



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

SILYBUM MARIANUM

SUMMARY REPORT

1. *Silybum marianum*, (synonyms: *Carduus marianus*, Milk thistle) is a plant of the family *Asteraceae* distributed in Southern Europe (Mediterranean). In veterinary homeopathy *Silybum marianum* is used as the mother tincture prepared by ethanolic extraction of the dried seeds of *Silybum marianum* according to homeopathic pharmacopoeias, and dilutions thereof. Major active constituents of *Silybum marianum* are flavonol-lignanes collectively referred to as silymarin (minimally 1% calculated as silibinin). Silymarin is a mixture of approximately 50% silibinin, 25% silychristin and 25% silydianin. Further, isosilybin, taxifoline, quercetin, dehydrodiconiferyl alcohol, silymonin, silandrin, 3-deoxy flavanones, β -sitosterol and apigenin have been identified. Other constituents are proteins and fatty oils (20 to 30%).
2. *Silybum marianum* is intended for use in all food-producing animals. The use follows the principles of homeopathic therapy where animals are diagnosed on basis of the individual pattern of clinical signs. The recommended maximum parenteral dose is 10 ml/animal. Treatment may be repeated but a fixed dose schedule is not common in homeopathy.

Silybum marianum is also used in human homeopathy as the mother tincture as well as in lower concentrations. *Silybum marianum* and silibinin, a major constituent thereof, are used in phytotherapy for oral treatment of toxic liver damage and for supportive therapy in chronic inflammatory liver diseases and in liver cirrhosis. Silymarin and its main isomer silibinin have been shown to possess antioxidant properties thus preventing lipid peroxidation and membrane destruction in cells of the liver. In addition, protein biosynthesis and cell regeneration are reported to be accelerated. The daily oral dose is normally 1 to 5 g but can be higher. Recommended oral doses of the constituent silymarin are 200 to 400 mg.

The fruit is used as herbal tea and therefore considered as foodstuff.

3. There are no reports on acute intoxications of humans or other significant effects of *Silybum marianum* described in literature. A dose of 20 g/kg bw has been reported to be tolerated by mice.
4. In a preliminary risk evaluation procedure by the Committee for Veterinary Medicinal Products (CVMP) considering all defended old substances used in veterinary homeopathy in concentrations greater than 1:10 000, the use of *Silybum marianum* and its individual constituents was considered as not giving rise to specific health concern. Further information made available and extensive search of published literature did not provide any further evidence for pharmacological or toxicological properties of *Silybum marianum* alerting to specific health risks which may result from residues in food producing animals following the intended uses. Special emphasis was put on identification of any suspicion pointing to genotoxicity or other potential of serious health effects of plant constituents.

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:

- *Silybum marianum* is used in a small number of individual animals and for non-regular treatments only,
- animals are unlikely to be sent for slaughter during or immediately after treatment,
- the substance and constituents thereof do not give rise to specific consumer health concern which may result from the use in veterinary homeopathy;

the Committee for Veterinary Medicinal Products concludes that there is no need to establish an MRL for any plant constituents following homeopathic use of *Silybum marianum* 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>Silybum marianum</i>	All food producing species	For use in homeopathic veterinary medicinal products prepared according to homeopathic pharmacopoeias at concentrations corresponding to the mother tincture and dilutions thereof only