BERIPLEX P/N 500 AND 1000 (HUMAN PROTHROMBIN COMPLEX) (ADULTS)  
ADVICE ON ADMINISTRATION

Please see www.beriplex.co.uk > UK healthcare professional > resources to access:
- Beriplex P/N dosage calculator smart phone app (which also contains reconstitution guide)
- The dosing and reconstitution guides provided in this document

What is Beriplex?

Beriplex, a prothrombin complex concentrate, is licensed for use in acquired deficiencies of factors II, VII, IX and X that occur following treatment with vitamin K antagonists such as warfarin and acenocoumarol.

Beriplex is a pooled plasma-derived product. The batch number of the Beriplex P/N MUST be recorded in order to maintain a link between the patient and the batch of the product. It is good practice to avoid mixing different batches in the same syringe, in case there is a reaction to an individual batch of product.

When is Beriplex indicated?

Beriplex is indicated if rapid correction of the deficiency is required, such as in situations of major bleeding or when immediate emergency surgery is required.

Dosing and prescription

Beriplex P/N is prescribed in “international units” (specifically for units of factor IX per kilogram body weight). Do NOT record as “IU” but write “units” to avoid prescription errors.

The dose should be calculated on an individual patient basis and will depend on the INR before treatment and the targeted INR, and the patient’s weight in kilograms (kg):

<table>
<thead>
<tr>
<th>Initial INR</th>
<th>Beriplex dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 – 1.9*</td>
<td>Approx 12.5 units / kg*</td>
</tr>
<tr>
<td>2.0 – 3.9</td>
<td>Approx 25 units / kg</td>
</tr>
<tr>
<td>4.0 – 6.0</td>
<td>Approx 35 units / kg</td>
</tr>
<tr>
<td>&gt; 6.0</td>
<td>Approx 50 units / kg</td>
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</tbody>
</table>

It is recommended that the maximum single dose should not exceed 5000 international units.

A helpful Beriplex P/N dosing guide is provided on page 6. This can also be accessed at www.beriplex.co.uk > UK healthcare professional > resources.

Once the appropriate dose for the patient has been calculated, this should be rounded to the nearest 500 international units (the transfusion laboratories generally stock 500 international unit and 1000 international unit vial sizes). If a calculated dose falls at the midpoint between two rounded doses, the dose should be rounded up rather than down, for example:

- Calculated dose: 2125 units = rounded dose 2000 units
- Calculated dose: 2800 units = rounded dose 3000 units
- Calculated dose: 1750 units = rounded dose 2000 units

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The rounded dose is then ordered from the transfusion laboratory.

**It is the rounded dose that is prescribed for the patient.**

Beriplex is prescribed in the patient’s drug kardex.

**Where and how to obtain Beriplex**

Beriplex issue does not require the authorisation of a haematologist.

- **Royal Infirmary** (telephone ext 27501/2):
  Beriplex is obtained from the transfusion laboratory upon telephoned request.

- **Western General Hospital** (telephone ext 31912):
  Beriplex is obtained from the transfusion laboratory via provision of a completed transfusion request form (no sample required). It is recommended that the clinician brings the completed request form in person to the transfusion laboratory as the Beriplex can then be issued immediately. If the Beriplex is collected some time after the request, the collector is asked to bring patient identification details with them (full name, date of birth and CHI) – this does not have to be a blood collection slip.

- **St John’s Hospital** (telephone ext 53354):
  Beriplex is obtained from the transfusion laboratory via provision of a completed transfusion request form (no sample required). It is recommended that the clinician brings the completed request form in person to the transfusion laboratory as the Beriplex can then be issued immediately. If the Beriplex is collected some time after the request, the collector is asked to bring patient identification details with them (full name, date of birth and CHI) – this does not have to be a blood collection slip.

A helpful hints guide will be issued from the transfusion laboratory with the product (see page 7).

**Reconstitution**

General instructions for the reconstitution of the product and its administration are provided by the manufacturer, CSL Behring, and should be followed carefully.

