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ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apovomin 1 mg/ml solution for injection for dogs
(AT, BG, CZ, EE, EL, ES, HR, HU, IE, IS, IT, LT, LV, PL, PT, RO, SI, SK, UK)
Apovomin vet 1 mg/ml solution for injection for dogs (DK, FI, NO, SE)
Apovomin 0.85 mg/ml solution for injection for dogs (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Apomorphine	0.85 mg
(equivalent to apomorphine hydrochloride hemihydrate	1.00 mg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	10.0 mg
Sodium metabisulfite (E223)	1.0 mg
Sodium chloride	
Water for injections	
Sodium hydroxide (for pH adjustment)	
Hydrochloric acid, diluted (for pH adjustment)	

Clear, colourless aqueous solution.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

Induction of emesis.

3.3 Contraindications

Do not use in case of depression of the Central Nervous System (CNS).
Do not use in cases of ingestion of caustic agents (acids or alkalis), foamy products, volatile substances, organic solvents and non-blunt objects (e.g. glass).
Do not use in animals which are hypoxic, dyspnoeic, seizuring, in hyperexcitation, extremely weak, ataxic, comatose, lacking normal pharyngeal reflexes, or suffering other marked neurologic impairments that could lead to aspiration pneumonia.
Do not use in cases of circulatory failure, shock and anaesthesia.
Do not use in animals which have been treated with Dopamine-Antagonists (Neuroleptics) in the past 24 hours.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

Expulsive efforts with or without vomiting are likely to be seen from 3 to 4 minutes after the injection of the veterinary medicinal product and may last up to half an hour.
If emesis is not induced following a single injection, do not repeat the injection as it will not be effective and may provoke clinical signs of overdose.

3.5 Special precautions for use

Special precautions for safe use in the target species:

In dogs with known severe hepatic failure, the benefit-risk balance for use of the veterinary medicinal product should be considered by the veterinarian.
Before administering the veterinary medicinal product, consideration must be given to the time of the ingestion of the substance (in relation to gastric emptying times) and the suitability of inducing emesis based on the type of substance ingested (see also section 3.3).

Special precautions to be taken by the person administering the veterinary medicinal product to animals:

This veterinary medicinal product may cause nausea and somnolence. In case of accidental self–injection, seek medical advice immediately and show the package leaflet or the label to the physician. DO NOT DRIVE, as sedation may occur.
Apomorphine has been shown to have teratogenic effects in laboratory animals and is excreted in breast milk. Pregnant and breastfeeding women should avoid handling the veterinary medicinal product.
This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to apomorphine or to any of the excipients should avoid contact with the veterinary medical product.
If the veterinary medicinal product comes into contact with the skin or eyes, rinse immediately with water. Wash hands after use.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Drowsiness [a], Decreased appetite [a] Hypersalivation [a] Immediate pain upon injection [a, b]
Common (1 to 10 animals / 100 animals treated):	Dehydration [a, c] Tachycardia [a], Bradycardia [a]
Undetermined frequency (cannot be estimated from the available data)	Low blood pressure

[a] Transient and may be related to the physiological response to expulsive efforts
[b] Mild to moderate
[c] Slight

Multiple episodes of vomiting may be observed, and vomiting may occur up to several hours after the injection.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation in dogs.

Pregnancy and lactation:
Apomorphine has been shown to have teratogenic effects in rabbits and foetotoxic effects in rats at doses higher than the recommended dose in dogs.
As apomorphine is excreted in breast milk, when used in lactating females, puppies should be monitored carefully for undesired effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 Interaction with other medicinal products and other forms of interaction

Neuroleptics with a dopaminergic antagonistic effect (e.g.: chlorpromazine, haloperidol), and anti-emetics (metoclopramide, domperidone) reduce or suppress the emesis induced by the administration of apomorphine.
The administration or the prior ingestion of opiates or barbiturates can induce additive CNS effects and respiratory depression with apomorphine.
Caution is advised when dogs are receiving other dopamine agonists, such as cabergoline, due to possible additive effects such as exacerbation or inhibition of vomiting.

