

Zoletil™ for Injection



(tiletamine and zolazepam for injection)

**PURCHASE
9 VIALS AND
RECEIVE 3
AT NO CHARGE**

June 1 - August 15, 2020

Convenient & Versatile

2 MOLECULES, 1 INJECTION

2-in-1 combined anesthesia

Dogs - for restraint and minor procedures

Cats - for restraint and anesthesia combined with muscle relaxation.

Zoletil™ for Injection delivers:

- Rapid onset of action
- Wide therapeutic window



A combination of 2 complementary molecules in an optimized formulation:

- **Tiletamine** - a dissociative agent that produces the following effects: anesthesia and analgesia.
- **Zolazepam** - a benzodiazepine molecule that produces the following effects: tranquilization and muscle relaxation.



VERSATILE

Dose-dependent duration and depth of dissociative anesthesia



CONVENIENT

Ready-to-use combination containing two molecules in a fixed ratio formulation



SHORT DURATION PROCEDURES

Suitable for common procedures requiring anesthesia and analgesia: e.g. short dental procedures, castration, lacerations, abscess treatment, foreign body removal



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www.jurox.com/us

Important Safety Information: As with all drugs, side effects may occur. Zoletil™ for Injection should not be used in dogs and cats with pancreatic disease, renal pathology or impairment of renal function, or severe cardiac or pulmonary dysfunction. Do not use at any stage of pregnancy or for Caesarean section. Do not use phenothiazine-derivative drugs concomitantly with Zoletil™ for Injection as the combination produces respiratory and myocardial depression, hypotension, and hypothermia. Pulmonary edema has been reported in cats. Respiratory depression may occur following administration of high doses of Zoletil. Copious salivation may occur during Zoletil anesthesia and may be controlled by giving atropine sulfate, USP as a concurrent medication. Vomiting upon emergence, involuntary muscle twitching and cardiac arrest have occasionally been reported with Zoletil. Refer to the prescribing information for complete details or visit jurox.com/us.

Summary of Prescribing Information

NDC 49480-718-05



Zoletil™ for Injection

(tiletamine and zolazepam for injection)

100 mg/mL total
(equivalent to 50 mg/mL tiletamine and 50 mg/mL zolazepam)
For Intramuscular Use in Dogs and Cats Only

CAUTION

Federal law restricts this drug to the use by or on the order of a licensed veterinarian.

DESCRIPTION

Zoletil™ for Injection (tiletamine and zolazepam for injection) is a nonbarbiturate, injectable anesthetic agent for dogs and cats. Chemically, Zoletil™ for Injection is a combination of equal parts by weight of base of tiletamine hydrochloride (2-[ethylamino]-2-[2-thienyl]-cyclohexanone hydrochloride), an arylaminocycloalkanol dissociative anesthetic, and zolazepam hydrochloride (4-[o-fluorophenyl]-6,8-dihydro-1,3,8-trimethylpyrazolo [3,4-e] [1,4] diazepin-7-[1H]-1-hydrochloride), a non-phenothiazine diazepinone having minor tranquilizing properties. The product is supplied sterile in vials. The addition of 5 mL diluent produces a solution containing the equivalent of 50 mg tiletamine base, 50 mg zolazepam base and 57.7 mg mannitol per milliliter. This solution has a pH of 2 to 3.5 and is recommended for deep intramuscular injection.

INDICATIONS

Dogs

Zoletil™ for Injection is indicated in dogs for restraint and minor procedures of short duration (30 min. avg.) requiring mild to moderate analgesia. Minor surgery is considered to be a laceration repair, draining of abscesses, castrations and other procedures requiring mild to moderate analgesia. (See Dogs under Dosage and Administration.)

Cats

Zoletil™ for Injection is indicated in cats for restraint or for anesthesia combined with muscle relaxation.

