The dosing syringe should be prepared to contain the above dose. The rate of intravenous injection should be such that the total dose, if required, be administered over the first 60 seconds. If, 60 seconds after complete delivery of this first induction dose, intubation is still not possible, one further similar dose may be administered to effect. This may be achieved by administering the calculated dose every 15 seconds. Administration should continue until the clinician is satisfied that the depth of anaesthesia is sufficient for endotracheal intubation, or until the entire dose has been administered. Maintenance of anaesthesia. Following the first induction, the animal may be intubated and maintained on Alfaxan or an inhalation anaesthetic agent. Maintenance doses of Alfaxan may be given as supplemental boluses or as constant rate infusion. Alfaxan has been used safely and effectively in both dogs and cats for procedures lasting for up to one hour. The following dosages suggested for maintenance of anaesthesia are based on data taken from controlled laboratory and field studies and represent the average amount of drug required to provide maintenance anaesthesia for a dose of 10 mg/kg (i.e. up to 25 mg/kg). For both dogs and cats, these excessive doses delivered over 60 seconds cause apnoea and a temporary decrease in mean arterial blood pressure. The decrease in blood pressure is not life threatening and is compensated for by changes in heart rate. These animals can be treated solely by manual positive pressure ventilation (if required) with extubation and oxygen. Recovery is rapid with no residual effects. 4.11. Withdrawal period(s): Not applicable. 5. PHARMACOLOGICAL PROPERTIES: Pharmacotherapeutic group: other general anaesthetics, ATCvet code: QN01AX05. Pharmacological properties: Alfaxalone (3a-hydroxy-5a-pregnane-11,20-dione) is a neuroactive steroid molecule with properties of a general anaesthetic. The primary mechanism for the anaesthetic action of alfaxalone is modulation of neuronal cell membrane chloride ion transport, induced by binding of alfaxalone to GABA(A) cell surface receptors. Alfaxalone has limited analgesic properties at clinical doses. 5.2. Pharmacokinetic particulars: The volume of distribution after a single injection of clinical doses of 2 and 5 mg/kg bw of alfaxalone in dogs and cats is 2.4 L/kg and 1.8 L/kg, respectively. In vitro cat and dog hepatocyte studies show that alfaxalone experiences both Phase I (cytochrome P450 dependent) and Phase II (conjugation dependent) metabolism. Both cats and dogs form the same Phase I alfaxalone metabolites. The Phase II metabolites observed in cats are alfaxalone sulphate and alfaxalone glucuronide, while alfaxalone glucuronide is observed in the dog. In cats, the mean terminal plasma elimination half-life (1/2) for alfaxalone is approximately 45 minutes for a 5 mg/kg dose. Mean plasma clearance for a 5 mg/kg dose is 1.1 - 1.7 L/min/kg. In dogs, however, the terminal elimination half-life (1/2) for alfaxalone is approximately 25 minutes for a 2 mg/kg dose. Plasma clearance for a 2 mg/kg dose is 9.4 - 12.9 ml/min/kg. In both dogs and cats the elimination of alfaxalone demonstrates non-linear pharmacokinetics. If repeated doses of alfaxalone are administered, the Phase II metabolites are likely to be eliminated from the dog and cat by the hepatic/renal routes, similar to other species. 6. PHARMACOLOGICAL PARTICULARS: 6.1. List of excipients: Hydroxypropylbetaes, Sodium Chloride, Disodium Phosphate Anhydrous, Potassium DiHydrogen Phosphate, Sodium Hydroxide (for pH adjustment), Hydrochloric Acid, Concentrated (for pH adjustment), Water for Injections. 6.2. Incompatibilities: In the absence of compatibility studies, the 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: 30 months. This product does not contain an antimicrobial preservative. Any solution remaining in the vial following withdrawal of the required dose should be discarded. 6.4. Special precautions for storage: Do not freeze. 6.5. Nature and composition of immediate packaging: Cardboard box containing one glass vial of 10 ml with a bromobutyl rubber stopper and aluminum cap. 6.6. Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from its use: The above veterinary medicinal product or waste materials should be disposed of in accordance with national regulations. 7. MARKETING AUTHORIZATION HOLDER: June (UK) plc, 3 Tenterden Technical Business Centre, Tenterden, Kent TN30 3DS. 8. MARKETING AUTHORISATION NUMBER(S): UK: Vm 25296/4000. Ireland: VPA 1066/001/001. 9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION: 23 November 2006. 10. DATE OF REVISION OF THE TEXT: March 2008. PROHIBITION OF SALE, SUPPLY AND/OR USE: Legal Category LG4.P.O. Legal Category Ireland: V.P.