The European Agency for the Evaluation of Medicinal Products

EMEA/MRL/564/99-FINAL
March 1999

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

LAURI FOLII AETHEROLEUM

SUMMARY REPORT

1. *Lauri folii aetheroleum* is the volatile oil obtained by steam distillation from bay leaves, the leaves of *Laurus nobilis.*

   Lauri folii aetheroleum contains 50 to 100 different constituents. Usually 1,8-cineole is the main component in Mediterranean bay leaf oils. In such oils 28 to 62% of cineole may be found. Other important constituents are α-pinene, β-pinene, sabinene (2.3 to 8.8%), citral, methylcinnamate, terpineol, cinnamic acid, eugenol, 3,4-dimethoxyallyl-benzene, geraniol, and α-terpineyl acetate.

   Sesquiterpene lactones such as costunolid, eremanthin and laurenobiolid are reported to be present in the volatile oil. They are responsible for allergic reactions (see below).

   Lauri folii aetheroleum is contained in a concentration of 0.5% (w/w) as one of 11 ingredients in an ointment for topical administration to the udder or mammary glands of cows, horses, sheep, goats and pigs used for disinfection and to prevent transmission of udder or mammary gland diseases. The ointment is to be used as frequently as required, no doses were given.

2. 3,4-Dimethoxyallyl benzene causes sedation at low doses and prevents death in mice treated with lethal doses of strychnine. Antibacterial properties are reported for 1,8-cineol.

   Given orally to mice, *Lauri folii aetheroleum* may cause reversible narcosis at doses of 40% and 80% in corn oil (no further figures given). A similar effect is observed in stickleback fish.

   Lauri folii aetheroleum has a depressive effect on the heart and causes hypotension.

3. No information was provided on the pharmacokinetics of *Lauri folii aetheroleum.*

4. The oral LD_{50} for *Lauri folii aetheroleum* is 3.95 g/kg bw for rats and 3.31 ml of volatile oil/kg bw for mice. The dermal LD_{50} is greater than 5 g/kg bw for rabbits.

   Excessive doses of the volatile oil are irritant to the gastrointestinal tract and may cause diarrhoea, nausea and vomiting.

   Oily solutions with 1,8-cineole as a major constituent have been associated with lipoid pneumonia.

5. No information was provided on the repeated dose toxicity, reproductive toxicity or on teratogenicity.

6. *Lauri folium* have no mutagenic effect in the *Salmonella*-microsomal assay. Considering this, and the knowledge of the constituents in the *Lauri folii aetheroleum* carcinogenicity studies were not considered necessary.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Switchboard: (+44-171) 418 8400 Fax: (+44-171) 418 8447
E_Mail: mail@emea.eudra.org http://www.eudra.org/emea.html

7. In humans the volatile oil of bay leaves may cause severe lesions of the skin. This dermatitis is known as "felt hat dermatitis", because the oil was being used in the felt hat industry as a glaze to improve luster. Also other professionals handling the volatile oil have been reported to suffer from this type of contact dermatitis. The use of the oil in cosmetics and as a flavouring agent has also caused dermatitis. This allergic manifestation has been found to be due to the presence of the above-mentioned sesquiterpene lactones. Cross reactions to a large number of other chemically related sesquiterpene lactones occurring in different species of the family *Asteraceae* have been observed. The use of the product in cosmetics is prohibited in one Member State.

   Sensitization tests on volunteers have given conflicting results.

8. The volatile oil and some of its constituents have antibacterial and fungicidal activity.

9. *Lauri folii aetheroleum* is used in perfumery and for flavouring of food products and liqueurs.

10. *Lauri folii aetheroleum* has been given Generally Recognized As Safe (GRAS) status by the Flavoring Extracts Manufacturers Association (FEMA) in 1965. Laurel leaf is included in the Council of Europe's list of substances, spices and seasonings deemed admissible for use with a possible limitation of the active principle in the final product. No limitation appears to have been established until now.

Conclusions and recommendation

Having considered the criteria laid down by the Committee for Veterinary Medicinal Products for the inclusion of substances in Annex II of Council Regulation (EEC) No. 2377/90 and in particular that:

- *Lauri folii aetheroleum* is of low acute oral toxicity,
- *Lauri folii aetheroleum* is used as a spice in human food,
- the animals are unlikely to be sent for slaughter during or immediately after treatment;

the Committee for Veterinary Medicinal Products concludes that there is no need to establish an MRL for *Lauri folii aetheroleum* and recommends its inclusion in Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Lauri folii aetheroleum	All food producing species	