DOSAGE AND ADMINISTRATION

The dose is determined by the total combined concentration of 100 mg/mL (see HOW SUPPLIED)

Dogs

Intramuscular (IM) For Restraint and Minor Procedures of Short Duration Requiring Mild to Moderate Analgesia:

In healthy dogs, an initial intramuscular dosage of 3 to 4.5 mg/lb (6.6 to 9.9 mg/kg) Zoletil™ for Injection is recommended for diagnostic purposes; 4.5 to 6 mg/lb (9.9 to 13.2 mg/kg) for minor procedures of short duration, such as treatment of lacerations and wounds, castrations and other procedures requiring mild to moderate analgesia. When supplemental doses of Zoletil™ for Injection are required, such individual supplemental doses should be less than the initial dose, and the total dose given (initial dose plus supplemental dose or doses) should not exceed 12 mg/lb (26.4 mg/kg). The maximum safe dose is 13.6 mg/lb (29.92 mg/kg). (See Animal Safety.) Results from Zoletil™ for Injection anesthesia in dogs will be more satisfactory if the procedures are completed within one hour and if the procedures can be completed following single dose administration. In order to maintain at least a 2X margin of safety in dogs, the use of this product is limited to procedures that call for low doses (see Indications). Studies show that there is variation in response to different dosages of tiletamine and zolazepam injection and that low doses do not give adequate levels of anesthesia, and in some instances do not give adequate analgesia, for extensive procedures.

Cats

In healthy cats, an initial Zoletil™ for Injection dosage of 4.4 to 5.4 mg/lb (9.7 to 11.9 mg/kg) IM is recommended for such procedures as dentistry, treatment of abscesses, foreign body removal and related types of surgery; 4.8 to 5.7 mg/lb (10.6 to 12.5 mg/kg) for minor procedures requiring mild to moderate analgesia, such as repair of lacerations, castrations and other procedures of short duration. Initial dosages of 6.5 to 7.2 mg/lb (14.3 to 15.8 mg/kg) are recommended for ovariohysterectomy and onychectomy. When supplemental doses of Zoletil™ for Injection are required, such individual supplemental doses should be given in increments that are less than the initial dose, and the total dose given (initial dose plus supplemental doses) should not exceed the maximum allowable safe dose of 32.7 mg/lb (72 mg/kg). (See Animal Safety.)

General Dosing Information

Fasting prior to induction of general anesthesia with Zoletil™ for Injection is not essential; however, when preparing for elective surgery, it is advisable to withhold food for at least 12 hours prior to Zoletil™ for Injection administration. As with other injectable anesthetic agents, the individual response to Zoletil™ for Injection is somewhat varied, depending upon the dose, general physical condition and age of the patient, duration of the surgical procedure, and any preanesthetics used. Therefore, recommendations for dosage regimens cannot be fixed absolutely. Specific dosage requirements must be determined by evaluation of the health status and condition of the patient and of the procedure to be performed. Recovery varies with the age and physical condition of the animal and the dose of Zoletil™ for Injection administered. Recovery is extended with high dose or multiple injections, particularly in cats.

Intramuscular injection in dogs and cats:

There may be pain on injection. This is especially prevalent in cats.

Following a single, deep intramuscular injection of Zoletil™ for Injection in cats and dogs, onset of anesthetic effect usually occurs within 5 to 12 minutes. Muscle relaxation is optimum for approximately the first 20 to 25 minutes after Zoletil™ for Injection is administered, and then diminishes.

Repeated doses increase the duration of the effect of Zoletil™ for Injection but may not further diminish muscle tone. The quality of anesthesia with repeated doses varies because the ratio of the two components within the animal's body changes with each injection. This is due to the difference in the rates of metabolism and elimination of the two components. The quality of anesthesia will be improved and more predictable if the entire dose is given as a single injection rather than in several doses. The best method of evaluating the depth of Zoletil™ for Injection anesthesia is to monitor the patient for deliberate conscious response to noxious stimuli.

