



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

MAJORANAE HERBA

SUMMARY REPORT

1. *Majoranae herba* is the dried upper parts of *Origanum majorana* L. (= *Majorana hortensis* Moench). The toxicological and pharmacological relevant components are: flavonoids and phenols (hydroquinone: 0.8%) including glycosides hereof (arbutin: approximately 0.4%), tannins, phenol carboxylic acids and 1 to 3% volatile oil. The main components of the essential oil are sabinene and sabinene derivatives which together add up to about 92% of the weight of the oil (*cis*-Sabinene hydrate 40 to 50%, *cis*-sabinene hydrate acetate 20 to 30%, *trans*-sabinene hydrate 2% and sabinene 10%).
2. *Majoranae herba* is used in two products in combination with other active principles. The one product containing *Majoranae herba* in a concentration of 10% is intended for oral use to induce rut and heat in cows, horses, pigs, sheep and goats. The dosage regime is 50 g of the product two times daily on two subsequent days for cows and horses, and 10 to 20 g of the product two times daily (depending on the weight of the animals) during three to four days for pigs, sheep and goats. The other product is intended for rinsing of the vagina and uterus with a concentration of 1.2% for use in cattle, horses and pigs. The dosages used are up to 50 ml of the product diluted to a suitable volume depending on the size of the animal. The treatment can be repeated, for some indications daily treatment is recommended.

In human medicine *Majoranae herba* is used for a wide range of symptoms including spasms, gastrointestinal problems, depressive conditions and colds. The dosages used are 1 to 2 teaspoons of the drug to 250 ml hot water, 1 to 2 cups of the infusion is recommended per day.

Majoranae herba is commonly used as a culinary herb.

3. In the summary information provided *Majoranae herba* is reported to have antiviral properties against Newcastle-Virus and Herpes-simplex-Virus. The oil has antibacterial and insecticidal effects.
4. No information on pharmacokinetics of the *Majoranae herba* has been provided for animals.

In humans given 420 mg arbutin (corresponding to 168 mg hydroquinone) 0.6% of the applied dose was excreted as free hydroquinone in the urine and 70% was found as hydroquinone conjugates to glucuronic and sulfuric acid.
5. The oral LD₅₀ for *Majoranae aetheroleum* in rats is reported to be 2.24 g/kg bw. A dermal LD₅₀ in rabbits is reported to be greater than 5 g/kg bw.
6. No information on repeated-dose toxicity has been provided.
7. No data on effects on reproduction and teratogenicity have been provided.

8. There is no information on mutagenicity or carcinogenicity of *Majoranae herba* but hydroquinone which is present in the plant in small amounts have shown carcinogenic potential in experimental animals. Arbutine also present in small amounts in *Majoranae herba* is a glucoside of hydroquinone and is hydrolysed to hydroquinone. In published literature it was found that the urine from human volunteers given 420 mg arbutin did not show genotoxic potential in the *in vitro* Ames test and in the *in vivo* micronucleus test

The total content of hydroquinone in the crude drug is about 1%. In published literature it is stated that “the only tumour type for which there is convincing evidence of tumourigenicity is the renal adenoma in the male rat”. This finding is from long-term exposure to doses ranging from 25 mg/kg bw per day, 5 days a week for 103 weeks (7% incidence of tumours) to 351 mg/kg bw per day for 104 weeks (47% incidence of renal adenoma). Tests for bacterial mutagenicity were mostly negative but induction of chromosomal aberrations and aneuploidy was prominent.

9. Hydroquinone is known to cause depigmentation to skin but such effect has not been reported from the use of ointments containing *Majoranae herba*.
10. *Majoranae aetheroleum* has a status as “Generally Recognised As Safe” in the USA.
11. A worst case calculation for the product containing the highest concentration of *Majoranae herba* (10%) shows that a person weighing 65 kg can get 1 mg hydroquinone from eating 1.5 kg of meat corresponding to 0.015 mg/kg bw. (Cow weighing 200 kg corresponds to 100 kg edible meat. The dose is 2 times 50 g of the product for two days giving 20 g *Majoranae herba* corresponding to 0.2 g hydroquinone) This is a single dose which is 0.0006 times the smallest dose (25 mg/kg bw) causing tumours in rats when given 5 days a week for 103 weeks and producing tumours with an incidence of 7%.

For the intake of milk the calculated intake is higher. It is assumed that a cow gets 2 times 50 g of the product per day corresponding to 10 g *Majoranae herba* and to 0.1 g hydroquinone. If the milk production is 10 l then the daily consumption of 1.5 l corresponds to 15 mg hydroquinone (0.231 mg/kg bw for a person weighing 65 kg) which is 0.0092 times the lowest tumourinducing dose in rats at long-term exposure.

12. The use *Majoranae herba* 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 in Annex II to Council Regulation (EEC) No. 2377/90 and in particular that:

- *Majoranae herba* is widely used as a spice in human food,
- *Majoranae herba* 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 *Majoranae herba* and recommends its inclusion in Annex II to Council Regulation (EEC) No. 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
<i>Majoranae herba</i>	All food producing species	