). As the most common contact allergen among active treating agents (excluding non-treating substances) causing contact dermatitis in the Helsinki area we regard the benefit/risk ratio of Melaleuca oil as negative.

Moreover, traditional herbal medicinal products should be safe to use without doctor's surveillance and without prescription, i.e. over-the counter. Tea tree oil is extremely poisonous when taken accidentally orally by children, which is not acceptable for an over-the-counter medication. Accidental ingestion of even small amounts of tea tree oil (10-25 ml) has caused severe poisoning with central nervous system depression, unresponsiveness, ataxia, and muscle weakness, requiring hospital treatment and respiratory support for several days in small children, according to several published case reports and also oral information from the Finnish Poison Centre in the Helsinki University Hospital.

Eeva Sofia Leinonen, HMPC member from Finland

London, 24 November 2014

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Olavi Pelkonen, Co-opted HMPC member

London, 24 November 2014

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

Data mentioned in AR, Part 5., Clinical Safety/Pharmacovigilance evoked my concerns on overall safe use of different preparations mentioned in Monograph for *Melaleuca alternifolia* (Maiden and Betch) Cheel, *M. linariifolia* Smith, *M. dissitiflora* F. Mueller and/or other species of *Melaleuca*, aetheroleum.

The irritation potential of undiluted preparation applied on cotton wool bunch is not suppressed as the irritation sensitivity in humans to essential oil from Melaleuca is highly variable and a simple dose decrease does not lead (from my point of view) to a clear decrease of irritation risk, as in local small skin area with a direct contact with undiluted essential oil fom Melaleuca stays its real concentration (calculated for 1 cm^2) always the same.

Also allergenicity of essential oil from Melaleuca is probably underestimated, especially for aged samples. These ones are for a long period in contact with air/oxygen, which leads to the autooxidaton of some essential oil components, e.g. α-terpinene, and creation of derivatives with skin allergy potential (Rudbäck, 2012; Christoffers 2013; Corazza 2013; Christoffers 2014 – **not involved in AR**). The autooxidation rate of an essential oil fom Melaleuca and concentration of allergenic substances (haptens) cannot be predicted for all types of preparations and their dilutions in real life conditions.

Thus, a risk of an allergic reaction and its intensity in humans with various sensitivity to haptens, often related to the genetic predisposition of humans, could be a serious argument for rejecting essential oil from Melaleuca from the class of a safe herbal medicine.

In AR not involved articles:

Rudbäck J. et al. (2012). α-Terpinene, an Antioxidant in Tea Tree Oil, Autoxidizes Rapidly to Skin Allergens on Air Exposure. *Chem. Res. Toxicol*., **25,** 713−721.

Christoffers W. A. et al. (2013). Co-sensitization to ascaridole and tea tree oil. *Contact Dermatitis*, **69**, 181–191.

Corazza M. et al. (2013). Topical botanically derived products: use, skin reactions, and usefulness of patch tests. A multicentre Italian study. *Contact Dermatitis*, **70**, 90–97.

Christoffers W. A. et al. (2014). The optimal patch test concentration for ascaridole as a sensitizing component of tea tree oil. *Contact Dermatitis*, **71**, 129–137.

Milan Nagy HMPC member from Slovakia

London, 24 November 2014

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

All data presented during the procedure indicated that safety of products containing Melaleuca oil do not fulfil criteria of safe use in a normal conditions of use. However I found three products, containing Melaleuca oil, registered by Therapeutic Good Administration in Australia, but all they are all labelled as toxic substances. Moreover the oil itself possesses strong skin irritating properties and could only be safely used in a specified concentration. Presented data indicate frequent adverse events (at level of 7% of group) in concentration of 5%.

Wojciech Dymowski the HMPC member from Polen

London, 24 November 2014

The member of the HMPC mentioned below did not agree with the HMPC's opinion for the following reason:

The posology, conditions of use and sensitisation risk of the undiluted essential oil are not enough justified by the scientific data available.

An Lé the HMPC member for France

London, 24 November 2014