3.9 Administration routes and dosage

For single subcutaneous use only.
0.1 mg of apomorphine hydrochloride hemihydrate per kg bodyweight (0.1 ml veterinary medicinal product per kg bodyweight).
To ensure a correct dosage, body weight should be determined as accurately as possible.
Do not use if the solution has turned green.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Excessive doses of apomorphine may result in respiratory and/or cardiac depression, CNS stimulation (excitement, seizures, stereotypy) or depression, protracted vomiting, slight decrease in body temperature or rarely in restlessness, excitement or even convulsion.
At higher doses apomorphine may also suppress vomiting.
Naloxone may be used to reverse the CNS and respiratory effects of apomorphine.
Anti-emetics such as metoclopramide and maropitant should be considered in case of protracted vomiting.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QN04BC07

4.2 Pharmacodynamics

Apomorphine is an aporphine derivative of the dibenzoquinoline class and a synthetic derivative of morphine with no analgesic, opiate or addictive properties. At low doses, apomorphine induces emesis by stimulation of the dopamine D2-receptors in the chemoreceptor trigger zone (CTZ). Higher doses of apomorphine, however, may suppress vomiting by stimulating the μ receptors in the vomiting centre in the brain.

4.3 Pharmacokinetics

Absorption
After subcutaneous administration apomorphine is rapidly absorbed. Peak plasma concentration (C_{max}) is 35.5 ± 7.46 ng/ml and is reached after about 13.5 ± 5.3 minutes.

Distribution
Apomorphine is very lipophilic and equilibrates rapidly between blood and tissue. Apomorphine binds extensively to plasma proteins in humans.

Metabolism
Apomorphine is extensively metabolised by the liver into-non-active metabolites.

Excretion
The metabolites and very little unchanged apomorphine (<2%) are excreted via the urine.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after opening of the immediate packaging: 28 days.

5.3 Special precautions for storage

Store in the original package in order to protect from light.
Store in a refrigerator (2 °C – 8 °C).

5.4 Nature and composition of immediate packaging

Clear Type I glass vials containing 5 ml, closed with a coated Type I bromobutyl rubber stopper and sealed with an aluminium cap. Each vial is packed into a cardboard box.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Outer carton

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apovomin 1 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Apomorphine	0.85 mg
(equivalent to apomorphine hydrochloride hemihydrate	1.00 mg)

3. PACKAGE SIZE

5 ml

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 28 days. Once broached use by…

9. SPECIAL STORAGE PRECAUTIONS

Store in the original package in order to protect from light.
Store in a refrigerator.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

5 ml glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apovomin
5 ml

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Apomorphine hydrochloride hemihydrate 1.00 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once opened use within 28 days.

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Apovomin 1 mg/ml solution for injection for dogs

2. Composition

Each ml contains:

Active substance:

Apomorphine	0.85 mg
(equivalent to apomorphine hydrochloride hemihydrate	1.00 mg)

Excipients:

Benzyl alcohol (E1519)	10.0 mg
Sodium metabisulfite (E223)	1.0 mg

Clear, colourless aqueous solution.

3. Target species

Dogs.

4. Indications for use

Induction of emesis.

5. Contraindications

Do not use in case of depression of the Central Nervous System (CNS).
Do not use in cases of ingestion of caustic agents (acids or alkalis), foamy products, volatile substances, organic solvents and non-blunt objects (e.g. glass).
Do not use in animals which are hypoxic, dyspnoeic, seizuring, in hyperexcitation, extremely weak, ataxic, comatose, lacking normal pharyngeal reflexes, or suffering other marked neurologic impairments that could lead to aspiration pneumonia.
Do not use in cases of circulatory failure, shock and anaesthesia.
Do not use in animals which have been treated with Dopamine-Antagonists (Neuroleptics) in the past 24 hours.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special warnings:
Expulsive efforts with or without vomiting are likely to be seen from 3 to 4 minutes after the injection of the veterinary medicinal product and may last up to half an hour.
If emesis is not induced following a single injection, do not repeat the injection as it will not be effective and may provoke clinical signs of overdose.

