



COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CARAZOLOL (2)

SUMMARY REPORT

1. Carazolol is a non-specific β -adrenergic receptor blocking agent which is used in pigs to prevent stress and death during transport.
2. On the basis of data available, provisional MRLs were established for porcine liver, kidney, muscle and fat as shown below:

Liver	30 $\mu\text{g}/\text{kg}$;
Kidney	30 $\mu\text{g}/\text{kg}$;
Muscle	5 $\mu\text{g}/\text{kg}$;
Fat	5 $\mu\text{g}/\text{kg}$.

There is a validated method of analysis using HPLC with a limit of quantification of 0.3 $\mu\text{g}/\text{kg}$.

3. The provisional MRLs were based on a pharmacological NOEL of 20 $\mu\text{g}/\text{kg}$ bw determined in the rabbit. This led to a temporary ADI of 0.1 $\mu\text{g}/\text{kg}$ bw using a safety factor of 200. Further information was required concerning the pharmacological NOEL in humans.
4. These data have now been considered. Studies of healthy subjects on the effects of a single dose of carazolol on cardiac function resulted in an extrapolated NOEL of 10 $\mu\text{g}/\text{kg}$ bw. In humans with either chronic bronchitis or asthma, a single dose of 0.1 or 0.7 mg/person resulted in reductions in vital capacity and forced expiratory volume. From the results, an overall NOEL of 0.5 $\mu\text{g}/\text{kg}$ bw was determined.
5. Humans with chronic bronchitis or asthma are highly sensitive to the effects of carazolol, and this group forms a substantial part of the general population. However, the previous temporary ADI of 0-0.1 $\mu\text{g}/\text{kg}$ bw provides a sufficient safety margin for both healthy subjects and for subjects suffering from chronic bronchitis or asthma. An ADI of 0-0.1 $\mu\text{g}/\text{kg}$ bw/day was therefore confirmed.
6. New residues data were also provided for pigs, after intramuscular injection. Animals were slaughtered in groups of 4 at 2, 12, 18 and 24 hours after administration. Residues at 2 hours were in the range of 2-10 $\mu\text{g}/\text{kg}$ in muscle, kidney, fat and skin but were high (56 $\mu\text{g}/\text{kg}$) at the injection site. Residues in muscle and fat were at the limit of detection (0.2 $\mu\text{g}/\text{kg}$) of the assay at 12 hours and all samples were below this limit at 24 hours.
7. On the basis of the ADI and the residues studies, MRLs were established in pigs as follows:

Muscle	5 $\mu\text{g}/\text{kg}$;
Liver	25 $\mu\text{g}/\text{kg}$,
Kidney	25 $\mu\text{g}/\text{kg}$;
Fat+skin	5 $\mu\text{g}/\text{kg}$.

Parent carazolol is the marker residue.

8. Residues of carazolol at the injection site may result in an intake which exceeds the ADI. Therefore, unless appropriate measures can be taken in order to ensure that injection site is not offered for human consumption, a withdrawal period for carazolol preparations must be established, which excludes the use of such preparations during the transport of animals to slaughter.