CVMP list of questions to be addressed in an oral explanation by the MAH for
Kexxtone 32.4 g continuous-release intraruminal device for cattle
(EU/2/12/145/001-003)

Procedure under Article 130(4) of Regulation (EU) 2019/6

Procedure number: EMEA/V/A/150

INN/active substance: monensin
With regard to the above-mentioned procedure, the MAH for Kexxtone is requested to address the following in an oral explanation:

1. The Corrective and Preventive Actions (CAPAs) proposed during the quality defect procedure

   The Corrective and Preventive Actions (CAPAs) proposed during the quality defect procedure were:
   - Modify the amount of water during the granulation process from 44 kg to a range of 41-47 kg and study the impact of increasing the upper limit. The range was not accepted during the quality defect procedure and instead a fixed amount of 47 kg was recommended to be notified via a variation. The MAH committed to assess the process control with higher amount of water.
   - Implement additional in-process controls for API pre-mill particle size, granule particle size distribution and loss on drying and submit respective variations.
   - Submit a variation to notify the already implemented change in the DNA inactivation unit, including a demonstration that this change did not contribute to the quality defect.
   - Complete the investigation regarding the introduced API surface properties changes after the fermenter purge (characterisation and physicochemical properties).
   - Add the mould number to the top of the barrel to ensure that the information is retained even if both wings are removed and submit the respective variation.

   The MAH is requested to investigate including an additional CAPA, to develop a method that can distinguish between batches of acceptable and unacceptable quality with respect to tablet payout in-vivo and adding this new test to the release specification. In the event that a suitable test is developed the appropriate variation should be submitted. If it is not possible to develop such a test, the MAH should discuss how they will demonstrate the effectiveness of the CAPAs.

   The CAPAs only relate to in-process controls and no changes are proposed to finished product release specification. It is therefore unclear how the MAH will demonstrate that the proposed CAPAs will be effective in-vivo.

2. Within the 8th PSUR, the CVMP discussed the MAH's proposal for an improvement to the intraruminal device in order to decrease the broken wings, and therefore, reduce the incidence of regurgitation, by replacing the material for a higher strain-to-break material. The MAH was requested to review the status of this possible improvement after application of this measure and to provide an update and a timetable of when it would be submitted to EMA. The MAH concluded that the change in the resin did not require a variation as the starting materials and finished product continued to meet all registered specifications. However, the MAH committed to assess the impact of this change by continuing to monitor reports of regurgitation of the bolus as part of ongoing monitoring of the safety profile of the veterinary medicinal product (VMP) in conjunction with routine signal detection processes. Apart from that, and given that regurgitated boluses with incomplete payout have been reported, the MAH is requested to provide an update on this matter.

3. In light of the currently available data including the MAH’s written responses within the quality defect procedure confirming that regurgitation of boluses with incomplete payout continues to be reported and affects batches other than those previously identified (focus period), the MAH is requested to provide an evaluation of the benefit-risk balance of this VMP, with particular attention...
to potential lack of efficacy in the target species and serious adverse events in non-target species (dogs).

It should be noted that in addition to the questions raised in this document, the CVMP may consider other available data related to the quality, safety and efficacy of the VMP concerned.