1. NAME OF THE VETERINARY MEDICINAL PRODUCT
Etorphine injection 2.25 mg/ml, vial 7 ml (7 ml = 15.75 mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
One ml contains:
Active substance: etorphine 2.25 mg (2.45 mg etorphineHCl)
Excipients: benzylalcohol, NaCl, HCl, water for injection

3. PHARMACEUTICAL FORM
Solution for injection.
Clear colourless solution.

4. CLINICAL PARTICULARS
4.1 Target species
Experience with large animals like elephants, rhino's, buffalo's, but also hoof stock like antelopes, giraffes and zebra's.

4.2 Indications for use, specifying the target species
Etorphine is used for sedation and immobilisation of zoo and wild life animals, often in combination with acepromazine, ketamine and (me)detomidine, by dart delivery systems.

4.3 Contraindications
Do not use in animals belonging to the family Felidae which have severe and adverse reactions to all opiate agonists.

4.4 Special warnings for each target species

4.5 Special precautions for use
Do not use etorphine unless an opiate antagonist is on hand.

Etorphine is a highly potent opiate agonist, up to 4000 times more potent than morphine and small doses like 30 microgram (0.01 ml of this drug) could be lethal in human.

Prevention first!
- Never work alone when handling etorphine
- Have running water in the near vicinity
- Wear gloves
- Use new rubbers for dart preparation
- Secure the needle tightly to the syringe
- Don't pressurize the dart without case-protection
- Always consider the darts and remaining patrons to be lethal weapons

4.6 Adverse reactions (frequency and seriousness)
Dizziness, nausea, constriction of the pupils, respiratory depression, hypotension, serious adverse events include apnoea, cyanosis, coma and cardiac arrest.

The effects of etorphine are rapidly reversed with naltrexone. Apnoea can be reversed with butorphanol (dose ratio mg butorphanol to etorphine 1:1).

4.7 Use during pregnancy or lactation
Can be used during pregnancy and lactation. Need for intervention should be weighed against potential negative effects for foetus or suckler.

4.9 Amounts to be administered and administration route
Intramuscularly (i.m.) by dart

SPECIES	**MASS KG**	**ETORPHINE**		
		µg/kg	ml product/**100 kg**	Common dose (mg)
African elephant	5000	1 – 1.5	0.044 – 0.067	5 – 15
Sq. Lipped Rhino	2000	1 – 2	0.044 – 0.089	2 – 3.3
Black Rhino	1000	2 – 4	0.089 – 0.178	2 – 4.5
Giraffe	1000	2 – 10	0.089 – 0.44	2 – 10
African Buffalo	700	7.5 – 15	0.33 – 0.67	5 – 12.5
Eland	700	7.5 – 15	0.33 – 0.67	5 – 10.5
Blue Wildebeest	200	10 – 20	0.44 – 0.89	2 – 4
Black Wildebeest	150	10 – 20	0.44 – 0.89	1.5 – 3
Red Hartebeest	140	15 – 25	0.67 – 1.1	2 – 3.5
Lichtenstein Hartebeest	200	15 – 25	0.67 – 1.1	3 – 4
Tsessebe	140	15 – 25	0.67 – 1.1	2 – 3.5
Blesbok	90	15 – 25	0.67 – 1.1	1.5 – 2.5
Greater Kudu	250	15 – 25	0.67 – 1.1	4 – 8
Nyala	100	15 – 25	0.67 – 1.1	1.5 – 2.5
Bushbuck	50	15 – 25	0.67 – 1.1	1 – 1.5
Reedbuck	70	15 – 25	0.67 – 1.1	1 – 2
Waterbuck	250	15 – 25	0.67 – 1.1	4 – 8.5
Roan Antelope	280	15 – 25	0.67 – 1.1	4.2 – 7
Sable Antelope	240	15 – 25	0.67 – 1.1	3.6 – 6
Gemsbok	200	15 – 25	0.67 – 1.1	3 – 6.5
Impala	50	15 – 25	0.67 – 1.1	0.8 – 1.5
Springbok	35	15 – 25	0.67 – 1.1	0.5 – 1
Steenbok antelope	12	15 – 25	0.67 – 1.1	0.2 – 0.3
Common Duiker	15	15 – 25	0.67 – 1.1	0.2 – 0.4
Zebra	250	15 – 25	0.67 – 1.1	4 – 6.5
Warthog	80	40 – 60	1.8 – 2.7	3 – 7

