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Veterinary Medicines Division

## Committee for Veterinary Medicinal Products (CVMP)

# CVMP assessment report for a grouped variation requiring assessment for Eluracat (EMEA/V/C/005948/VRA/0002/G)

INN: Capromorelin tartrate

**Assessment report as adopted by the CVMP with all information of a commercially confidential nature deleted.**

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# 1. Introduction

## *1.1. Submission of the variation application*

In accordance with Article 64 of Regulation (EU) 2019/6, the marketing authorisation holder, Elanco GmbH (the applicant), submitted to the European Medicines Agency (the Agency) on 26 July 2024 an application for a group of variations requiring assessment for Eluracat.

## *1.2. Scope of the variation*

| **Variations requested** | |
|---|---|
| G.I.19 | Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet to implement the outcome of the MAH's signal management process according to Article 81(2) of Regulation (EU) 2019/6 |
| G.I.4 | Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data. |

These variations are to implement the outcome of the MAH's signal management process and to move the warning for use of the product in cats with hypersomatotropism (acromegaly) from special precautions section to contraindications.

As per standard procedure at EMA the specific details of the G.I.19 VRA have been redacted.

## *1.3. Changes to the dossier held by the European Medicines Agency*

This application relates to the following sections of the current dossier held by the Agency:

Part 1.

## *1.4. Scientific advice*

Not applicable.

## *1.5. Limited market status*

Not applicable.

# 2. Scientific Overview

Eluracat contains the active substance capromorelin. The product is indicated for body weight gain in cats experiencing poor appetite or unintended weight loss resulting from chronic medical conditions. Eluracat was authorised in the EU on 29 June 2023.

Two variations have been submitted by the applicant within the current procedure:

- VRA G.I.19 – the aim is to update the product information to implement the outcome of the MAH's signal management process according to Article 81(2) of Regulation (EU) 2019/6
- VRA G.I.4 – the aim is to move the warning on the use of the product in cats with

hypersomatotropism (acromegaly) from special precautions (section 3.5 of the SPC and section 6 of the PL) to contraindications (section 3.3 of the SPC and section 5 of the PL).

## *2.1. VRA G.I.19 – Update of the adverse events sections of the product information*

On 21 June 2024, the MAH submitted two adverse event signals (bradycardia and hypotension) for Eluracat 20 mg/ml oral solution for cats in the IRIS system. Additionally, the applicant submitted a Signal Assessment Report in order to support the amendment of the product information to include those VeDDRA PTs.

Based on the data presented, the CVMP agrees with the applicant's proposal to include 'Bradycardia' and 'Hypotension' as new adverse events in the product information (section 3.6 of the SPC and section 7 of the PL), with the frequency 'Very rare'.

## *2.2. VRA G.I.4 – Relocation of the warning on the use of the product in cats with hypersomatotropism (acromegaly)*

Capromorelin is a selective ghrelin receptor agonist. Capromorelin binds to ghrelin receptors in the hypothalamus to stimulate appetite and in the pituitary to stimulate secretion of growth hormone (GH). Increased GH stimulates release of insulin like growth factor 1 (IGF-1) from the liver, which in turn stimulates weight gain.

Acromegaly was previously thought to be rare and therefore usually featured only infrequently or sparsely during the basic training of veterinarians. This has changed very recently in light of studies revealing that its prevalence amongst diabetic cats is higher than expected. Since that time, screening diabetic cats for acromegaly or hypersomatotropism has increased and it has become evident that it is a rather common cause for diabetic cats to become diabetic in the first place, as well as being difficult to control once diabetes mellitus has occurred. Prevalence of acromegaly amongst diabetic cats in North America and the UK was found to be around 1 in 4 diabetic cats seen in primary practice. The disease is therefore likely currently underdiagnosed. The prevalence of hypersomatotropism amongst non-diabetic cats is currently unknown although these cats would be expected to become diabetic in the long-run[1].

In section 3.5 "Special precautions for use - Special precautions for safe use in the target species" of the Eluracat SPC, it is stated that the use of the product in cats with diabetes mellitus has not been evaluated, and, in cases of diabetes mellitus, it is advised to use it only according to the benefit-risk assessment by the responsible veterinarian.

Currently, section 3.5 of the SPC - "Special precautions for use - Special precautions for safe use in the target species" - states that the product should be used with caution in cats with hypersomatotropism (acromegaly).

