

## GENERAL

### 1. ORDERING

**How do I order?** VIL's preference, particularly for new customers, is that orders are made on the standard faxback form. This ensures accurate information is recorded relating to both the details of each order as well as customer information. This must be kept up to date to ensure continuing trouble free communication and prompt delivery. The Faxback can be down loaded from the website.

Nevertheless, VIL is pleased to take orders by office telephone, email or mobile for established customers.

### 2. SHIPPING

**How is Hypermune shipped?** Hypermune equine plasma is always stored frozen at  $-25^{\circ}\text{C}$  and wrapped in two layer bubble plastic to provide protection and hygiene. The bags are placed in special insulated boxes and packed with polystyrene void filler along with the appropriate documentation.

**In the UK and the rest of Europe** shippers which guarantee next day delivery are used whenever possible, but each is selected for its efficiency in a particular area.

**Outside the UK and Europe** the shortest shipping time available is selected even if that means dispatching outwith normal working hours or using an independant shipper.

To avoid potential delays which may impinge on weekends the preference is to dispatch frozen plasma Monday to Thursday within the UK and Monday to Wednesday outwith the UK.

Shipping out of the UK adds cost but this can be minimised on a per litre basis for orders of 5 litres as air freight is costed on a dimensional weight basis. This is further reduced on a per litre basis as the number of litres in each consignment increases.

**Will the plasma be frozen on arrival?** Validation studies using digital data loggers have confirmed that even a single litre retains a frozen core temperature at 24 hours in VIL's packaging. Multiples of up to 5 litres remain frozen longer than that, up to 48 hours and more depending on ambient temperatures.

**Can the plasma be re frozen?** If plasma arrives partially or even completely thawed it will not have deteriorated and can be re frozen. It is a sterile product and is more like "long life" milk, there being no bacteria to exploit thawing conditions. Validated stability studies have been satisfactorily completed on thawed plasma stored at  $+4^{\circ}\text{C}$  for 20 days.

However, it is not recommended that bags which have been thawed **and warmed to body temperature** are re frozen.

### 3. STORING

**What is the frozen shelf life?** It has been proven that Hypermune products can be stored frozen for in excess of two years from the date of production but current stability studies indicate that stability is robust for three years.

**What conditions should be provided for trouble free storage?** Although the defined storage temperature is  $-25^{\circ}\text{C} \pm 5^{\circ}\text{C}$  it is acceptable to store the frozen product in a domestic freezer at  $-18^{\circ}\text{C}$ . It is also very important that the plasma is kept in its bubble wrap in a dedicated box, basket or other suitable container in the freezer to ensure it is not bumped or knocked inadvertently. In this way damage occurring to the plastic of the plasma bag which can become brittle at low storage temperatures is avoided.

### 4. USAGE

**What is the best way to thaw the plasma?** Instructions on thawing are provided on the package insert. Hypermune has a very high content of proteins which are easily denatured by excess heat and from time to time investigations of problems encountered accidentally have revealed unusual causes such as:

1. A frozen litre being placed in the passenger side foot well of the car and the heater being turned on full.
2. A bag being left on the laboratory bench and the hot summer sun shining on to it.
3. A bag being allowed to float in a water bath under a stream of very hot tap water being added to the water bath.

**Hypermune products should not be exposed to temperatures above  $40^{\circ}\text{C}$ .**

**How do I know when it is at blood heat?** The bubble wrap should remain on the bag when initially placed in the water. From time to time, as it cools, the water can be topped up with warm water but the bag must **not** come into contact with hot tap water, even briefly. After five minutes the bubble wrap can be removed and periodically the bag picked up and inverted a few times to mix the thawed plasma near the bag surface with the cold plasma at its centre. As there is no single focus of heat source, convection will not occur to distribute heat by particle movement of the plasma. Once the bag is completely thawed it will have a "clammy" feel until it has acquired the temperature of the water bath throughout and is ready for transfusing.

**Is it essential to use a giving set?** It is absolutely essential to use a blood giving set which has a large mesh filter. This will trap any cryoprecipitate or fibrin strands and thus permit a smooth transfusion.

## TECHNICAL

**Is there likely to be a reaction from the foal?** Adverse reactions to plasma products are extremely rare in both human and veterinary transfusion medicine. It is essential, however, before using Hypermune or Hypermue-RE to read the package insert very carefully. Over the past 16 years VIL has supplied tens of thousands of litres of plasma but been asked investigate less than 0.1% of Suspect Adverse Reactions. **In all cases investigated no fault could be found with the quality of the plasma used.**

It is accepted in human medicine that acute immunological reactions to peanuts, shell fish etc are more often than not due to an idiosyncratic immune response rather than a defect in the causal agent and no doubt similar incidents can occur in animals. In addition evidence does suggest that drug incompatibilities or drugs used for chemical restraint may be implicated when complications arise as well as sub clinical disease or sub clinical physiological problems.

It is essential that administration is slow and careful monitoring takes place throughout the transfusion.

Veterinary Immunogenics Ltd has sponsored independent safety studies in compliance with regulatory requirements. It has also gathered data from field studies and much anecdotal evidence all of which confirm the safety of Hypermune products even when transfusions are repeated at short or relatively long intervals.

**Can Hypermune be used in donkey foals?** Yes, but adhere to the correct dose of 20ml/kg.

**My boss delivered a premature foal yesterday and ordered a bag of your plasma. How do I administer it?** Read the instructions very thoroughly and follow them methodically. Thaw the product carefully, ensuring it is warmed through to body temperature. Do not use chemical restraint for the foal. Do use a blood giving set and ensure only 20ml/kg is administered slowly monitoring heart and respiration carefully by placing and keeping one hand on the chest wall.

When the correct dose has been administered the giving set tap can be closed and the bag and set stored in the refrigerator overnight. At 24 hours after the first dose a second dose can be given using a new giving set spiked into the second port.

**I have thawed a bag of plasma and it is a green colour. Is it safe to use?** Yes. There are a number of donors which consistently give plasma with a green tinge which is not significant.

**I have thawed a bag of plasma and it is faulty because it has lumps in it.** Numerous small "white/grey" lumps which sink in the plasma are usually the result of excess heat denaturing the proteins and therefore should not be used. Stringy strands of mucoid material floating in the plasma is usually indicative of the plasma still not being

warmed thoroughly throughout to body temperature and will tend to block the filter in the giving set if used. In extreme cases the bag will be requested to be returned for investigation and a report issued by VIL.

**I have thawed a bag of plasma and it is faulty – it is leaking plasma.** A bag which has showed a leak when thawed should not be used. It should be emptied and posted back to VIL for investigation and a report issued following the investigation. VIL does not accept responsibility for bags broken or damaged after delivery.

**I have never used plasma before – please advise?** Read and follow the instructions carefully; do not use chemical restraint if at all possible and slowly administer the correct volume for the weight of foal, while monitoring heart and respiration. If there are additional queries after that please contact VIL again.

**The plasma was delivered late and is thawed. Is it still OK to use?** It is fine to use immediately, after warming to body temperature or to re freeze the plasma which has been in transit **for up to 4 days.**