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

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COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

CORTICOTROPHIN

SUMMARY REPORT

1. Corticotrophin (ACTH, adrenocorticotrophic hormone, CAS 9002-60-2) is a naturally occuring polypeptide hormone secreted by the anterior lobe of pituitary gland. It is also produced synthetically. Corticotrophin is used in human medicine to test the functioning of the adrenal cortex. In veterinary medicine both short-acting and depot preparations for parenteral use in horse, cattle, sheep, goat and swine are available. It is used as a depot injection in metabolic disorders, intoxications, allergies and inflammatory disorders of the locomotor systems as well as after long-term glucocorticoid treatment for stimulation of the adrenal glands (10-100 IU/animal intramuscularly every 2-3 days; for cattle the dose is 200-600 IU/animal intramuscularly or subcutaneously on the first day and 200-300 IU/animal/every other day thereafter).

2. Corticotrophin is a polypeptide of 39 amino acids derived from a precursor polypeptide (pro-opiomelanocortin). It is secreted from the hypophysis in response to corticotrophin-releasing hormone in pulses about once an hour. Corticotrophin binds to a high-affinity receptor that is a member of the receptors coupled to G proteins. It is a trophic hormone and stimulates immediate secretion of cortisol and other adrenal steroids. The corticotrophins from various species do not differ structurally very much from each other. Twenty milligrams of corticotrophin are released daily from the human hypophysis as several pulses.

3. Corticotrophin is not active when administered by mouth due to digestion in the gastrointestinal tract neither when applied topically. In humans, the plasma half-life is less than 15 minutes when given intravenously (dose not given). Long-acting preparations with 12 to 24 hours effect have been introduced. The daily dose for human is 40-80 IU of depot preparation every 24-72 hours intramuscularly or subcutaneously.

4. There are no data available on pharmacokinetics of corticotrophin in animals. Instead, the effect of corticotrophin on plasma cortisol levels was measured using corticotrophin long-acting depot formulation (200 IU/horse intramuscularly, 8 horses). Plasma cortisol levels increased during the first 3 hours after the injection. From 3 to 6 hours the cortisol level was stable but declined from 6 to 12 hours to a value near the initial level. Between 12 to 24 hours plasma cortisol levels were half of the initial level and returned to normal by 48 hours.

5. No toxicological data have been provided other than adverse effects related to use in humans. These effects include allergic reactions and central nervous signs. No information is given about the frequency of these effects in relation to the doses used in humans.

6. The lack of toxicological studies is not considered to result in a risk to the consumers because corticotrophin is neither active via the oral route due to digestion in the gastrointestinal tract nor when applied topically. There is no need to establish an ADI for corticotrophin.

7. Residue data were not considered necessary because of the rapid elimination of the substance and any residues ingested being inactive when administered by mouth.

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Conclusions and recommendation

Having considered that:

- corticotrophin is used only for individual animals;
- corticotrophin is not active via the oral route;
- corticotrophin is rapidly excreted in target species;

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

Pharmacologically active substance(s)	Animal species	Other provisions
Corticotrophin	All food producing species	