If adequate anesthesia is not produced by the recommended dosage regimen, supplemental anesthesia or another agent is indicated. This includes the use of barbiturates and volatile anesthetics. When used concurrently with Zoletil™ for Injection the dosage of these agents should be reduced.

PREPARATION OF SOLUTION FOR ADMINISTRATION

To each vial add 5 mL sterile water for injection, USP. Slight agitation will facilitate complete reconstitution. The resultant solution will contain 100 mg total Zoletil™ for Injection per one milliliter (50 mg tiletamine and 50 mg zolazepam per mL).

Discard unused solution after 4 days when stored at room temperature or after 14 days when kept refrigerated. Only use clear solution. Color of solution may vary from colorless to light amber.

CONTRAINDICATIONS

The use of Zoletil™ for Injection is contraindicated in dogs and cats with pancreatic disease. Zoletil™ for Injection should not be used in dogs and cats with severe cardiac or pulmonary dysfunction.

Because the teratogenic potential of Zoletil™ for Injection is unknown, it should not be used in pregnant bitches or queens at any stage of pregnancy. Also, a study has shown that tiletamine and zolazepam injection crosses the placental barrier and produces respiratory depression in the newborn; therefore, its use for Cesarean section is contraindicated.

WARNINGS

FOR USE IN DOGS AND CATS ONLY.

When using Zoletil™ for Injection for induction of anesthesia, patients should be continuously monitored. Facilities for the maintenance of a patent airway, artificial ventilation and oxygen supplementation should be available.

Pulmonary edema has been reported to occur in cats with the use of tiletamine and zolazepam injection. Signs and symptoms include dyspnea, lethargy, anorexia and abnormal heart rate. Deaths have been reported occasionally in severely affected individuals. Cats should be observed closely for any signs and symptoms which may suggest pulmonary edema so that appropriate therapy may be instituted.

The principal route of excretion of both components in the cat is the urine; therefore, Zoletil™ for Injection is not recommended for use in cats suffering from renal insufficiency. Balance studies in dogs indicated extensive biotransformation of both components with less than 4% of the dose excreted unchanged in the urine.

Zoletil™ for Injection is excreted predominantly by the kidneys. Preexistent renal pathology or impairment of renal function may be expected to result in prolonged duration of anesthesia.

Phenothiazine-derivative drugs should not be used with Zoletil™ for Injection at dosages indicated for intramuscular (IM) injection because the combination produces respiratory and myocardial depression, hypotension and hypothermia.

The safe use of Zoletil™ for Injection in pregnant animals or on reproduction has not been established. Zoletil™ for Injection crosses the placental barrier and causes respiratory depression in the neonate.

PRECAUTIONS

The dosage of Zoletil™ for Injection should be reduced in geriatric dogs and cats, in animals in debilitated condition and in animals with impairment of renal function. Death has occurred in both cats and dogs following intramuscular Zoletil™ for Injection administration. Preexisting pulmonary disease, renal disease (see Contraindications and Warnings) and shock were causally implicated at necropsy; however, death was drug attributable in at least one dog (of 1072) and one cat (of 1095).

Intravenous Zoletil™ for Injection has been demonstrated to be safe in a field study in dogs when used in conjunction with phenothiazine-derivative drugs (acepromazine) administered at dosages from 0.04-0.06 mg/kg IM.

Cats and smaller dogs with small body masses in relation to large body surfaces should be protected from heat loss during Zoletil™ for Injection anesthesia. Body temperature should be monitored, and supplemental heat may be required to control hypothermia. As with other anesthetics, it is prudent to provide for hemostasis during any surgical procedure.

During Zoletil™ for Injection anesthesia, ataxic movement may occur. This ataxia should not be mistaken for lack of anesthesia nor is it indicative of lack of analgesia. Do not give additional anesthesia in an attempt to abolish the ataxic movement. Efforts to eliminate ataxic movement with additional doses of Zoletil™ for Injection can result in anesthetic overdose.

