The European Agency for the Evaluation of Medicinal Products
*Veterinary Medicines Evaluation Unit*

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# COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

## AMITRAZ (Cattle and sheep)

## SUMMARY REPORT (2)

1. Amitraz is a formamidine acaricide and insecticide used on top fruit, cotton and hops, and as veterinary medicine for the treatment of ectoparasites in pigs, cattle, sheep, goats and dogs. Amitraz should be applied topically, as a spray for cattle (0.25 g/l; 5-10 l/cow) and goats (0.5 g/l), and as a dip for sheep (0.5 g/l). If necessary, treatment can be repeated.

2. Amitraz has been previously assessed for pigs. A final ADI of 0.003 mg/kg was established, based on a NOEL of 0.25 mg/kg bw/day from a 2-year dog study, using a safety factor of 100. This figure was rounded in accordance with the ADI established by the WHO/FAO Joint Meeting on Pesticide Residues (1984, 1990) based on the same toxicity data. For pig tissues final MRLs of 200 µg/kg for liver and kidney and 400 µg/kg for skin + fat were established, based on the sum of amitraz and all metabolites containing the 2,4-dimethylaniline (2,4-DMA) moiety, expressed as amitraz.

   Pending the provision of fully validated routine analytical methods, and, if relevant, additional residue data for the establishment of MRLs for ovine and caprine milk and caprine tissues, amitraz is currently entered in annex III to Council Regulation (EEC) No 2377/90 as follows:

| Pharmacologically active substance(s) | Marker residue | Animal species | MRLs | Target tissues | Other provisions |
|---|---|---|---|---|---|
| Amitraz | Sum of amitraz and all metabolites containing the 2,4-DMA moiety, expressed as amitraz | Bovine | 200 µg/kg | Liver, kidney, fat | Provisional MRLs expire on 1.7.98 |
| | | | 10 µg/kg | Milk | |
| | | Ovine | 400 µg/kg | Fat | |
| | | | 200 µg/kg | Liver, kidney | |

3. In calves, after repeated spraying with 0.025% amitraz (twice, with an interval of 7 days) no residues (expressed as amitraz equivalents) above 50 µg/kg could be detected in muscle and fat at day 1, 3, 7 and 14 after treatment. In liver and kidney residues could be detected only at day 1 and 3 (respectively 90 and 150 µg/kg at day 1, and 70 and 90 µg/kg at day 3). Residues in milk of dairy cows after repeated spraying with 0.025% amitraz (twice, with an interval of 7 days) were highest at 7 hours after treatment (6 to 24 µg/l). All milk samples were below 10 µg/l at 48 hours after treatment, and reached 2 µg/l within 72 to 96 hours.

4. In sheep, residues (expressed as µg equivalents amitraz/kg) can be found in all tissues after single dip treatment with 0.05% amitraz. Highest levels were found in back fat (260 to 270 µg/kg at days 1, 3 and 5, and 120 µg/kg at day 7) and kidney (270 µg/kg at day 1, 90 and 70 µg/kg at days 5 and 7). Lower levels were found in omental fat (80 to 100 µg/kg at all time points), liver (130 µg/kg at day 1, and 40 µg/kg at days 5 and 7) and muscle (lower than 50 µg/kg at all time points).

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5. In a new tissue residue study, sheep were dipped twice with 0.05% amitraz with an interval of 14 days. Compared to the single treatment, repeated administration resulted in the same tissue distribution, but higher residue concentrations (expressed as µg equivalents amitraz/kg). Highest levels were found in subcutaneous fat (600 µg/kg at days 1 and 3, declining to 300 µg/kg at day 14 and at or below 20 µg/kg thereafter) and in kidney (500 µg/kg at day 1, 200 µg/kg at day 7, declining at or below 20 µg/kg at day 28). In liver, residues were lower: 300 µg/kg at day 1, 100 µg/kg at day 7 and at 20 µg/kg or below at day 28. Residues in muscle were lowest (lower than 100 µg/kg at all time points).

6. After a single dip treatment in 0.05% amitraz, residues in sheep milk (expressed as µg/l amitraz) showed a fast decline from 84 µg/l at day 1, 34 µg/l at day 2, lower than 24 µg/l at day 3, to less than 20 µg/l at later time points.

7. In line with the final MRLs for pig tissues and the EU MRLs for amitraz for food products of plant origin, the marker residue for amitraz for food commodities of animal origin is defined as "sum of amitraz and all metabolites containing the 2,4-DMA moiety, expressed as amitraz".

8. Fully validated routine analytical GC methods (with nitrogen selective detection) are available for the determination of residues of amitraz and its metabolites in tissues and milk from cattle and sheep. These methods are based on hydrolysis of amitraz and all its derivatives containing the 2,4-DMA moiety to 2,4-DMA, and the results can be expressed as amitraz. For both species, the limits of quantification are 10 µg/kg in milk and 50 µg/kg in tissues, except for sheep fat (20 µg/kg).

9. No residue data and no routine analytical methods were provided for goats, including lactating goats.

**Conclusions and recommendation**

Having considered that:

- a toxicological ADI for amitraz has been set at 0.003 mg/kg/bw (0.180 mg/person),
- 70% of the ADI is already occupied by consumption of food commodities of plant origin, leaving only 30% of the ADI for products of animal origin,
- validated routine analytical methods are available to detect residues of amitraz in tissues and milk of bovine and ovine species,
- the concentration of residues in muscle was very low, therefore no muscle MRL was considered necessary,
- no MRLs can be set for goats including lactating goats, as no residue data and no routine analytical methods were provided;

the Committee recommends the inclusion of amitraz in Annex I to Council Regulation (EEC) No 2377/90 for bovine and ovine species in accordance with the following table:

| Pharmacologically active substance(s) | Marker residue | Animal species | MRLs | Target tissues | Other provisions |
|---|---|---|---|---|---|
| Amitraz | Sum of amitraz and all metabolites containing the 2,4-DMA moiety, expressed as amitraz | Bovine | 200 µg/kg | Fat | |
| | | | 200 µg/kg | Liver | |
| | | | 200 µg/kg | Kidney | |
| | | | 10 µg/kg | Milk | |
| | | Ovine | 400 µg/kg | Fat | |
| | | | 100 µg/kg | Liver | |
| | | | 200 µg/kg | Kidney | |
| | | | 10 µg/kg | Milk | |

With these MRLs, the total theoretical daily intake, taking into account both the veterinary use (including bees) and the pesticidal use of amitraz, will result in 103% of the ADI.