

PRASCEND® tablets for horses: be aware of the risk of accidental ingestion and the steps to take in the event of an accident

Accidental ingestion of PRASCEND® (pergolide) tablets, a drug for horses with equine Cushing's disease, poses a significant risk to human health. Accidents occur when the product, often hidden in fruit and prepared well before administration, ends up being eaten by a person. ANSES-ANMV has identified 37 cases of accidental ingestion since the drug was first placed on the market in 2012. As a result, the Agency has asked for the summary of product characteristics to be updated and reminds horse owners and keepers of the risks inherent in preparing this medicine in advance of administration. If someone accidentally swallows PRASCEND®, they should seek prompt medical attention, while avoiding driving due to its potential neurological effects. Preventive measures should be taken to avoid such accidents occurring.



Photo credit : Eric Fresnay

Background

PRASCEND® (pergolide) is a veterinary medicinal product indicated for the treatment of clinical signs associated with pituitary *pars intermedia* dysfunction in horses, a condition better known as equine Cushing's disease (see photo). It is an endocrine disease that mainly affects older subjects: at least 15% of horses over 15 years old are thought to be affected [1]. This syndrome is linked to dopaminergic neurodegeneration in the hypothalamus, leading to disrupted functioning of the pituitary gland, the brain gland responsible for the synthesis of many hormones. The pituitary gland then increases in size, inducing an overproduction of steroid hormones by the adrenal glands, which results in symptoms that are highly suggestive of the disease such as lethargy, emaciation, polyuria-polydipsia, hirsutism, excessive sweating and laminitis [2]. Once the diagnosis has been made, Cushing's disease requires daily treatment throughout the animal's life.

PRASCEND® has been considered the reference treatment for this syndrome for some years. However, horses are distrustful and difficult when it comes to food. Giving the horse a substance it does not know is often a source of conflict and risk, both for the horse itself and anyone around it. Long-

term administration of this drug therefore requires ploys to maintain good compliance. This is often done by mixing the drug with food that the horse likes. However, once it has been prepared, administration can then be delayed, leaving time for an uninformed third party to accidentally ingest it.

The effects of pergolide, the active substance in PRASCEND®

Pergolide is a synthetic derivative of rye ergot. It stimulates dopamine receptors by mimicking the effects of dopamine (i.e. it is a dopamine agonist).

Dopamine plays a complex role in the central nervous system and is involved in various key functions such as behaviour, cognition, motor functions, motivation, reward, sleep and memory.

Pergolide was used in humans in some countries for treating Parkinson's disease at doses of 1 to 3 mg/day, but due to serious adverse effects — particularly cardiac problems [3] — it is no longer used in human medicine. It is generally well tolerated in Equidae, however. PRASCEND®, available in 1 mg tablets, is used in horses at an average dose of 2 µg/kg.

1. Syndrome combining intense thirst with large urine volumes.
2. Metabolic disorder leading to inflammation of the horse's foot.

Cases regularly reported

Since it was placed on the market in 2012, 37 human cases of accidental ingestion of PRASCEND tablets have been reported to the French Agency for Veterinary Medicinal Products (ANMV). The annual number of reports increased from 2018 onwards. However, this increase is biased: starting from this date, poisonings recorded by poison control centres were added to the reports transmitted directly to the ANMV via the veterinary pharmacovigilance network. Since 2018, there have been six or more reports involving PRASCEND® every year (Figure 1).

A study carried out on all human reports of adverse events

notified in France in 2018 following the use of a veterinary drug [4] showed that with 11 cases over the year, PRASCEND® was the veterinary drug most frequently involved in human poisonings, just behind external antiparasitics.

The main clinical signs, reported at least twice to the ANMV, are listed in Figure 2. These signs, observed following ingestion, can be explained by the dopaminergic properties of pergolide. The main symptoms are nausea and/or vomiting, fatigue, malaise or asthenia, sometimes mental confusion, dizziness, headaches, and/or cardiovascular disorders such as hypotension, bradycardia or palpitations. The first signs appear quickly, usually within an hour of ingestion.

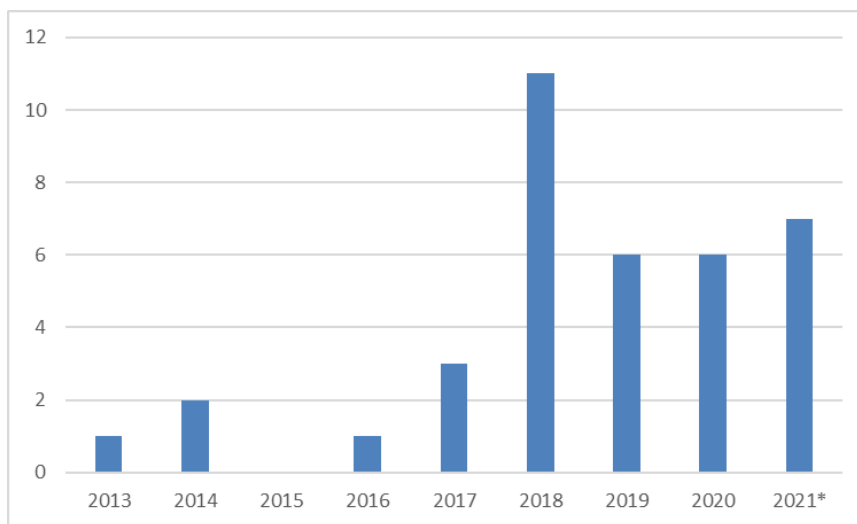


Figure 1: Change over time in the number of cases of adverse effects in humans after accidental ingestion of PRASCEND® (source: ANMV).