A helpful step-by-step product reconstitution guide is provided on page 5 and a copy of the same will be issued from the laboratory with the product. Full manufacturer’s instructions are enclosed along with the product.

Please follow the step-by-step reconstitution guidance to ensure swift and effective reconstitution and reduce risk of delay.

The product must not be mixed with other medicinal products, diluents or solvents.

**Administration**

It is good practice to avoid mixing different batches in the same syringe, in case there is a reaction to an individual batch of product.

The reconstituted product should be administered immediately. The reconstituted solution should
be administered intravenously (slow intravenous injection) at a rate of not more than 8 mLs per minute \(\text{(NB for patients with body weight less than 70 kg use administration rate of 0.12 mL / kg / minute)}\)

Due to the rate and volume to be infused, Beriplex is unable to be given via an infusion pump and will require manual administration by a nurse or doctor who is competent to administer an IV bolus.

The method of administration in elderly people (defined in the Summary of Product Characteristics as “over 65 years”) is equivalent to general recommendations. There is no experience in children or neonates.

**The effect of Beriplex and general requirement to administer concurrent vitamin K**

The correction of the vitamin K antagonist-induced impairment of haemostasis is reached 30 minutes after the injection and will persist for approximately 6-8 hours. If vitamin K is administered simultaneously, the effect is usually achieved within 6-8 hours. Repeated treatment with human prothrombin complex is not usually required when vitamin K has been administered.

Therefore administer 5 mg IV vitamin K along with Beriplex P/N, and check the PT and APTT 30 minutes following administration, as per the NHS Lothian Guide to Reversal of Oral Anticoagulation on Warfarin (based on National Plasma Product Expert Advisory Group protocol) which can be found at: [http://intranet.lothian.scot.nhs.uk/Directory/Haematology/policy/Documents/Warfarin%20Reversal.pdf](http://intranet.lothian.scot.nhs.uk/Directory/Haematology/policy/Documents/Warfarin%20Reversal.pdf)

If there is lack of correction further discussion is necessary with the on call haematologist.

**Contraindications**

There is a risk of thrombosis and caution should be taken if there is a history of previous thrombosis, angina pectoris, thrombotic stroke or recent myocardial infarction when the risks of administration of the product must be weighed against the correction of life-threatening bleeding.

Prothrombin complex concentrate should not be given in disseminated intravascular coagulation.

The product contains a trace of heparin and is contra-indicated if there is a known history of heparin-induced thrombocytopenia.

Infusion of prothrombin complex concentrate may worsen an underlying hypercoagulable state.

**Special warnings**

In patients receiving warfarin or vitamin K antagonists, Beriplex P/N should only be used when rapid correction of the anticoagulant effect is required, such as emergency bleeding or emergency surgery. In other cases, reduction of the dose of vitamin K antagonist and / or administration of vitamin K is usually sufficient.

If allergic or anaphylactic-type reactions occur, the administration of Beriplex P/N has to be stopped immediately.
There is a risk of thrombosis or disseminated intravascular coagulation (DIC) when patients are treated with human prothrombin complex concentrate, and particularly with repeated dosing. Patients given human prothrombin complex concentrate should be closely observed for signs or symptoms of DIC or thrombosis.

Close monitoring should be exercised when administering Beriplex P/N to patients with liver disease, patients in the post-operative period and those at increased risk of thrombosis.

Beriplex contains up to 343mg sodium, and this should be taken into consideration in patients on a controlled sodium diet.

**Virus safety**

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation / removal of viruses. However, the possibility of transmitting emerging viruses or other pathogens cannot be totally excluded.

**Further advice and resources**

For more advice regarding the administration of Beriplex P/N please contact the haematologist on call.

