



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CINCHONAE CORTEX

SUMMARY REPORT

1. *Cinchonae cortex* is the dried bark of *Cinchona pubescens* Vahl. (synonym: *Cinchona succirubra* Pavon ex Klotzsch). Also the bark of other species of *Cinchona* such as *Cinchona calisaya* Wedd, *Cinchona ledgeriana* Moens ex Trim. and *Cinchona officinalis* are used industrially for production of the alkaloid quinine. Some pharmacopoeias define also these barks as *Cinchonae cortex*.

The bark contains about 34 different quinoline alkaloids (total content 5 to 15%; the German pharmacopoeia DAB 10 requires at least 6%) of which the stereoisomeric pairs quinine-quinidine and cinchonine-cinchonidine constitute the main part. Only the pair quinine/quinidine is used in medicine. The quinine content is variable (2 to 9%). Quinidine is present at a concentration of approximately 1%. Tannins (8%) of the catechin type and bitter triterpenic glycosides are also present.

2. In veterinary medicine *Cinchonae cortex* is used in a preparation containing also *Rhei radix*, *Anisi stellati fructus*, *Torula* yeast, calcium hydroxide, calcium carbonate, magnesium oxide, cobalt sulphate heptahydrate and, as excipients, sodium lauryl sulphate and sucrose. The concentration of *Cinchonae cortex* in the preparation is 2.88%. The indications for use are various gastric complaints including forestomach atony, acute indigestion with ruminal atony and gastric catarrh. The preparation is intended to be used for cattle, sheep and goats in doses corresponding to 20 g of *Cinchonae cortex* to cattle weighing more than 200 kg and 5 g to sheep and goats (up to 50 kg bw).

In human medicine *Cinchonae cortex* is used as a bitter stomachic and - traditionally - for treatment of malaria and common flu at individual doses of 1 g and a daily dose of 3 g. The pure alkaloids quinine and quinidine are important drugs for treatment of malaria and cardiac arrhythmia respectively. The therapeutic oral dose of quinine is 600 mg 3 times per day. For quinidine the daily therapeutic oral dose is 0.8 to 2.0 g.

Quinine is used as a bitter flavouring in soft drinks (tonic water) at a concentration of about 70 mg/litre. *Cinchonae cortex* is also used for the preparation of bitter liqueurs and aperitifs.

3. The bitter taste of *Cinchonae cortex* stimulates the appetite and favours salivation and secretion of gastric juices. Quinine exerts its antimalarial activity by interference with synthesis of DNA in the merozoite phase of protozoa of the genus *Plasmodium*. Also quinidine, cinchonine and cinchonidine have antimalarial properties but these alkaloids are not as effective as quinine. The anti-arrhythmic effect of quinidine is due to a direct interference with the electrophysiological properties of the cardiac cells, which causes rapid sodium influx and a decrease of the atrial and intraventricular conduction velocity.
4. No information was provided on pharmacokinetics.

5. No reports were provided on acute toxicity or on repeated dose toxicity. *Cinchonae cortex* is contraindicated in pregnancy and in cases of gastric or intestinal ulcer. Overdosage (more than 3 g) or long-term administration of quinine can cause nausea, summer cholera, headache, fall of body temperature, intravascular haemolysis, cardiac arrhythmia, buzzing in the ears and hearing and visual disorders. A single dose of 2 to 8 g of quinine is reported to be fatal to an adult.
6. No information was provided on reproductive toxicity, teratogenicity, mutagenicity or cancerogenicity.
7. Quinine and quinidine can cause sensibilisation (eczema, itching). Even with therapeutic doses an enhanced pseudohaemophilia can occur through the triggering of a thrombocytopenia.
8. No information on antimicrobial activity was provided.
9. No information on residues was provided.

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:

- *Cinchonae cortex* is expected to be used in a small number of individual animals only, for infrequent or non-regular treatments,
- the animals treated with *Cinchonae cortex* are unlikely to be sent for slaughter during or immediately after treatment,
- *Cinchonae cortex* is used as a flavouring for bitter liqueurs and aperitifs and its main active constituent quinine is contained as a flavouring in soft drinks;

the Committee for Veterinary Medicinal Products concludes that there is no need to establish an MRL for *Cinchonae cortex* 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>Cinchonae cortex</i> , standardised extracts and preparations thereof	All food producing species	