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Committee for Veterinary Medicinal Products (CVMP)

Recombinant equine Chorionic Gonadotropin (reCG): Summary of assessment

Request on whether a full MRL evaluation is required in accordance with Commission regulation (EU) 2018/782

I Background

Syn Vet-Pharma Ireland Limited submitted, on 19 December 2025, an application for the evaluation of reCG (recombinant equine chorionic gonadotropin) to determine whether a full MRL application is required, based on Annex I of Commission Regulation (EU) 2018/782, specifically Sections I.6 and I.7 thereof.

Where an MRL evaluation is not required, the substance is included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 pursuant to Section I.7 of Annex I of Commission Regulation (EU) 2018/782.

The Committee for Veterinary Medicinal Products (CVMP) appointed Andrea Golombiewski as rapporteur during its meeting of June 2025.

II Summary of assessment

Recombinant equine chorionic gonadotropin (reCG) is a macromolecular protein with a MW higher than 103 Dalton. Its glycosylation is not precisely defined. It has a complex composition as the secondary and tertiary structures are required for biological function. Finally, its biological activity is determined by biological testing. Based on these characteristics, reCG can be considered a chemical-unlike biological substance in the sense of Section I.6 of Annex I of Commission Regulation (EU) 2018/782.

In accordance with Sections I.6 and I.7 of Annex I of Commission Regulation (EU) 2018/782, biological substances other than those identified in Article 1(2)(a) of Regulation (EC) No 470/2009 that are chemical-unlike shall be evaluated on a case-by-case basis and a report describing the scientific basis for the request on whether a full MRL evaluation is required or not shall contain information as set forth in the following sections A to E.

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A. Nature of the biological substance (e.g. cell, tissue, live or killed organism) and a comparison with similar biological substances to which consumers are known to be routinely exposed

The reCG can be considered a chemical-unlike biological. It is a single-chain construct containing the identical amino acid sequences of the α- and β-subunits of natural eCG, but covalently linked and modified by additional O-glycosylation sites. As a result, some differences in glycosylation pattern are expected due to both the added sites and the expression system used. Although the exact structural details are unknown, the tertiary structure is assumed to be comparable to that of natural eCG to ensure efficacy.

Since consumers may be exposed to natural eCG via edible tissue and milk of pregnant horses, it is considered a component of the human diet.

B. Description of the mechanism of action underlying the substance's therapeutic effect and, if available, information on its potency

The eCG/reCG is a gonadotropin of equine origin and functions as a LH (luteinizing hormone) in horses and binds to the equine corpus luteum during early gestation. Its veterinary use is based on the fact that it interacts with both LH and FSH (follicle-stimulating hormone) receptors of various domestic species. The biological basis for the dual LH/FSH activity is considered to be the result of promiscuity of the mammalian FSH receptors to eCG/reCG, while the species-specific CG is not a ligand for FSH receptors. In mammalian species, FSH and LH are essential regulators of ovarian and testicular function.

C. Fate of the substance in the treated animal (i.e. is it bioavailable, are residues expected in food commodities)

No residue data are provided for reCG, and similarly no residue depletion studies in treated animals exist for eCG.

Furthermore, no NO(A)EL was established in the MRL assessment of eCG (CVMP Summary report Pregnant mare serum gonadotrophin (PMSG)) which would have enabled derivation of an ADI. Residue depletion studies were not requested during the MRL assessment of eCG, since residues were considered as orally inactive in humans.

While it appears likely that modification of the glycosylation pattern and the covalent bond between the α- and β-subunit would have some effect on the substance's pharmacokinetics, it can be concluded that the monomeric reCG would be as inactive as eCG in humans when consumed via food obtained from treated animals.

D. Any activity that the substance may have in the human gut (are the residues inactive or do they produce local effects)

Like eCG, reCG has LH/FSH specific activity by binding surface receptors on specific target cells that are involved in reproduction. No activity in the human gut or microbiota effects are expected.

E. Systemic availability of residues following ingestion of residues by consumers, along with a worst-case consumer exposure estimate

Although there is no data on consumer exposure to reCG through food obtained from treated animals, it is reasonable to assume that, for a recombinant eCG analogue designed to have a similar biological effect, the substance would also be deactivated in the human gastrointestinal tract, resulting in negligible oral bioavailability. On the one hand, this is due to the loss of its tertiary structure, which is crucial for the

molecule's biological function; on the other hand, it is the result of rapid enzymatic digestion. Furthermore, the size of the monomeric molecule would prevent ready transmucosal absorption during its passage to the stomach.

The entry for pregnant mare serum gonadotrophin in Table 1 of the Annex to Regulation (EU) No 37/2010 applies to all food producing species while the current application was submitted specifically for cattle, sheep and pigs. Noting that, from a consumer safety perspective, reCG is not expected to be different from eCG, and in line with Article 5 of Regulation (EC) No 470/2009, the CVMP considers that it is appropriate to extrapolate the recommended MRL status for reCG to all food producing species.

Conclusions

Having considered that:

- recombinant equine chorionic gonadotropin is a biological substance,
- the substance as presented by the applicant is similar to the naturally occurring, endogenous equine chorionic gonadotropin, and expected to follow the same degradation process in the human digestive tract, resulting in negligible systemic bioavailability,
- the reCG is therefore expected not to be bioactive in humans when orally ingested via food obtained from treated animals,
- no relevant local or systemic effects are anticipated after oral ingestion of food commodities derived from treated animals,
- intake of potential treatment-related reCG residues is not anticipated to significantly increase daily protein or carbohydrate consumption,
- while the current application was made specifically for cattle, sheep and pigs, the conclusions can be extrapolated to all food producing species,

the Committee concludes that no further MRL assessment is necessary for reCG (recombinant equine chorionic gonadotropin) and that the substance can be included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 with a "No MRL required" classification in accordance with Section I.7 of Annex I of Commission Regulation (EU) 2018/782 as follows:

Pharmaco-logically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Recombinant equine chorionic gonadotropin (reCG, recombinant analogues of pregnant mare serum gonadotrophin) – chemical-unlike biological substance	NOT APPLICABLE	All food producing species	No MRL required	NOT APPLICABLE	NO ENTRY	NO ENTRY