* For 2021: period from 1 January to 30 June only

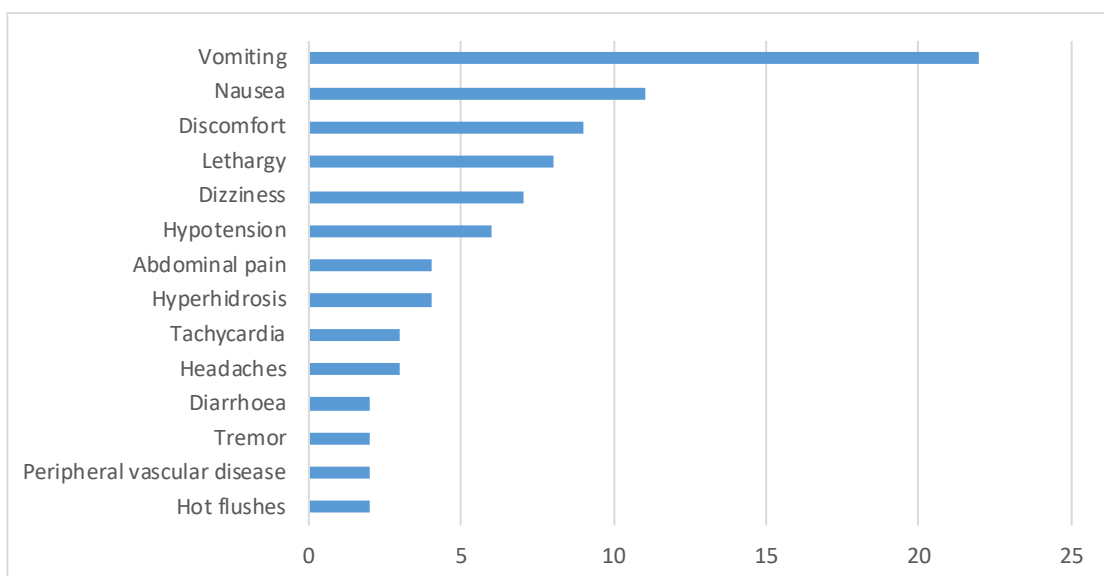


Figure 2: Distribution of clinical signs reported after human ingestion of PRASCEND, for 2018 (source: ANMV).

Precautions to be taken to avoid these accidents

Given the methods conventionally used for administering this drug to horses, it is important that owners be informed of the risks of accidental ingestion whenever PRASCEND® is prescribed.

The treatment should be prepared at the stable where the horse is kept and at the very last moment, just before administration. However, if advance preparation cannot be avoided:

- prepare only one dose at a time, to limit the severity of poisoning in case of accidental ingestion;
- minimise the time between preparation and administration to the horse;

In the period before administration:

- place the treatment in a sealed box, correctly labelled (with the horse's name, for example);
- place this box somewhere where people will not be passing through (in an isolated room), out of immediate reach (at the top of a cupboard for example), the best place being in a locked room.

References

- [1]. DOLIGEZ P. & DELERUE P (2019): Le syndrome de Cushing, fréquent chez les chevaux âgés [Equine Cushing's disease: comon in elderly horses]. Cheval Santé, **125**: 48-51
- [2]. SCHOTT HC (2002): Pituitary *pars intermedia* dysfunction: equine Cushing's disease. Vet Clin North Am Equine Pract, **18**: 237-270
- [3]. ADRAC (2004): Cardiac valvulopathy with pergolide. Aust Adv Drug React Bull, **23** (4): 12-15
- [4]. ANSES (2019): Cases of human exposure to veterinary medicinal products – Retrospective study of cases recorded in the veterinary pharmacovigilance database in 2018 – Study report

Where should reports be made?

To report an adverse effect in an animal following the use of a veterinary drug:

<https://pharmacovigilance-anmv.anses.fr>

To report an adverse effect in a human following the use of a veterinary drug:

https://signalement.social-sante.gouv.fr/psig_ihm_utilisateurs/index.html#/accueil

The ANMV also wishes to reiterate that in the event of accidental ingestion, medical advice must be sought rapidly from a poison control centre, emergency services (dial 15 in France) or a general practitioner, for example.

Conclusion

Due to the number of regularly reported cases of poisoning, the summary of product characteristics for PRASCEND® was amended in October 2020 to update the precautions to be taken by the person administering the drug (Section 4.5). The risk of accidental ingestion is not unique to PRASCEND®, as it is inherent in any veterinary medicine prepared in advance of administration, such as antiparasitic solutions for dilution. However, the very nature of this treatment and its serious risks to humans call for major preventive measures. Veterinarians should be aware of this risk from the moment that administration of PRASCEND® is delegated to a third party. It is therefore their responsibility to remind people of the good practices to be followed here.

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FOR MORE INFORMATION ABOUT THIS MEDICINAL PRODUCT:

<http://www.ircp.anmv.anses.fr/rcp.aspx?NomMedica-ment=PRASCEND+1+MG+COMPRIMES+POUR+CHEVAUX>