

NOTIFICATION TO THE EUROPEAN MEDICINES AGENCY OF A REFERRAL UNDER ARTICLE 82 OF REGULATION (EU) 2019/6

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This notification is a referral under Article 82 of Regulation (EU) 2019/6 to the European Medicines Agency (the 'Agency') made by Germany:

A range of veterinary medicinal products, all containing the same active substance	Veterinary medicinal products containing albendazole as a single active substance presented as oral suspension
Active substance	Albendazole
Route of administration	Oral use
Target species	Sheep
Applicant(s)/marketing authorisation holder(s)	To be identified

Detailed explanation of the matter involving Union interest:

This referral procedure concerns the doses or lower dose limits of 3.75 – 5.0 mg/kg bodyweight (bw) of veterinary medicinal products (VMPs) containing albendazole as a single active substance presented as oral suspension indicated against gastrointestinal (GIT) nematodes (*Ostertagia* spp., *Haemonchus contortus*, *Nematodirus* spp., *Chabertia ovina*, *Gaigeria* spp., *Oesophagostomum* spp., *Bunostomum* spp., *Trichostrongylus* spp.) in sheep.

Albendazole is a broad spectrum anthelmintic of the benzimidazole class. In susceptible parasites, benzimidazoles act by disrupting the intracellular microtubular transport system of parasites by binding selectively and damaging tubulin, preventing tubulin polymerization, and inhibiting microtubule formation (Plumb, 6th edition).

Veterinary medicinal products containing albendazole have been widely used for decades in cattle, sheep, goats, pigs, rabbits, birds, dogs and cats. In ruminants, and in particular in sheep, albendazole-containing VMPs are used for the treatment of GIT nematodes, lungworms, tapeworms and adult liver flukes. However, emerging benzimidazole resistance has been reported throughout Europe for GIT nematodes in sheep (Borgsteede et al., 2007, Cernanská et al., 2006, Kaplan & Vidyashankar, 2012, Scheuerle et al. 2009).

During the recent decentralised procedure ES/V/0431/001/DC submitted in accordance with Article 18 of Regulation (EU) 2019/6, it has been noticed that there are several VMPs on the market, including the reference product of the aforementioned decentralised procedure "Valbazen 1,9% Suspension zum Eingeben für Schafe", which are indicated for the treatment of GIT nematodes in sheep with doses or lower dose limits of 3.75 mg-5 mg albendazole/kg bw. In fact, a number of scientific publications suggest that doses up to 5 mg albendazole/kg bw may pose a serious risk of insufficient efficacy against GIT nematodes in sheep (Borgsteede et al., 2007, Cernanská et al., 2006, Claerebout et al. 2020, Domke et al., 2012, Höglund et al., 2022, Kowal et al., 2016, Scheuerle et al. 2009, Untersweg et al., 2021, Vineer et al., 2020, Voigt et al., 2022), and, in addition, of selecting for albendazole resistance in the context of the benzimidazole resistance already present in sheep GIT nematodes in Europe.

Moreover, Germany has noticed that the doses of albendazole-containing VMPs against GIT nematodes in sheep are disharmonised across the EU, ranging between 3.75 – 15 mg albendazole/kg bw.

For these reasons, Germany considers that a review of VMPs containing albendazole as a single active substance presented as oral suspensions against gastrointestinal (GIT) nematodes in sheep with doses or lower dose limits of 3.75 mg- 5 mg albendazole/kg bw is required to ensure the safe and effective use of those VMPs and to avoid an unnecessary risk of antiparasitic resistance development, for the environment and the consumer.

Questions to be addressed by the Agency's Committee for Veterinary Medicinal Products (CVMP):

The CVMP is requested to review the available data for veterinary medicinal products containing albendazole as a single active substance presented as oral suspension for sheep with doses or lower dose limits of 3.75 – 5.0 mg/kg bw and to provide an opinion on the following questions:

- Considering the available data, what dosage regimen (i.e. dose rate and treatment duration) of albendazole provides adequate efficacy against gastrointestinal nematodes in sheep while limiting the risk of development of resistance to albendazole?
- In case the need for a change to the dosage regimen is identified, then consideration should be given to establish an adequate withdrawal period for sheep and to assess the potential impact on the target animal safety as well as the environmental risk assessment of the concerned VMPs.

In view of the elements described above and the necessity to take action at EU level, Germany considers that it is in the interest of the Union to refer the matter to the Agency and requests that the CVMP gives its opinion under Article 83 of Regulation (EU) 2019/6 as to whether the marketing authorisations for the above-mentioned products should be maintained, varied, suspended, or revoked.

Signed [REDACTED]

Date 11-06-25

[REDACTED]

¹References:

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