*Note: Approved by UHD D&T Committee Dec 2016 – subject to FAF3 application approval.*
Reconstitution Technique

Mix2Vial - Needle-Free Reconstitution and Transfer System

1. Prepare the vials
   - Unpack the product and diluent vial flip top cover and remove the vials.
2. Blue for the water
   - Open the Mix2Vial package by pulling away the lid.
   - Place the vial on a flat, hard surface and hold the vial upright.
3. Pull off the package
   - Carefully remove the package from the Mix2Vial set. Make sure that you only pull up the package and not the Mix2Vial set.
4. Invert the diluent vial
   - Place the product vial on a hard, flat surface. Invert the diluent vial with the flip top cover attached and push the transparent diluent straight down through the product vial.
5. Reconstitute on a hard, flat surface
   - Unpack the set.
6. Gently swirl the product vial until the product is fully dissolved. Do not shake.
7. Load the syringe
   - Draw air into an empty, sterile syringe while the product vial is upright. Connect the syringe to the Mix2Vial unit.
   - Inject air into the product vial.
   - While keeping the syringe-plunger pressed, invert the syringe until it is upside down and draw the concentrate into the syringe by pushing the plunger back slowly.
8. Beriplex® P/N
   - Rapid infusion rate - up to 80 ml/min
   - Flexible dosing - 3 presentations available
   - Mix2Vial needleless transfer device - minimises the risk of needle stick injury

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## Rapid Warfarin Reversal

### Beriplex® P/N Dosage Guide

#### Human Prothrombin Complex

<table>
<thead>
<tr>
<th>Body weight (kg):</th>
<th>Initial INR</th>
<th>2.0 - 3.9</th>
<th>4.0 - 6.0</th>
<th>&gt;6.0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ml</td>
<td>IU</td>
<td>ml</td>
<td>IU</td>
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<tr>
<td>30</td>
<td>30</td>
<td>750</td>
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<tr>
<td>&gt;100</td>
<td>100</td>
<td>2500</td>
<td>140</td>
<td>3500</td>
</tr>
</tbody>
</table>
Beriplex Administration – Helpful Tips

This plasma-derived blood product has been issued for your patient because they either have life / limb threatening bleeding or require emergency surgery. Beriplex must be administered to the patient as a priority. Maximal reversal of anticoagulation will be achieved within 30 minutes of administration.

1. The number of vials of Beriplex issued for your patient will have been calculated based on the patient’s INR and body weight.

2. Please refer to the step-by-step guidance on how to reconstitute Beriplex which will accompany each issue of the product (instructions are also found within each vial box).

3. Once reconstituted, Beriplex should be withdrawn from the vials into an empty syringe using the Luer lock fitting supplied.

4. The reconstituted solution should be administered to the patient immediately. Once reconstituted, Beriplex is stable for 24 hours at room temperature (maximum 25°C); however, from a microbiological point of view, the product should be used immediately.

5. Beriplex should be administered by slow intravenous bolus (not more than 8 mL / minute) (NB for patients with body weight less than 70 kg use administration rate of 0.12 mL / kg / minute)

Due to the rate and volume to be infused, Beriplex is unable to be given via an infusion pump and will require manual administration by a nurse or doctor who is competent to administer an IV bolus.

In many cases the volume required may result in more than one syringe load needing to be administered.

6. It is usually appropriate for intravenous vitamin K 5 – 10 mg to be prescribed at the same time as Beriplex to prevent a rebound rise in the INR once the effect of the Beriplex has worn off.

7. Repeat coagulation screen and INR should be checked at 30 minutes and 4-6 hours post Beriplex administration. In some cases additional doses of Beriplex or vitamin K may be required.

8. Contact the duty haematologist if further advice is required.

Beriplex is listed under “Prothrombin Complex, Dried” in the NHS Lothian IV Guide (intranet and hard-bound red folder).

The NHS Lothian Guide to Reversal of Oral Coagulation on Warfarin is found on the intranet at Directory > Haematology > Policy Documents > Warfarin Reversal

Advice on the Administration of Beriplex is found on the intranet at Directory > Haematology > Policy Documents > Beriplex Administration

The authors acknowledge NHS Forth Valley Haematology Department whose original document these ‘Helpful Tips’ are based on.