The European Agency for the Evaluation of Medicinal Products

EMEA/MRL/036/95

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

PAPAIN

SUMMARY REPORT

1. Papain is a cysteinproteinase isolated from Carica papaya L. and constituted of one folded polypeptide chain which contains 212 amino acids.

2. Papain is frequently administered in cattle, horses, goats, sheep, sows, dogs and cats by parenteral, oral and intramammary routes in combination with other enzymes (chymotrypsin, trypsin and/or pancreatin).

   It is a proteolytic agent used for the cleaning of wounds, ulcers, abscesses, empyemas, sinuses and fistulas.

3. After oral administration, papain is absorbed intestinally and keeps its biological active structure. It interacts with the endogenous occurring antiproteinases (α2-Macroglobulin) and forms a α2-Macroglobulin-proteinase-complex which is rapidly degraded by the cells of the mononuclear-phagocytic system and eliminated.

   In the healthy man, these complexes are eliminated from the circulation with an half-time about 5 to 10 minutes.

4. The oral administration of Papain in combination with other enzymes to mice, rats and dogs induced no mortality. So, the median lethal doses could not be determined in any mammalian species.

   No aggravating toxicologic appearances or pathological findings were reported after the single, repeated and long-term local applications of Papain in combination with other enzymes at doses up to 10 g/kg b.w.

5. Pregnant rats or rabbits were treated orally for 10 or 12-15 days, respectively. No disorders of the fertility, of numbers of uterine implantations, no anatomo-pathological variations have been reported after doses of 0.140 g up to 4 g/kg b.w. After daily administration at 4 g/kg b.w in pregnant rats for 10 days, the foetuses skeleton ossifications (calvaria, terminal phalanges and breastbones) were delayed.

6. Papain did not give positive results in the *in vitro* mutagenic tests reported (Ames, Saccharomyces-D7-cells, DNA repair test system and EUE-cells test).

7. In 1971, the JECFA established no limitation for the Acceptable Daily Intake (Report NMRS 50/TRS 488-JECFA 15/11).

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

- Papain is a proteolytic enzyme present naturally in the diet compounds,
- The α2-Macroglobulin-Papain-complexes are eliminated rapidly from the circulation.

The Committee for Veterinary Medicinal Products concluded that maximum residue limits for tissues are not necessary to ensure consumer safety and recomments the inclusion of Papain in Annex II of Council Regulation (EEC) No 2377/90. as indicated in the following table:

Pharmacological active substance(s)	Animal species	Other provisions
Papain	All food producing species	

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