



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

THYMI AETHEROLEUM

SUMMARY REPORT

1. *Thymi aetheroleum* is obtained from *Thymus vulgaris* L. (synonym: thyme) by steam distillation of the aerial parts of the fresh flowering plant, in which it is contained at concentration of 0.3 to 0.5%. It contains thymol (30 to 50%), carvacrol (1 to 5%), *p*-cymene (15 to 20%), γ -terpinene (5 to 10%). The following monoterpenes are present in concentrations between 1 and 3%: Borneol, camphor, limonene, linalool, myrcene, β -pinene, *cis*-sabinene hydrate and α -terpinene. Present in concentrations lower than 1% are: bornyl acetate, camphene, 1,8-cineol, *p*-cymene-8-ol, linalyl acetate, *cis*-myrcene-8-ol, terpineol, terpinene-4-ol, terpinolene and terpinyl acetate. The sesquiterpene derivative β -caryophyllene is present in a concentration of 1 to 3%.
2. *Thymi aetheroleum*, in combination with 5 other active principles, is contained at a concentration of 1% in a veterinary medicinal product intended for disinfection of wounds and to prevent infection of wounds. The product is sprayed on the wound. It should not be used for more than a week. The target species are cattle, horses, pigs, sheep and goats. Another product, a solution for topical administration, contains 0.9% *Thymi aetheroleum* in combination with 7 other active principles. It is used topically in cattle, sheep, goats, horses, pigs, rabbits and poultry as an antiseptic on wounds. No information was provided on further veterinary products, which also contain *Thymi aetheroleum* and are covered by a valid application.

In human medicine *Thymi aetheroleum* is used for treatment of acute and chronic inflammations of the upper respiratory tract. It is also used against itching and for other dermatological purposes. It can be used externally for baths containing at least 4 mg of *Thymi aetheroleum*/l or internally 4 to 5 drops 3 to 5 times a day.

Thyme is commonly used as a culinary herb, and *Thymi aetheroleum* is used in food flavouring.

Thyme is indigenous to the Mediterranean regions of Europe and grazing animals like to eat it.

3. *Thymi aetheroleum* has antitussive, expectorant and spasmolytic actions. *Thymi aetheroleum* has produced hypotensive and respiratory stimulant effects in rabbits following oral or intramuscular administration and in cats following intravenous injection (doses not reported). An increase in rhythmic heart contraction was observed in rabbits (dose and route of administration not given). *Thymi aetheroleum* has strong antibacterial and antifungal activity. Its main constituent thymol has anthelmintic (especially hookworms), antibacterial and antifungal properties.
4. No information on pharmacokinetics of the *Thymi aetheroleum* has been provided. Thymol the main constituent of *Thymi aetheroleum* is readily absorbed in the gastrointestinal tract. A small amount is oxidised to thymohydroquinone. About 50% of the absorbed substance is excreted via the kidney, either unconjugated or as a glucuronide or sulfate conjugate in 24 hours. The metabolite thymohydroquinone is also excreted via the kidney.

5. The oral LD₅₀ for *Thymi aetheroleum* in rats is in the range of 2.8 to 4.7 g/kg bw. An LD₅₀ in mice is reported as 1.25 g/kg bw (no information on route of administration). For thymol the oral LD₅₀ is 980 mg/kg bw in rats, 1800 mg/kg bw in mice, and 880 mg/kg bw in guinea pigs.
6. No information on the long-term toxicity of *Thymi aetheroleum* was provided. For thymol no effects were seen in a 19 week oral study when rats were given 10000 mg/kg feed (450 to 530 mg/kg bw) or 1000 mg/kg feed (45 to 53 mg/kg bw) thymol in the diet (5 male and 5 female rats per group).
7. No data on effects on reproduction and teratogenicity have been provided.
8. *Thymi aetheroleum* is not mutagenic in the Ames test. No damage to chromosomes in the Bacillus subtilis Rec-test was recorded.
9. There is no information on carcinogenicity. However, this is not considered necessary due to the conclusion on mutagenicity above.
10. No sensibilisation was observed from 8% of the oil in vaseline.
11. High doses of *Thymi aetheroleum* is toxic and should not be taken internally and only applied externally if diluted in suitable carrier oil.

There are no known problems with the use of thyme (the dried plant) during pregnancy and lactation, providing that doses do not greatly exceed the amounts used in foods. Thyme is reputed to affect the menstrual cycle and therefore large amounts should not be ingested.
12. *Thymi aetheroleum* has status as "Generally Recognised As Safe" in the USA. Thymol has been evaluated 1992 by the Committee of Experts on Flavouring Substances of the Council of Europe. Thymol is listed among the substances that are permitted as flavouring agents. An upper limit for inclusion of thymol in food is established at 50 mg/kg and in beverages at 10 mg/kg.
13. Thymol the main constituent of *Thymi aetheroleum* is included in Annex II of Council Regulation (EEC) No. 2377/90
14. The use *Thymi aetheroleum* in the doses recommended is unlikely to result in residues in edible tissues posing a risk to the health of the consumer.

Conclusions and recommendation

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

- *Thymi aetheroleum* is obtained from the leaves of *Thymus vulgaris* which are used as a spice in human food,
- thymol the main constituent of *Thymi aetheroleum* is already included in Anne II,
- *Thymi aetheroleum* is used only for occasional treatment of individual animals,
- the animals are unlikely to be sent to slaughter immediately after treatment;

The Committee concludes that there is no need to establish an MRL for *Thymi 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
<i>Thymi aetheroleum</i>	All food producing species	