

Additional Medical and Product information requested by CBS Hospital Customers

Why do you recommend warming the contents of the Octaplasma bag to reach approximately +37°C? Why is it important?

The objective of thawing any kind of plasma for transfusion is not just to get frozen FFP or Octaplasma to their respective liquid states.

Plasma comprises about 90% water. A cocktail of over 1,000 individual proteins plasma makeup 6-8% of plasma; mostly albumin (55-60%), (α , β and γ) globulins (35-38%) and fibrinogen (4-7%). There are also several vital regulatory proteins and coagulation factors (<1%) – as well as electrolytes (e.g., Na^+ and Cl^-), nutrients [e.g., sugars (glucose) and amino acids], fat (e.g., lipids), hormones (e.g., cortisol and thyroxine), wastes (e.g., urea), and dissolved gasses (e.g., O_2 and CO_2). Therefore, plasma is a complicated, natural, and multifunctional solution.

Plasma proteins have primary, secondary, and tertiary structures, shaping molecules with specialized functions under different physical conditions. In frozen plasma, these special functions of plasma proteins are in a static state and need to be regained through thawing, being eventually natural and optimal at around +37°C. Inadequately thawed plasma can result in the aggregation of plasma proteins (precipitate formation). The recommended thawing temperature helps plasma protein maintain its normal folding.

Therefore, Octaplasma must be allowed to be brought to 'at or around +37°C'. This is true for frozen products as it is for products in a liquid but refrigerated state. Octaplasma is a high-quality medicinal product. Thaw it adequately at +37°C, use it quickly, thereafter, and it is best not to under or overheat the product at any time.

What is the recommended approach to handling and storing previously thawed plasma?

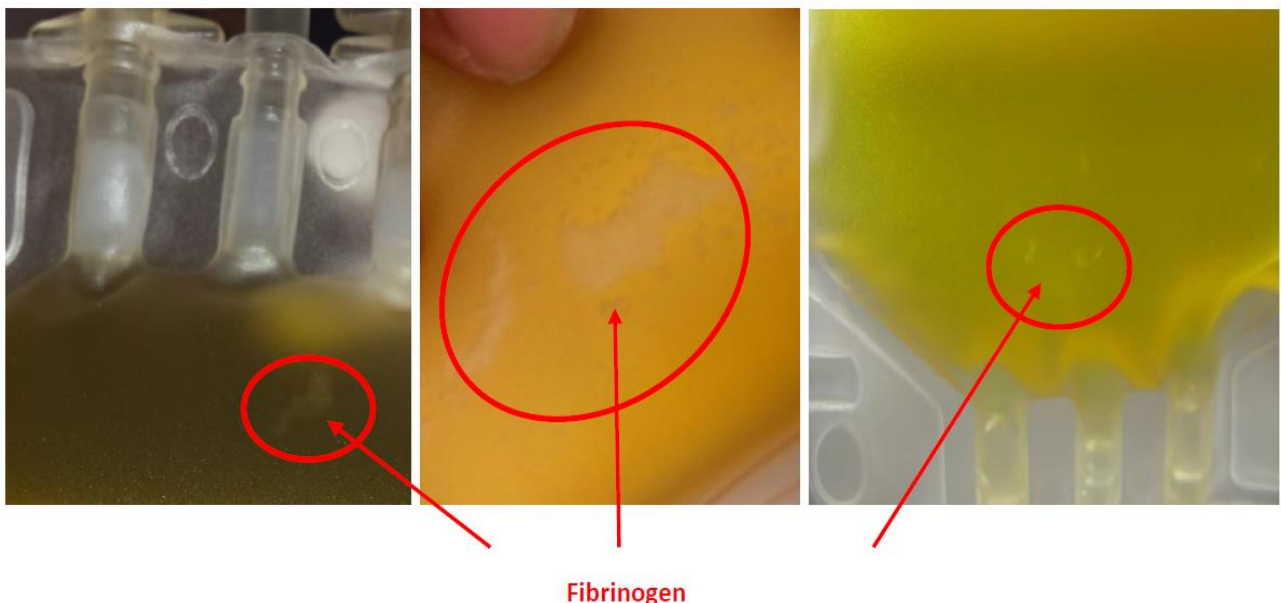
Octaplasma can be stored at $\leq -18^\circ\text{C}$ for up to 4 years after manufacturing. All coagulation-active products, including Octaplasma, should ideally be thawed shortly before use (within 1-2 hours) to ensure the best quality. If, however, the product cannot be administered after thawing, it can be stored at 2°C to 8°C for up to 5 days or at $+20^\circ\text{C}$ to 25°C for up to 8 hours. Pre-thawed, long-term-stored Octaplasma should therefore be used only as an exception in cases where time plays a crucial role, such as e.g., massive transfusions caused by major trauma.

If the thawed product cannot be used immediately, it is important to let the product reach 37°C, and then let the product rest at room temperature (temperature prevailing in a work area) to gradually cool down to reach ambient temperature (15°C to 25°C) before placing it in the fridge at 2°C to 8°C for up to 5 days of storage. This reduces the chance for protein precipitates to form later-especially after 3-5 days.

Is it safe to administer the product in the presence of precipitates in the bag after thawing?

When precipitation is visible in a thawed bag, thawing is deemed incomplete. This indicates the thawing time was either too short or the thawing temperature was low. See the example images below.

The precipitate like those seen in the pictures is fibrinogen/cryoprecipitate, generated due to 'cold precipitation', and goes again into solution when plasma is thawed completely.



When the thawing time is too short, plasma in the bag may be incompletely thawed and some ice pieces are still available. These ice pieces can be small and may not necessarily be visible. When an incompletely thawed bag is placed in the fridge, and subsequently taken out for use, local cold precipitation may occur, leading to fibrinogen precipitation as the ice may still be present in the bag.

When the plasma, upon rewarming to reach 37°C in a water bath becomes clear (i.e. fibrinogen/cryoprecipitate resolved), the product can be used. If the cryo-precipitate doesn't disappear, the product should be discarded. In general, the time required to dissolve the cryo-precipitate in a pre-thawed Octaplasma bag that was previously stored in the fridge may take anywhere between 7-12 minutes when placed in a circulating water bath.

What are the signs of denatured proteins in the bag and is it safe to administer the product?

When the temperature during thawing is too high such that the product temperature is higher than +37°C, some plasma proteins may be subject to denaturing. See the example image below.



This indicates that the thawing temperature is too high. Should denatured protein become visible, the product should be discarded.

For further information on product handling, please contact Octapharma Medical information by email at medinfo.canada@octapharma.com