SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Sympagesic 500 mg/ml + 4 mg/ml solution for injection for horses, cattle, pigs and dogs (BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, HR, HU, IE, IT, IS, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI, SK, UK)
Sympagesic solution for injection for horses, cattle, pigs and dogs (FR)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Metamizole sodium monohydrate (equivalent to 443 mg metamizole)	500.0 mg
Hyoscine butylbromide (equivalent to 2.76 mg hyoscine)	4.0 mg

Excipients:

Phenol	5.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, yellowish solution.

4. CLINICAL PARTICULARS

4.1 Target species

Horses, cattle, pigs, dogs

4.2 Indications for use, specifying the target species

Horses, cattle, pigs, dogs: treatment of smooth muscle spasms and pain associated with underlying disorders of the gastro-intestinal tract, urogenital system and bile excretory organs.

Horses only: Spasmodic colics.
Cattle, pigs, dogs: Supportive therapy for acute diarrhoea and gastroenteritis.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substances or to any of the excipients.
Do not use in cases of:
- gastro-intestinal ulceration
- chronic gastro-intestinal disorders
- mechanic obstruction in the gastro-intestinal system
- paralytic ileus
- disorders of the haematopoietic system
- coagulopathies
- renal insufficiency
- tachyarrhythmia
- glaucoma
- prostate adenoma.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Due to the risk of anaphylactic shock, metamizole-containing solutions should be administered slowly when given intravenously.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In a very small number of people, metamizole can cause reversible, but potentially serious agranulocytosis and other reactions such as skin allergy. Take care to avoid self-injection.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Avoid skin and eye contact. People with known hypersensitivity to metamizole or hyoscine butylbromide should avoid contact with the veterinary medicinal product.
Avoid use of the product if you are known to be sensitive to pyrazolones, or are sensitive to acetylsalicylic acid.
Wash splashes from skin and eyes immediately.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, anaphylactic reactions may occur and should be treated symptomatically.
In very rare cases, cardiovascular shock may occur if the intravenous injection is administered too fast.
In horses, mild tachycardia may be observed occasionally due to the parasympatholytic activity of hyoscine butylbromide.
In dogs painful reactions at the injection site can occur immediately after injection, which abate rapidly and have no negative impact on the expected therapeutic benefit.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Studies in laboratory animals (rabbit, rat) have not produced any evidence of a teratogenic effect. No information on use during pregnancy in the target species is available. Metabolites of metamizole cross the placental barrier and penetrate into milk. Therefore this product should be used only according to the benefit-risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

The effects of metamizole and/or hyoscine butylbromide may be potentiated by concurrent use of other anticholinergic or analgesic substances.
Concomitant use of inducers of hepatic microsomal enzymes (e.g. barbiturates, phenylbutazone) reduces the half-life period and hence the duration of action of metamizole. Simultaneous administration of neuroleptics, especially phenothiazine derivatives, may lead to severe hypothermia. Furthermore the risk of gastro-intestinal bleeding is increased upon concurrent use of glucocorticoids. The diuretic effect of furosemide is attenuated.
Co-administration of other weak analgesics increases the effects and side-effects of metamizole.
The anticholinergic action of quinidine and antihistaminics as well as the tachycardic effects of β sympathomimetics may be enhanced by this veterinary medicinal product.

4.9 Amounts to be administered and administration route

Horse: slow intravenous use
Pig: slow intravenous use or intramuscular use
single injection of 20 - 25 mg metamizole sodium monohydrate/kg body weight and 0.16 - 0.2 mg hyoscine butylbromide/kg body weight i.e. once 4 - 5 ml per 100 kg.
For pigs, maximum injection volume is 5 mL per injection site.

Cattle: slow intravenous use or intramuscular use
Up to twice daily for three days, 20 - 25 mg metamizole sodium monohydrate/kg body weight and 0.16 - 0.2 mg hyoscine butylbromide/kg body weight i.e. 4 - 5 ml per 100 kg twice daily up to three days.

Dog: intravenous (slow) or intramuscular use,
single injection of 50 mg metamizole sodium monohydrate/kg body weight and 0.4 mg hyoscine butylbromide/kg body weight i.e. once 0.5 ml per 5 kg. Treatment can be repeated after 24 hours if necessary.

The stopper must not be punctured more than 25 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

In case of overdosage, the symptoms of atropine intoxication can be observed (dryness of the mucous membranes, mydriasis, tachycardia), due to the parasympatholytic activity of hyoscine butylbromide.
In case of overdosage, treatment should be discontinued. Parasympaticomimetics, such as physostigmine and neostigmine, are recommended as antidotes to hyoscine butylbromide. A specific antidote for metamizole sodium is not available. Therefore symptomatic treatment should be initiated in case of overdosage.

4.11 Withdrawal period(s)

Cattle
Meat and offal: 18 days following intravenous administration
Meat and offal: 28 days following intramuscular administration
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 2 months of expected parturition.

Horses
Meat and offal: 15 days
Not authorised for use in animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 2 months of expected parturition.

Pigs
Meat and offal: 15 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Drugs for functional gastrointestinal disorders, Belladonna and derivatives in combination with analgesics, butylscopolamine and analgesics
ATCvet code: QA03DB04.

5.1 Pharmacodynamic properties

Hyoscine butylbromide (butylscopolamine bromide) is a quaternary ammonium compound of hyoscine and is an antispasmodic agent which relaxes smooth muscle of the organs of the abdominal and pelvic cavities. It is believed to act predominantly on the intramural parasympathetic ganglia of these organs. Hyoscine antagonises the actions of acetylcholine mediated through the muscarinic receptor. It also has some antagonist effect at nicotinic receptors. Due to its chemical structures as a quaternary ammonium derivative, hyoscine is not expected to enter the central nervous system therefore, does not produce secondary anticholinergic effects in the central nervous system.

Metamizole belongs to the group of pyrazolone derivatives and is used as an analgesic, antipyretic and spasmolytic agent. It has significant central analgesic and antipyretic, but only low anti-inflammatory effect (weak analgesics). Metamizole inhibits the synthesis of prostaglandins by blocking the cyclooxygenase. The

analgesic and antipyretic effect is mainly due to inhibition of prostaglandin E_2 synthesis. In addition, metamizole has a spasmolytic effect on smooth muscle organs. Metamizole sodium further antagonises the effects of bradykinin and histamine.

5.2 Pharmacokinetic particulars

Hyoscine butylbromide is 17 – 24% bound to plasma proteins. The elimination half-life is 2 – 3 hours. Hyoscine butylbromide is mainly eliminated unchanged in urine (approx. 54%).

Metamizole sodium is rapidly metabolised by hydrolysis into the primary pharmacologically active metabolite 4 methyl-aminoantipyrine (MAA). Other metabolites (4 acetyl aminoantipyrine (AAA), 4 formyl aminoantipyrine (FAA) and aminoantipyrine (AA)) are present in smaller quantities. Plasma protein binding of the metabolites is as follows: MAA: 56%, AA: 40%, FAA: 15%, AAA 14%. The elimination half-life of MAA is 6 hours. Metamizole is primarily eliminated renally.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Tartaric acid (E 334)
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

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

6.4 Special precautions for storage

After first opening the immediate packaging do not store above 25°C.

6.5 Nature and composition of immediate packaging

Cardboard box with amber glass vial (type II) with bromobutyl rubber stopper and aluminium cap.
Pack sizes: 100 ml, 5 x 100 ml

Not all pack sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 50406/4008

9. DATE OF FIRST AUTHORISATION

21 May 2019

10. DATE OF REVISION OF THE TEXT

May 2019

Approved: 21 May 2019