Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Spasmalgan compositum 500 mg/ml + 4 mg/ml Solution for injection for horses, cattle, pigs and dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:

Metamizole sodium monohydrate (equivalent to 443.00 mg metamizole)	500.00 mg
Hyoscine butylbromide (equivalent to 2.76 mg hyoscine)	4.00 mg

Excipients:

Benzyl alcohol (E1519)	10.00 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Clear, yellow solution

4 CLINICAL PARTICULARS

4.1 Target Species

Horses, cattle, pigs and dogs

4.2 Indications for use, specifying the target species

Treatment of spasms or sustained increased tonus of smooth muscles of the gastro-intestinal tract or of the urine and bile excretory organs associated with pain.

Horse:
Spasmodic colics

Cattle/Calf, pig, dog:
As supportive therapy for acute diarrhoea.

4.3 Contraindications

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.
Due to the content of metamizole sodium, do not use in case of:
- disorders of the haematopoietic system
- gastrointestinal ulcers
- chronic gastro-intestinal disorders
- renal insufficiency
- coagulopathies

Due to the content of hyoscine butylbromide do not use in case of:
- mechanic stenoses in the gastro-intestinal system
- 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. Hyoscine butylbromide can potentially effect gastrointestinal tract motility and cause tachycardia. 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.
People with known hypersensitivity to metamizole, hyoscine butylbromide or benzyl alcohol 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.
This veterinary medicinal product can cause skin and eye irritation. Avoid contact with skin and eyes. In the case of contact with skin, wash with soap and water immediately. If the product comes into contact with the eyes, rinse the eyes immediately with plenty of water. If skin or eye irritation persists, seek medical advice.
Fetotoxicity was sporadically observed following metamizole intake in the third trimester of pregnancy in humans. Furthermore, metamizole intake by breast-feeding women might be harmful for their babies. Therefore, pregnant women in the third trimester and breast-feeding women should not administer this veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, anaphylactic reactions and cardiovascular shock may occur. In dogs painful reactions can occur immediately after injection, which abate rapidly and have no negative impact on the expected therapeutic benefit.
In horses and cattle, a slight increase in heart rate may be observed occasionally due to the parasympatholytic activity of hyoscine butylbromide.
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 1000 animals treated)
- Rare (more than 1 but less than 10 animals in 10000 animals treated)
- Very rare (less than 1 animal in 10000 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. However, hyoscine butylbromide may have effects on smooth muscle of the birth canal. Metabolites of metamizole can cross the placental barrier and penetrate into milk. Therefore, this product should be used in pregnant and lactating animals only according to the benefit risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interactions

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

Administration route:
Horses, cattle: slow intravenous use
Pig: intramuscular use
Dog: intramuscular and slow intravenous use
Due to the risk of anaphylactic shock metamizole-containing solutions should be administered slowly when given intravenously.

Dosage instructions:
Horse: 25 mg metamizole sodium monohydrate/kg bw and 0.2 mg hyoscine butylbromide/kg bw (equivalent to 2.5 ml of the veterinary medicinal product per 50 kg bw)
Cattle: 40 mg metamizole sodium monohydrate/kg bw and 0.32 mg hyoscine butylbromide/kg bw (equivalent to 4 ml of the veterinary medicinal product per 50 kg bw)
Calf: 50 mg metamizole sodium monohydrate/kg bw and 0.4 mg hyoscine butylbromide/kg bw (equivalent to 1 ml of the veterinary medicinal product per 10 kg bw)
Pig: 50 mg metamizole sodium monohydrate/kg bw and 0.4 mg hyoscine butylbromide/kg bw (equivalent 1 ml of the veterinary medicinal product per 10 kg bw)
Dog: 50 mg metamizole sodium monohydrate/kg bw and 0.4 mg hyoscine butylbromide/kg bw (equivalent to 0.1 ml of the veterinary medicinal product per kg bw)

Treatment frequency:
Cattle and Calf: up to twice daily for three days.
Horse and pig: single injection
Dog: single injection that can be repeated after 24 hours if necessary.
The stopper must not be punctured more than 100 times. The user should select the most appropriate vial size according to the target species to be treated.

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

The acute toxicity of both compounds is very low. In studies with rats, the symptoms were non-specific and included ataxia, mydriasis, tachycardia, prostration, convulsions, unconsciousness and respiratory signs.
In case of overdosage treatment should be discontinued. Physostigmine is recommended as an antidote to hyoscine butylbromide. A specific antidote for metamizole sodium is not available. Therefore, symptomatic treatment should be initiated in case of overdosage.

Due to the parasympatholytic activity of hyoscine butylbromide a slight increase in the heart rate was observed in some cases in horses and cattle following administration of the double therapeutic dose.

4.11 Withdrawal period(s)

Horse, Cattle (i.v.):	Meat and Offal:	12 days
Cattle (i.v.):	Milk	96 hours
Pig (i.m.):	Meat and Offal:	15 days

Not authorised for use in horses producing milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antispasmodic in combination with analgesic
ATC vet 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 butylbromide is not expected to enter the central nervous system and 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 E2 synthesis. In addition, metamizole has a spasmolytic effect on smooth muscle organs. Metamizole sodium monohydrate 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%).
After intravenous injection the onset of action is immediate, after intramuscular injection it is delayed for 20 - 30 minutes. Depending on administration route and clinical picture the spasmolytic effect lasts for approximately 4 - 6 hours.

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

Benzyl alcohol (E1519)
Tartaric acid (pH adjustment)
Sodium hydroxide (pH adjustment)
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

Do not store above 25°C.
Keep the vial in the outer carton in order to protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

Clear type I glass vial closed with a fluorinated bromobutyl rubber stopper and an aluminium cap.

1 vial of 10 mL in a cardboard box.
1 vial of 100 mL in a cardboard box.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Veyx-Pharma GmbH
Soehreweg 6
34639 Schwarzenborn
Germany

8 MARKETING AUTHORISATION NUMBER(S)

VPA10539/007/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th May 2020

10 DATE OF REVISION OF THE TEXT

August 2021