The European Agency for the Evaluation of Medicinal Products

EMEA/MRL/565/99-FINAL
March 1999

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

LAURI FRUCTUS

SUMMARY REPORT

1. *Lauri fructus* are the dried, ripe, berries of *Laurus nobilis*.

   Lauri fructus contains 1 to 4.1% volatile oil with approximately the same composition as the leaf oil containing 28 to 62% of cineole. 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. *Lauri fructus* contains 24 to 55% fixed oil.

   In veterinary medicine pulverised *Lauri fructus* is used orally in cows and mares to facilitate removal of the afterbirth. The product is used when the afterbirth has not appeared 6 hours after parturition in cows and 30 minutes after parturition in mares. The dose is 3 tablespoons in 1 litre warm bran gruel every 12 hours.

2. No information on the pharmacology of *Lauri fructus* was provided. However, due to the similarity of the volatile oils of the berries and the leaves the data observed for bay leaf oil, *Lauri folii aetheroleum*, can be considered relevant.

   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-cineole.

   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 pharmacokinetics.

4. No information of the acute toxicity of *Lauri fructus* was provided. However, due to the similarity of the volatile oils of the berries and the leaves the data observed for bay leaf oil, *Lauri folii aetheroleum*, can be considered relevant.

   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 or more 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* has 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 the 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.

   Sensitisation tests on the volatile oil have given conflicting results.

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

9. *Lauri fructus* was previously used in human medicine as a bitter, carminative, emmenagogue and diuretic. It is also used as a spice.

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:

- the volatile oil contained in *Lauri fructus* is of low acute oral toxicity,
- *Lauri fructus* is used as a spice in human food,
- *Lauri fructus* is used only in a small number of individual animals, for infrequent or non-regular treatments,
- 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 fructus* 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 fructus	All food producing species	