Zoletil™ for Injection does not abolish laryngeal, pharyngeal, palpebral, and pedal reflexes, and may not be adequate as the sole anesthetic for surgical procedures in these areas. Endotracheal tubes are not well tolerated in connection with Zoletil™ for Injection anesthesia in the cat and their use may result in impaired respiration. After removal of the tube, normal respiration should resume.

The stimulation of surgical procedures aids in maintaining adequate ventilation.

The anesthetized patient must be monitored throughout the procedure, and if cardiopulmonary problems do occur, measures must be taken to assure that alveolar ventilation and cardiovascular functions are maintained.

The eyes normally remain open with the pupils dilated. The use of a bland ophthalmic ointment is advisable to protect the corneas from desiccation. The concurrent use of chloramphenicol will prolong the duration of anesthesia in cats.

Copious salivation may occur during Zoletil™ for Injection anesthesia. Ptyalism may be controlled in dogs and cats by administering atropine sulfate, 0.02 mg/lb (0.04 mg/kg) body weight (IV, IM, or SC) as concurrent medication. Exaggerated swallowing, reflex action and accumulation of saliva may give rise to vomiting and retching.

ADVERSE REACTIONS

For Restraint and Minor Procedures of Short Duration Requiring Mild to Moderate Analgesia

Respiratory depression may occur following administration of high doses of Zoletil™ for Injection. If at any time respiration becomes excessively depressed and the animal becomes cyanotic, resuscitative measures should be instituted promptly. Adequate pulmonary ventilation using either oxygen or room air is recommended as a resuscitative measure.

Adverse reactions reported include emesis during emergence, excessive salivation, transient apnea, vocalization, erratic recovery and prolonged recovery, excessive tracheal and bronchial secretions when atropine sulfate was not given before anesthesia, involuntary muscular twitching, hypertonicity, cyanosis, cardiac arrest, pulmonary edema and muscle rigidity during surgical procedures. Central nervous system stimulation and convulsions have also been reported. Tachycardia frequently occurs, particularly in the dog. This rise in heart rate usually lasts about 30 minutes. Either hypertension or hypotension may also occur.

Insufficient anesthesia has been reported in dogs. Death has been reported in dogs and cats following Zoletil™ for Injection administration.

For a copy of the Safety Data Sheet (SDS) or to report adverse reactions call Jurox at 1-844-253-2926. Additional information can be found at <http://www.jurox.com/us>. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VEFS or online at www.fda.gov/reportanimalae.

CLINICAL PHARMACOLOGY

Mechanism of Action

Zoletil™ for Injection is a rapid-acting anesthetic combination of tiletamine hydrochloride and zolazepam hydrochloride. Tiletamine hydrochloride is a dissociative anesthetic agent whose pharmacologic action is characterized by profound analgesia, normal pharyngeal-laryngeal reflexes and cataleptoid anesthesia. The anesthetic state produced does not fit into the conventional classification of stages of anesthesia, but instead Zoletil™ for Injection produces a state of unconsciousness which has been termed "dissociative" anesthesia in that it appears to selectively interrupt association pathways to the brain before producing somesthetic sensory blockade.

Cranial nerve and spinal reflexes remain active; however, these reflexes must not be confused with inadequate anesthesia. Analgesia results from apparent selective interruption of sensory inputs in the brain and usually persists after the anesthetic effect has subsided.

Protective reflexes, such as coughing and swallowing, are maintained under tiletamine anesthesia. Other reflexes, e.g., corneal, pedal, are maintained during tiletamine anesthesia, and should not be used as criteria for judging depth of anesthesia. The eyes normally remain open with the pupil dilated. It is suggested that a bland ophthalmic ointment be applied to the cornea if anesthesia is to be prolonged.

Used alone, tiletamine hydrochloride does not provide adequate muscle relaxation for abdominal surgical procedures. When combined with zolazepam hydrochloride, good muscle relaxation is generally attained during the phase of deep surgical anesthesia.