At the time of submission of the initial marketing authorisation application, it was assumed that elevations of growth hormone induced by Eluracat will be small compared to those occurring in clinical cases of acromegaly, and, therefore, deleterious effects would be negligible. Additionally, cats with acromegaly are less likely to have low body weight or poor appetite, and therefore would not commonly be the target population for Eluracat therapy.

[1] Stijn J.M. Niessen. Acromegaly in Cats. World Small Animal Veterinary Association World Congress Proceedings, 2014. https://www.vin.com/doc/?id=7054862

However, after considering the statement further, it has been concluded that many cases of acromegaly in cats cannot be optimally treated (e.g. by surgery as done in humans). Thus, to limit any further increases in growth hormone in these cats, the MAH proposes to contraindicate the use of the product in such cases.

As such, the MAH has proposed to delete the wording "*Use with caution in cats with hypersomatotropism (acromegaly)*" from section 3.5 of the SPC "Special precautions for use - Special precautions for safe use in the target species" and add the wording "*Do not use in cats with hypersomatotropism (acromegaly)*" in section 3.3 "Contraindications" of the SPC as risk minimisation measure. The same changes are proposed in the corresponding sections of the package leaflet.

Based on the information provided, the CVMP is in agreement with the MAH's proposal to amend the product information as mentioned above. It is also recommended that the applicant closely monitors the use of the product in diabetics cats, due to the potential risk of no-diagnosed acromegaly in that population.

# 3. Benefit-risk assessment of the proposed change

Eluracat is authorised for body weight gain in cats experiencing poor appetite or unintended weight loss resulting from chronic medical conditions. The product contains capromorelin as the active substance and is available as a 20 mg/ml oral solution.

The proposed grouped variation is to implement the outcome of the MAH's signal management process and to move the warning for use of the product in cats with hypersomatotropism (acromegaly) from special precautions section to contraindications.

## *3.1. Benefit assessment*

The benefits of the product remain unaffected by this variation.

## *3.2. Risk assessment*

New risks in the form of additional adverse events (bradycardia and hypotension) have been identified through routine signal management procedures performed by the MAH. Additionally, there is a potential risk with the use of the product in cats with hypersomatotropism (acromegaly).

The CVMP considers the mitigation measures (product information updates) proposed by the MAH as being proportionate and appropriate.

## Quality:

Quality remains unaffected by this variation.

## Safety:

Safety (user, environmental) remains unaffected by this variation.

*Risks for the target animal:*

Administration of capromorelin tartrate in accordance with SPC recommendations is generally well

tolerated.

The main reported adverse reactions already included in the product information include:

- Hypersalivation (very common);
- Diarrhoea, Vomiting, Anaemia, Skin lesions (on the mouth and chin), Dehydration, Lethargy (common).

Bradycardia and hypotension have additionally been observed very rarely, in post authorisation use. Specific advice to veterinarians is necessary to address this risk.

Concerns have been raised regarding the use in cats with hypersomatotropism (acromegaly). Specific advice to veterinarians is necessary to address this risk.

### *3.3. Risk management or mitigation measures*

New risks to the target animal have been identified through routine signal management procedures. Through this variation, appropriate information has been included in the product information to inform on the potential new risk of this product relevant to the target species cats and to provide advice on how to prevent or reduce these risks.

The update of the product information to add two new adverse events resulting from signal detection process (bradycardia and hypotension) and the contraindication of use of the product in cats with hypersomatotropism (acromegaly) are considered as routine risk minimisation measures.

### *3.4. Evaluation of the benefit-risk balance*

No change to the impact of the product is envisaged on the following aspects: quality, safety, user safety, environmental safety, or efficacy.

Appropriate precautionary measures have been included in the product information in relation to the impact of the product on target animal safety.

The benefit-risk balance remains unchanged.

## 4. Conclusion

Based on the original data presented on safety, the Committee for Veterinary Medicinal Products (CVMP) concluded that the application for variation to the terms of the marketing authorisation for Eluracat can be approved, since the data satisfy the requirements as set out in the legislation (Regulation (EU) 2019/6), as follows: to implement the outcome of the MAH's signal management process and to move the warning for use of the product in cats with hypersomatotropism (acromegaly) from special precautions section to contraindications.

The CVMP considers that the benefit-risk balance remains positive and, therefore, recommends the approval of the variation to the terms of the marketing authorisation for the above mentioned medicinal product.

Changes are required in the following Annexes to the Community marketing authorisation:

I and IIIB.

As a consequence of these variations, sections 3.3, 3.5 and 3.6 of the SPC are updated. The corresponding sections of the package leaflet are updated accordingly.