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

EMEA/MRL/062/96-FINAL

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

PANCREATIN

SUMMARY REPORT

Name of the substance:

Pancreatin

Indication for use:

Local (topical) treatment of panaritium, sole ulcer, treatment of slow healing necrotic wounds, vestibular wounds, abscesses, fistulas, local treatment of warts, haematomas, saddle sore and decubitat sore in combination with papain, trypsin, chymotrypsin, vitamin A palmitate and alfa-tocopherolacetate.

Pharmacological activity:

Pancreatin is an extract from pancreas of pigs and cattle and contains enzymes with protease activity (trypsin, chymotrypsin, carboxipeptidases) as well as amylase, lipase and other enzymatic activities.

Pancreatin hydrolyses fats to glycerol and fatty acids, breaks down proteins into peptides, proteoses and derived substances, and converts starch into dextrins and sugars.

Pharmacokinetics:

Based on studies on rabbits, guinea pigs and rats, after oral administration of enzymes labelled with ^{3}H or ^{125}I, 10-70% of radioactivity was absorbed. Non-absorbed part was either digested or eliminated in faeces. In serum about 17% of these hydrolytic enzymes were bound to antiproteolytic macromolecules (α_1-antitrypsin, α_1-macroglobulin). These complexes were rapidly eliminated. A part of orally administered enzymes undergoes enteropancreatic circulation as do the endogenous enzymes. The half-life of radioactivity in serum, lung and liver was 3.8, 2.3 and 6.3 h, respectively.

Toxicological profile:

After single oral doses up to 4000 mg of pancreatin in combination with other enzymes per kg to mice, rats, and dogs, no mortality was observed. After intraperitoneal administration LD_{50} was 36 mg of ingredients/kg in guinea pigs and 730 mg/kg in rats and mice. Daily dose of 1000 mg of ingredients/kg orally for 4 weeks caused no changes in rats. The six-month-study in rats and mini-pigs revealed no toxicological changes.

Pregnant rats and rabbits were treated orally for 10 and 12-15 days, respectively. No pathological changes were seen in fertility, number of uterine implantations or in pathological examination after administration of pancreatin in combination with other enzymes at daily doses under 4000 mg/kg. At daily dosage level of 4000 mg/kg to pregnant animals delayed ossification of skeleton was seen in foetuses (calvaria, terminal phalanges, breastbones, rips).

No mutagenic activity was detected when Ames, Saccharomyces-D7-cells, DNA repair system, EUE-cell and S9-supernatants for liver microsomal fraction tests were used.

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Conclusions and recommendation :

Having considered the criteria laid down by the Committee for the inclusion of substances into Annex II of Council Regulation (EEC) No 2377/90 and in particular that:

- is a mixture of pancreatic enzymes and therefore normal constituents of the body;
- has low toxicity;
- is rapidly eliminated;
- is also given orally for humans in conditions of pancreatic insufficiency;
- is intended for use in a small number of individual animals;
- the residues of pancreatin in animal products are not likely to be of toxicological concern to humans.

The Committee considers that there is no need to establish an MRL for pancreatin and recommends its inclusion into Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal species	Other provisions
Pancreatin	All mammalian food producing species	For topical use only