Arti-Cell® Forte and RenuTend®: market recall of select product batches

Dear Animal Healthcare Professionals,

Boehringer Ingelheim Animal Health, in agreement with the European Medicines Agency and <National Competent Authority>, would like to inform you of the following:

Summary

- A horse that provided donor material for Arti-Cell® Forte and RenuTend® returned intermittently positive results for low levels of DNA associated with equine parvovirus (EqPV-H). The horse has shown no clinical signs of disease and remains healthy.
- To date, Boehringer Ingelheim has not received any reports of adverse events associated with EqPV-H in horses treated with these products.
- As a precautionary measure, Boehringer Ingelheim is pursuing a market recall of select batches of Arti-Cell® Forte and RenuTend® (see below).
- Horses treated with the affected batches should be monitored for any adverse events, including signs associated with EqPV-H for up to 13 weeks for treatment.

Background information

Arti-Cell® Forte is indicated for reduction of mild to moderate recurrent lameness associated with non-septic joint inflammation in horses. RenuTend® is indicated to improve healing of injuries of tendons and suspensory ligaments in horses. Both medicinal products contain equine allogeneic mesenchymal stem cells derived from donor horses.

The market recall relates to the following batches of Arti-Cell® Forte and RenuTend®:

Arti-Cell® Forte	**Batch #**	**Country**	**Distribution timeframe**
	F2741119	Finland, Sweden	between August 26, 2022 and December 12, 2022
	F4141133	Finland, Sweden	between December 16, 2022 and December 19, 2022
	F4127135	Finland, Sweden	between January 2, 2023 and January 13, 2023
	F3641121	Germany	between October 26, 2022 and December 20, 2022
	F4141125	Austria	between October 24, 2022 and December 14, 2022
	F4127128	France	between October 26, 2022 and January 9, 2023

RenuTend®	**Batch #**	**Country**	**Distribution timeframe**
	T41091/01	Germany	between July 8, 2022 and September 22, 2022
	T41092/01	Germany	between July 8, 2022 and October 17, 2022

	T41092/01	France	between October 10, 2022 and December 26, 2022

No impacted RenuTend® batches were distributed in Sweden, Finland or Austria.

Any unused product from these batches should be returned to Boehringer Ingelheim, and replacement products will be provided as soon as they are available.

Equine parvovirus-hepatitis virus (EqPV-H) is a newly discovered virus that has been associated with cases of hepatitis (Theiler's disease), as well as can be found in apparently healthy horses[1-6]. To learn more about the clinical signs and epidemiology of EqPV-H please contact the technical service team members as listed below.

Asymptomatic infection is most common, and it is estimated that approximately 2% of infected horses may develop clinical liver disease, ranging from mild illness to acute fulminant liver failure.

Clinical signs in affected horses may include one or more of the following[7]((AAEP Infectious Disease Guidelines: Equine Parvovirus-Hepatitis Virus (EqPV-H)): 'lethargy, anorexia, jaundice, and/or neurological signs associated with hyperammonaemic encephalopathy (altered mentation, maniacal behaviour, head pressing, blindness, staggering), discolored urine (secondary to hemolysis and/or bilirubinuria), colic, recumbency.

The prognosis for horses with acute fulminant hepatitis is guarded to poor, with a mortality rate of 50-90%, typically in first 72 hours.

Transmission can occur by administration of allogeneic biological products, most commonly tetanus antitoxin or blood/plasma transfusion[8] containing EqPV-H. Described cases generally presented 4-13 weeks after receiving the biological product[8,9].

Company contacts

If you have any of the aforementioned products to return to Boehringer Ingelheim or if you seek further information, please contact one of the following equine technical services team members:

- Dr. Ela Misuno, Sr. Global Franchise Technical Manager
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- Dr Simon Lang, Technical Manager, France
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Call for reporting

In line with standard pharmacovigilance procedure for any veterinary medicinal product, should any horse treated with Arti-Cell® Forte or RenuTend® experience any abnormal clinical or laboratory findings, please contact your Boehringer Ingelheim technical service manager.

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References:

1. Altan, E., Li, Y., Sabino-Santos Jr, G., Sawaswong, V., Barnum, S., Pusterla, N., Deng, X. and Delwart, E., 2019. Viruses in horses with neurologic and respiratory diseases. *Viruses*, *11*(10), p.942.

2. Badenhorst, M., de Heus, P., Auer, A., Tegtmeyer, B., Stang, A., Dimmel, K., Tichy, A., Kubacki, J., Bachofen, C., Steinmann, E. and Cavalleri, J.M., 2022. Active equine parvovirus-hepatitis infection is most frequently detected in Austrian horses of advanced age. *Equine Veterinary Journal*, *54*(2), pp.379-389.

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4. Lu, G., Sun, L., Ou, J., Xu, H., Wu, L. and Li, S., 2018. Identification and genetic characterization of a novel parvovirus associated with serum hepatitis in horses in China. *Emerging microbes & infections*, *7*(1), pp.1-7.

5. Lu, G., Wu, L., Ou, J. and Li, S., 2020. Equine parvovirus-hepatitis in China: Characterization of its genetic diversity and evidence for natural recombination events between the Chinese and American strains. *Frontiers in veterinary science*, *7*, p.121.

6. Meister, T.L., Tegtmeyer, B., Brüggemann, Y., Sieme, H., Feige, K., Todt, D., Stang, A., Cavalleri, J.M. and Steinmann, E., 2019. Characterization of equine parvovirus in thoroughbred breeding horses from Germany. *Viruses*, *11*(10), p.965.

7. AAEP Guidelines Equine_Parvovirus_Hepatitis_Virus_Control_Guidelines.pdf (aaep.org)

8. Tomlinson, J.E., Kapoor, A., Kumar, A., Tennant, B.C., Laverack, M.A., Beard, L., Delph, K., Davis, E., Schott II, H., Lascola, K. and Holbrook, T.C., 2019. Viral testing of 18 consecutive cases of equine serum hepatitis: A prospective study (2014-2018). *Journal of veterinary internal medicine*, *33*(1), pp.251-257.

9. Ramsauer, A.S., Badenhorst, M. and Cavalleri, J.M., 2021. Equine parvovirus hepatitis. *Equine Veterinary Journal*, *53*(5), pp.886-894.

Communication Plan for Direct Healthcare Professional Communication

DaHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Arti-Cell® Forte and RenuTend®
Marketing authorisation holder	Boehringer Ingelheim Vetmedica GmbH
Safety concern and purpose of the communication	Market recall of six batches of Arti-Cell® Forte and two batches of RenuTend® due to possible contamination with EqPV-H
DaHPC recipients	Specialty equine veterinarians and pharmacies that received product from the affected batches of Arti-Cell® Forte and from the affected batches of RenuTend®
Member States where the DaHPC will be distributed	Austria, Finland, France, Germany, Sweden

Timetable	Date
DaHPC and communication plan (in English) agreed by CVMP	3 April 2023
Submission of translated DaHPCs to the national competent authorities for review	<date>
Agreement of translations by national competent authorities	<date>
Dissemination of DaHPC start date	<date>