Special precautions for safe use in the target species:
In dogs with known severe hepatic failure, the benefit-risk balance for use of the veterinary medicinal product in such animals should be considered by the veterinarian.

Before administering the veterinary medicinal product, consideration must be given to the time of the ingestion of the substance (in relation to gastric emptying times) and the suitability of inducing emesis based on the type of substance ingested (see also the section on "*Contraindications"*).

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product may cause nausea and somnolence. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. DO NOT DRIVE, as sedation may occur.
Apomorphine has been shown to have teratogenic effects in laboratory animals and is excreted in breast milk. Pregnant and breastfeeding women should avoid handling the veterinary medicinal product.
This veterinary medicinal product may cause hypersensitivity reactions. People with known hypersensitivity to apomorphine or to any of the excipients should avoid contact with the veterinary medical product.
If the veterinary medicinal product comes into contact with the skin or eyes, rinse immediately with water. Wash hands after use.

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy and lactation in dogs.
Apomorphine has been shown to have teratogenic effects in rabbits and foetotoxic effects in rats at doses higher than the recommended dose in dogs.
As apomorphine is excreted in breast milk, when used in lactating females, puppies should be monitored carefully for undesired effects.
Use only according to the benefit-risk assessment by the responsible veterinarian.

Interaction with other medicinal products and other forms of interaction:
Neuroleptics with a dopaminergic antagonistic effect (e.g. chlorpromazine, haloperidol), and anti-emetics (metoclopramide, domperidone) reduce or suppress the emesis induced by the administration of apomorphine.
The administration or the prior ingestion of opiates or barbiturates can induce additive CNS effects and respiratory depression with apomorphine.
Caution is advised when dogs are receiving other dopamine agonists, such as cabergoline, due to possible additive effects such as exacerbation or inhibition of vomiting.

Overdose:
Excessive doses of apomorphine may result in respiratory and/or cardiac depression, CNS stimulation (excitement, seizures, stereotypy) or depression, protracted vomiting, slight decrease in body temperature or rarely in restlessness, excitement or even convulsion.
At higher doses apomorphine may also suppress vomiting.
Naloxone may be used to reverse the CNS and respiratory effects of apomorphine.
Anti-emetics such as metoclopramide and maropitant should be considered in case of protracted vomiting.

<Special restrictions for use and special conditions for use:>

Major incompatibilities:
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Dogs:

Very common (>1 animal / 10 animals treated):	Drowsiness[a], Decreased appetite[a] Hypersalivation (increased salivation)[a] Immediate pain upon injection[a, b]
Common (1 to 10 animals / 100 animals treated):	Dehydration[a,c] Tachycardia (rapid heart rate)[a], Bradycardia (slow heart rate)[a]
Undetermined frequency (cannot be estimated from the available data)	Low blood pressure

[a] Transient and may be related to the physiological response to expulsive efforts
[b] Mild to moderate
[c] Slight

Multiple episodes of vomiting may be observed, and vomiting may occur up to several hours after the injection.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

For single subcutaneous use only.
0.1 mg of apomorphine hydrochloride hemihydrate per kg bodyweight (0.1 ml veterinary medicinal product per kg bodyweight). To ensure a correct dosage, body weight should be determined as accurately as possible.

9. Advice on correct administration

Do not use if the solution has turned green.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
Store in the original package in order to protect from light.
Store in a refrigerator (2°C to 8°C).
Do not use this veterinary medicinal product after the expiry date which is stated on the carton and label after Exp. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Cardboard box with 1 x 5 ml vial.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:

Manufacturer responsible for batch release:
Produlab Pharma B.V.
Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information