4.10 Overdose (symptoms, emergency procedures, antidotes)
Symptoms of opiate intoxication:
- dizziness, incoordination, lethargy, sedation
- nausea, vomiting
- pin point pupil
- respiratory depression, apnoea
- cold skin, weak pulse
- unconsciousness, coma
- cardiovascular collapse due to hypoxia
- death

In case of human emergencies:
Remain calm and evaluate the possible exposure to etorphine. In case of superficial scratches without systemic exposure, remove all contaminants immediately with plenty of water and stay with the exposed person for 15 minutes. If no effects are observed in this period, no further actions are needed, although it is advisable to maintain an observation period for several hours.
In case of symptoms or accidental injection of etorphine immediate administration of opiate antagonists is warranted. Naloxone (Narcan) or naltrexone are safe in humans, don't use diprenorphine.

Naloxone: 10 mg antagonizes 1 mg of etorphine, so 1 ml of etorphine 2,25 mg/ml needs 60 ampoules of Narcan 0,4 mg=1 ml.

Naltrexone: 20-25 mg antagonizes 1 mg of etorphine, therefor Naltrexone 50mg/ml can be given intravenously in the same volume as the accidently administered volume of etorphine 2.25 mg/ml, the minimum dose is 10 mg = 0.2 ml.

Re-dosing is possible in case of recurring symptoms, naloxone's activity (30-81 minutes) may be shorter than etorphine, Naltrexone's activity (>24 hours) lasts longer than etorphine. Both antagonists are well tolerated in humans.

4.11 Withdrawal periods
Not applicable, animals sedated with etorphine are excluded from human consumption.

5. PHARMACOLOGICAL PROPERTIES
The chemical name for etorphine hydrochloride is 6,14-Ethenomorphinan-7-methanol, 4,5-epoxy-3-hydroxy-6-methoxy-ά,17-dimethyl-ά-propyl-, (5ά,7á-(R))-hydrochloride.
Pharmacotherapeutic group: analgesics, opioids, oripavine derivatives
ATCvet code: QN02AE90

5.1 Pharmacodynamic properties
Etorphine is a full opiate agonist and binds to multiple opiate sites in the central nervous system. It is believed to produce its clinical effects through binding the μ-, δ-, and κ- opiate sites. It has a potent effect on depressing the respiratory centers of the CNS thus resulting in apnoea being commonly seen in immobilized animals.

Etorphine is chemically related to morphine. In laboratory animals, etorphine resembles morphine by causing analgesia, catatonia, blockade of conditional reflexes, and anti-diuretic effect. It also resembles morphine by causing excitement in mice, cats and bradycardia and hypotension in rats, dogs, cats and monkeys. When given subcutaneously, etorphine is 1000-4000 times more potent than morphine as an analgesic, depending on the test situation. Its use for immobilizing game animals results largely from its ability to cause catatonia at very low dose levels.

5.2 Pharmacokinetic particulars
Absorption
Following i.m. administration by dart: 5 min for ataxia, 15 minutes for recumbence
Distribution

In rats was found that at least 85% of the dose was cleared from the blood in the first 2 min, with the highest brain concentrations observed at the earliest time point examined (7 min). Blood levels continued to fall slowly from about 5% of the administered dose after 15 min to less than 2% after 3 hours. Although more than 15% of the dose was found in the liver and kidney after 15 min, labelled material did not further accumulate in these organs, but decreased to about 3% after 3 hours.

Metabolism

Excretion into the bile as etorphine glucuronide (96%) and etorphine (<4%). Enterohepatic circulation was shown in rats.

Elimination

Duration of complete sedation in most species is about 1 hour.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

benzylalcohol
sodiumchloride
HCl 4N qs
water for injection

6.2 Incompatibilities

None known. Experience with admixtures of etorphine with ketamine, xylazine, acepromazine and medetomidine.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf-life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product should be stored at room temperature, with strictly controlled, limited access.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 injection vial of 7 ml closed with a rubber stopper and sealed with an aluminium cap.

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 products should be disposed of in accordance with local requirements.

7. MANUFACTURER

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10. DATE OF REVISION OF THE TEXT

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