EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Medicinal Products and Innovation
Veterinary Medicines
Head of Unit

Brussels
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Subject: Request under Article 130(4) of Regulation 2019/6 for the opinion of the CVMP in connection with the quality defects and adverse events reported for the centrally authorised veterinary medicinal product "Kexxtone".

Dear Dr Schefferlie,

Following the increase of adverse events reported for the centrally authorised veterinary medicinal product "Kexxtone" as discussed at the CVMP meeting on 12 March 2024, the CVMP is asked to give an opinion in accordance with Article 130(4) of Regulation (EU) 2019/6 addressing the questions identified below.

Background

Shortcomings in the quality for "Kexxtone" leading to events of regurgitation of the device while still containing tablets have been identified since 2021. Such events raise the following concerns:

a) Failures in the scheduled release of the tables from the device to the treated animals raise doubts as to whether the treated animals receive the right dose; sub-optimal dosing could -in turn- raise questions as to the efficacy of the veterinary medicinal product. Reports of lack of efficacy have been received under pharmacovigilance.

b) Regurgitation of devices that still contain capsules can lead to the exposure of other animal species and the environment to the veterinary medicinal product. The deaths of [redacted] dogs have been reported in 2023 as being linked to the exposure of the dogs to regurgitated devices of Kexxtone.

The marketing authorisation holder of Kexxtone has claimed that the problems of quality are limited to batches manufactured between July to November 2021 and has indicated that it has withheld [redacted] batches from that period. It is unclear how many batches manufactured during that period have been released, as well as the reason why the marketing authorisation holder decided to only block some of batches manufactured

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during that period in spite of the fact that it is claimed that all of the batches met the specifications set forth in the marketing authorisation.

Further, the marketing authorisation holder claims to have made some adjustments to manufacturing parameters -within approved specifications/ranges- implemented as from March 2022 to address the quality defects identified. No variation application(s) to amend the manufacturing and control methods or the current specifications have been submitted by the marketing authorisation holder with a view to address the quality problems identified. It is also understood that the manufacturing and control process for Kexxtone is the same for all batches manufactured after March 2022.

Batches other than those manufactured from July to November 2021 have been involved in adverse events reported. Further, the number of adverse events reported (linked to "regurgitation", "movement of implant", "lack of efficacy" or "product defect") increased in the course of 2023 and this trend continues during the first two months of 2024.

From all the above, it does not seem plausible to conclude that adjustments in the manufacturing process introduced in March 2022 have been able to satisfactorily resolve the quality problems identified.

Questions addressed to the CVMP:

1) Does the CVMP consider that the benefit-risk balance for Kexxtone continues to be positive under the current terms of the marketing authorisation, including aspects of manufacturing and control contained in the dossier?

2) Does the CVMP consider that the batches of Kexxtone that have been released on the market pose a risk to animal health or the environment such that the benefit-risk balance for those batches can no longer be considered positive and that the marketing authorisation holder should be ordered to recall those batches?

3) Does the CVMP consider that the marketing authorisation holder should implement specific measures/actions to ensure the positive benefit-risk balance for Kexxtone? In the affirmative, please identify such measures/actions.

The CVMP is asked to provide an opinion with statement of reasons addressing the above-referred questions **by 23 April 2024** at the latest. It is noted that, in accordance with Article 130(4), the marketing authorisation holder shall be invited to provide oral or written explanations, which should be taken into consideration by CVMP when providing its opinion within the above-referred deadline.

Your sincerely,

[e-signed]

Eva Zamora Escribano

[redacted]