ANIMAL SAFETY

Tiletamine and zolazepam injection has a wider margin of safety in cats than in dogs. Dogs have survived repeated IM dosage regimens of 13.6 mg/lb (30 mg/kg) (maximum safe dose) for eight successive days. This is approximately two times the maximum recommended therapeutic dose. Cats have survived IM dosage regimens of up to 32.7 mg/lb (72 mg/kg) (maximum safe dose) on alternate days for seven episodes. This is 4.6 times the maximum recommended therapeutic dose for cats. However, these reports should not obviate prudent anesthetic practices. Some degree of tolerance has been reported. This tolerance appears to be species-variable.

Cats

In cats, the duration of effect of zolazepam exceeds that of tiletamine so that as the animal recovers there is a greater degree of tranquilization than anesthetization. There is a slight lowering of blood pressure during the first hour after injection. Heart rate and electrocardiogram readings are unaffected by tiletamine and zolazepam injection. Arterial pO₂ levels are decreased three minutes after injection but usually return to normal within 15 to 35 minutes.

Dogs

In dogs, the duration of effect of tiletamine exceeds that of zolazepam so there is a lesser degree of tranquilization than anesthetization in this species. The total effect of tiletamine and zolazepam injection in dogs is of shorter duration than in cats.

Following administration of tiletamine and zolazepam injection in dogs, a marked, persistent tachycardia occurs within two minutes following either 4.5 or 9 mg/lb (10 or 20 mg/kg) tiletamine and zolazepam injection intramuscularly. Stroke volume decreases proportionately to the increased rate at the 4.5 mg/lb (10 mg/kg) dose, with little change in the net cardiac output. There is an initial increase in systolic blood pressure, with a slight drop in pressure within five minutes. The systolic blood pressure remains at this decreased level throughout the duration of the anesthetic effect. Diastolic pressure increases throughout this same period. Following a 9 mg/lb (20 mg/kg) dose of tiletamine and zolazepam injection in dogs, the relationship between stroke volume and heart rate is disproportionate, with a resultant substantial decrease in cardiac output. Contractility and mean blood pressure are decreased, indicating direct myocardial depression. Ventricular function is adequate. During surgical manipulations, tachycardia and hypertension may be observed, and may be brought on by sympathetic reaction to painful stimuli. Epinephrine is markedly less arrhythmogenic in animals under tiletamine and zolazepam injection anesthesia than in those under halothane anesthesia.

During tiletamine and zolazepam injection anesthesia, the assurance of a patent airway is greatly enhanced by virtue of maintaining pharyngeal-laryngeal reflexes. During the first 15 minutes after intramuscular administration of 9 mg/lb (20 mg/kg) of tiletamine and zolazepam injection, the respiratory rate is doubled while the tidal volume is decreased to less than one-half of control values. Arterial pO₂ levels also decrease. This may be evidenced by hypoxemia and cyanosis. The pulmonary function usually returns to normal within 35 minutes after the administration of tiletamine and zolazepam injection.

STORAGE CONDITIONS

Store at controlled room temperature 20° to 25° C (68° to 77° F). Discard unused solution after 4 days when stored at room temperature or after 14 days when kept refrigerated. Only use clear solution. Color of solution may vary from colorless to light amber.

HOW SUPPLIED

Zoletil™ for Injection (tiletamine and zolazepam for injection) is available in individual vials of 5 mL solution when reconstituted. The addition of 5 mL diluent produces a solution containing the equivalent of 50 mg tiletamine base, 50 mg zolazepam base and 57.7 mg mannitol per milliliter. 5 mL vial - 100 mg/mL total (equivalent to 50 mg/mL tiletamine and 50 mg/mL zolazepam) when reconstituted.

Approved by FDA under ANADA # 200-618

Manufactured in France for Virbac AH, Inc.

Zoletil™ for Injection is a trademark of Virbac SA

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(tiletamine and zolazepam for injection)

Think anesthesia...
think **JUROX**