Conclusions

In this guide

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108. Three *Echinacea* species – *E. purpurea*, *E. angustifolia* and *E. pallida* have been used medicinally to relieve the symptoms and shorten the duration of cold and flu infections. *Echinacea* preparations can be made from the dried roots of all three species, the fresh or dried aerial parts and the pressed juice from *E. purpurea*. Ethanolic extracts are also often used in many *Echinacea* products. The

effects of *Echinacea* are due to the combination of bioactive metabolites including alkylamides, caffeic acid derivatives and polysaccharides. The composition of these compounds varies across the species, the plant parts, season, growing conditions and extraction methods used.

109 There is evidence from *in vitro* and *in vivo* studies that *Echinacea* preparations can inhibit viral entry and modulate immune responses following infection. Herbal products containing *E. purpurea*, *E. angustifolia* and *E. pallida* have herbal medicinal licenses in EU/EEA member states and THR license from the MHRA based on traditional use for the relief of common cold symptoms in adults and children over 12 years of age. Regulatory authorities, including the EMA and MHRA, do not recommend the use of *Echinacea* containing medicinal products during pregnancy or lactation due to the absence of high-quality, guideline-conforming reproductive and developmental toxicity studies and the limited human evidence available. THR licensed *Echinacea* products in the UK also carry warnings advising against use in these populations. Nevertheless, survey data indicate that up to 10% of pregnant women may use *Echinacea* for the treatment or prevention of cold and flu symptoms or for immune support.

110. In addition to products with a THR license, there is a range of foods and food supplements containing *Echinacea* and its extracts. The most common food supplements are tablets and capsules, and the majority of these products carry a warning against their use in pregnancy/lactation and a recommendation for short term use only. There are also food products such as tea and honey which contain *Echinacea.* Whilst products with THR are acknowledged in this paper, the focus in the conducted exposure assessment has been the consumption of *Echinacea* foods and food supplements.

111. The *in vivo* toxicological studies on *Echinacea* suggested that it has low toxicity. Clinical studies reported that *Echinacea* products are well tolerated with minor and reversible side effects including gastrointestinal disturbances and allergic skin reactions. There are isolated case reports of *Echinacea* causing erythema nodosum, hyperoesinophilia, leucopenia, thrombocytopenia and hepatotoxicity, but causality has not been confirmed. Pharmacovigilance cases and follow up investigation of selected patients also suggested that *Echinacea* can trigger allergic reactions, as serious as anaphylaxis in some cases, in patients with pre-existing atopic diseases. EMA (2014) recommends *Echinacea* preparations should be used with caution in patients with asthma or history of atopy. Due to its potential for immune system modulation, *Echinacea* is also not recommended for people with autoimmune diseases, immunodeficiencies,

immunosuppression and diseases of the white blood cell system.

112. There is an uncertainty around the potential of *Echinacea* to interact with prescription medicines during pregnancy. *In vitro* and *in vivo* studies demonstrated that *Echinacea* could affect the activity of CYP enzymes leading to inhibition of CYP1A2 and CYP3A4. However, the clinical relevance of these *in vitro* and *in vivo* studies is unknown as there are limited number of human studies investigating the interactions of *Echinacea* with over the counter or prescription medicines.

113. Contaminants such as heavy metals, fungi, bacteria, mycotoxins and pesticides are sometimes found in herbal preparations. There is an uncertainty of how much risk the potential contaminants in *Echinacea* preparations pose to pregnant consumers due to lack of research. Whilst studies have reported that cadmium and lead levels detected in *Echinacea* preparations have been lower than the WHO limits, the presence of fungal contaminants and mycotoxins found in some *Echinacea* products can pose an additional risk during pregnancy.

114. There is a lot of uncertainty around the safety of using *Echinacea* products during pregnancy or lactation due to limited data from *in vitro*, *in vivo* and clinical studies. *In vitro* and *in vivo* OECD guideline conforming studies suggested that *Echinacea* is not genotoxic. There are two studies in mice, one in pigs and two studies in rabbits looking at the effects of *Echinacea* supplementation during pregnancy. Whilst the two mice studies highlighted potential increase in foetal loss and altered angiogenesis with *Echinacea*, the sample sizes were small and some of the results reported on foetal angiogenesis were conflicting. The pig and rabbit studies did not report any significant differences in relation to birth weight, pregnancy outcomes and frequency of malformations between *Echinacea* and control groups. There are human observational studies describing the effects of *Echinacea* on pregnancy outcomes and they did not highlight any adverse effects associated with gestational use of *Echinacea*. These studies rely on self-reported use of *Echinacea* during pregnancy and the dose, preparation or duration of use were not specified.

115. The doses used in clinical studies on the efficacy of *Echinacea* are comparable to the estimated exposures to *Echinacea* in women of child-bearing age, calculated by the FSA Exposure Assessment Team. *Echinacea* was well-tolerated in these clinical studies, but they did not include pregnant or lactating women. In addition, an exact comparison between different *Echinacea* products is challenging due to products containing different combinations of the three medicinally used species, their dried plant parts and extracts. Some food products

such as tea and honey often lack information on the exact species, plant parts or extracts used.

116. Overall, Members emphasised that the available information is insufficient to support a robust risk assessment or the derivation of any health-based guidance values. However, the Committee did not identify any reason to expect adverse effects in humans from the current levels of exposure of *Echinacea* as part of the maternal diet.