Adverse effects in humans

In this guide

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65. The adverse effects of Echinacea preparations in humans have been described in several literature reviews, EMA assessment reports, individual case studies and pharmacovigilance data. Although these findings relate to the general population and not specifically to pregnant women or exposure through the maternal diet, they have been included to provide broader insight into the

potential toxicities of Echinacea in humans, while acknowledging their limited relevance to pregnancy specific risk assessment.

66. The EMA assessment report on E. purpurea concluded that based on the analysis of pharmacovigilance reports from EU member states, hypersensitivity reactions such as rash, urticaria, itching and swelling were possible adverse effects of Echinacea and in a case of allergic reaction, Echinacea should not be taken again. The EMA report stated that there were cases of severe reactions such as Stevens-Johnson Syndrome, angioedema, bronchospasm, asthma and anaphylactic shock with confirmed/probable causality. The report acknowledged that cases of autoimmune diseases such as encephalitis disseminata, erythema nodosum, immunothrombocytopenia, Sjögren's syndrome with renal tubular dysfunction were reported, but that their causality was inconclusive. The report further stated that gastrointestinal side effects reported were unlikely to be linked to Echinacea as their frequency was similar between the placebo and treatment groups in clinical trials (EMA, 2014).

67. A meta-analysis of six randomised controlled trials (Schapowal et al., 2015), evaluating various Echinacea preparations for respiratory tract infections, also reported on adverse events in 1,440 Echinacea treated participants and 1,326 placebo treated controls. Although the trials primarily assessed potential benefits, the safety data indicated no significant difference in the overall number of adverse events between Echinacea (491 events) and placebo (474 events). The Echinacea products used varied across studies, including ethanol/glycerol extracts of E. purpurea and E. angustifolia (500–4,000 mg extract/day) and pressed juices of E. purpurea (6,200–10,000 mg/day). Most reported adverse effects were mild, transient gastrointestinal disturbances. Two severe adverse events (stridor) occurred in the Echinacea group, and one severe event (glandular fever requiring hospitalisation) occurred in the placebo group. No significant differences in clinical biochemistry were observed. Although the meta-analysis also concluded that Echinacea may reduce respiratory tract infections, these findings are beyond the scope of the present assessment and only the safety data have been considered here to inform understanding of the potential adverse effects associated with Echinacea use in humans.

68. A systematic review summarised evidence of the safety of Echinacea based herbal medicinal products from 36 clinical studies, case reports, and spontaneous reporting programmes from regulatory agencies in Australia, Germany, UK, USA and Sweden (Huntley et al., 2005). The oral doses used in the clinical trials were typically 4-8 mL expressed juice/liquid extract twice daily, 250-1,000 mg daily in

the form of capsules/tablets or 5-30 drops daily for the tinctures. The review concluded that Echinacea had a good safety profile when taken short-term, with short-term use being defined as ‘days as opposed to weeks’. Adverse effects were mild, transient and reversible with gastrointestinal disturbances and skin-related reactions being most commonly reported. The review discussed that in rare cases Echinacea use can be associated with allergic reactions, which can be severe. However, the authors noted that in about a quarter of these cases, Echinacin ® (E. purpurea) was administered intramuscularly or intravenously. Nevertheless, the authors suggested that atopic and asthmatic patients should be cautious when using Echinacea supplements.

69. An Australian study looking at adverse reactions associated with Echinacea reviewed 51 reports of adverse drug reactions (ADRs) in the Australian Adverse Drug Reactions Advisory Committee’s database (Mullins and Heddle, 2002). There were 26 cases which were suggestive of IgE-mediated hypersensitivity reactions (4 anaphylaxis, 12 acute asthma,10 urticaria/angioedema). Seventy eight percent of the affected patients were female, the median age was 32 years and over half had a history of asthma, allergic rhinitis or atopic dermatitis. In addition to the review of the ADR reports, five cases of adverse reactions to Echinacea were personally evaluated by the authors. Two patients suffered anaphylaxis and a third had an acute asthma attack 10 minutes after their first ever dose of Echinacea. All three patients were female, had a history of atopy including allergic rhinitis or latex allergy and tested positive on skin prick tests to aqueous Echinacea. A fourth case described a 56-year-old man who developed recurrent mild asthma with Echinacea tablets, resolving upon discontinuation. The fifth case involved a 48-year-old woman who developed a maculopapular rash within two days of Echinacea tablets ingestion, recurring on rechallenge. Both latter patients had allergic rhinitis but negative skin prick test. The overall conclusion of the study was that there is a possible cross-reactivity between Echinacea and other environmental allergens and atopic patients should be warned accordingly (Mullins and Heddle, 2002).

70. There are individual case reports of adverse effects experienced by people after taking Echinacea preparations including an autoimmune disease supposedly triggered by Echinacea (Lee and Werth, 2004), isolated case of erythema nodosum in a 41-year old male (Lee Soon and Crawford, 2001), hypereosinophilia in a 58-year old male patient with history of asthma and allergic rhinitis (Maskatia and Baker, 2010), leucopenia in a 51 year old woman who took 450 mg Echinacea capsules for 2 months (Kemp and Franco, 2002), thrombocytopenia with E. pallida in a 32 year old man (George et al., 2006) and hepatotoxicity in a 45-year old male who took 1,500 mg Echinacea root for the treatment of cold (Kocaman et

al., 2008). However, limited information was available in these case reports about the doses taken, and it was uncertain whether the adverse effects described were related to Echinacea consumption or to other factors, such as the use of other herbal products such as St John’s wort (Lee Soon and Crawford, 2001) or Gingko biloba (Kemp and Franco, 2002). In the case report of hepatotoxicity associated with Echinacea the authors concluded that this was a case of Echinacea-induced acute cholestatic autoimmune hepatitis (ACAH) due to the immunostimulatory effects of Echinacea (Kocaman et al., 2008).