Our Ref: CJC/JP

21st November 1979

Department of Health and Social Security,
Medicines Division,
Finsbury Square House,
33/37a Finsbury Square,
London, EC2A 1PP

For the Attention of Mr. G. C. Taylor

Dear Sir,

PL 0231/0044

High Potency Factorate

Notification that formal documents for the above product were to be issued was made to us in your letter of 13th June, 1979. Your letter requested that a copy of any data sheets issued in connection with the product be forwarded to you. It is our intention to make this product available early in 1980 and in connection with this we have now finalised the data sheet text. Two copies are attached for your reference. We would like to point out that because of the specialised nature and use of the product, it is not our intention to include the text of this data sheet in the ABPI Compendium.

We trust this is in order.

Yours faithfully,
ARMOUR PHARMACEUTICAL CO. LTD.

C. J. COLLINS
Regulatory Affairs Manager

c.c.: Mr. R. Butchart
R78/16 File
DHSS File

Encs.

Licence Number: PL 0231/0044 **Your reference:** R80/83

Name of Product: HIGH POTENCY FACTORATE

Give the present particulars and the change or proposed change. If the particulars appear on the licence document itself, you should give them exactly as they are given on the licence, or as you propose they should be given. (The items in the lefthand column of (3) are usually specified on product licences.)

Present	Proposed
(i) selling or supplying product in the U.K. (ii) procuring the manufacture or assembly of the product for sale or supply in the U.K. (iii) importing or procuring the importation of the product.	As before with the addition of (iv) exporting the product.

(continue on a separate sheet if necessary)

Reason for the change

Commercial purposes.

I hereby make application for the above licence to be varied in accordance with the proposals given above.

Signed: GRO-C Date: 19th May, 1980

ARMOUR000510

ARMO0000046_0002

ARMOUR PHARMACEUTICAL COMPANY LIMITED, Eastbourne, East Sussex.

HIGH POTENCY FACTORATE DATA SHEET

PRESENTATION

Dried Human Antihaemophilic Fraction HIGH POTENCY FACTORATE is a stable lyophilised concentrate of Factor VIII (AHF, AHG) prepared from pooled human plasma. It conforms to the monograph for Dried Human Antihaemophilic Factor B. P.

Each vial contains the labelled amount of antihaemophilic activity in International Units (one International Unit is the activity equivalent to the average Factor VIII content of I ml aliquots of I67 samples of fresh normal plasma, as determined in an international collaborative study). Each vial also contains sufficient sodium chloride to make the reconstituted solution approximately isotonic when Water for Injections B: P. is added as directed.

USES

For use in therapy of classic haemophilia (Haemophilia A).

DOSAGE

HIGH POTENCY FACTORATE is for intravenous administration only. As a general rule one unit of Factor VIII activity per kg will increase by 2% the circulating Factor VIII level, and although dosage must be adjusted according to the needs of the patient (weight, severity of haemorrhage, presence of inhibitors) the following general dosages are suggested.

I. Overt bleeding

Initially 20 units per kg. of body weight followed by IO units per kg every eight hours for the first 24 hours and the same dose every I2 hours for the next 3 or 4 days. For massive wounds, give until bleeding stops and maintain with 20 units per kg 8-hourly to achieve a minimum Factor VIII level of 40%.

2. Muscle Haemorrhages

(a) Minor Haemorrhages in extremities or non-vital areas: IO units per kg. once a day for 2 or 3 days.

(b) Massive Haemorrhages in non-vital areas: IO units per kg. by infusion at I2 hour intervals for 2 days and then once a day for 2 more days.

(c) Haemorrhages near vital organs (neck, throat, subperitoneal), 20 units per kg. initially; then IO units per kg. every 8 hours. After 2 days the dose may be reduced by one-half.

3. Joint Haemorrhages

IO units per kg. every 8 hours for a day; then twice daily for I or 2 days. If aspiration is carried out, IO units per kg. just prior to aspiration with additional infusions of IO units per kg. 8 hours later and again on the following day.

4. Surgery

Dosages of 30 to 40 units per kg. body weight prior to surgery are recommended. After surgery 20 units per kg. every 8 hours should be administered. Close laboratory control to maintain the blood level of Factor VIII above 40% of normal for at least 10 days post-operatively is suggested.

5. Dental Extractions

For simple extractions a pre-operative dose of 20-25 units per kg. sufficient to raise the Factor VIII level to 50% should be given, followed by intravenous administration of tranexamic acid. For multiple extractions further doses of Factor VIII may be advisable 24 or 36 hours after the operation. (Dormandy 1977).

RECOMMENDED RECONSTITUTION

Reconstitute HIGH POTENCY FACTORATE using 30 ml Water for Injections B. P. using standard aseptic precautions.

Warm both diluent and HIGH POTENCY FACTORATE vials to between 20°C and 30°C. Direct diluent down the side of the vial and gently rotate the vial until contents are dissolved. DO NOT SHAKE VIAL. Vigorous shaking will cause frothing and prolong the reconstitution time. Complete solution usually takes approximately 10 minutes. The solution is now ready for administration. If a gel forms on reconstitution, the preparation should not be used. The solution should be used within three hours of reconstitution.

ADMINISTRATION

Standard aseptic techniques should be used at all times.

Intravenous Injection

Plastic disposable syringes are recommended with Factor VIII solution. The ground glass surfaces of all-glass syringes tend to stick with solutions of this type.

1. Attach a filter needle to a sterile disposable syringe. Insert filter needle into stopper of Factor VIII vial; inject air and withdraw the reconstituted solution from the vial.

2. Discard the filter needle and attach a suitable intravenous needle.

3. Administer solution by slow intravenous injection, at a rate comfortable to the patient, and not exceeding 2 ml per minute.

Intravenous Infusion

The infusion equipment used should comply with that described in sections 3 or 4 of British Standard 2463:1962, Transfusion Equipment for Medical Use.

1. Prepare solution of HIGH POTENCY FACTORATE as recommended under Reconstitution.

2. Attach suitable infusion set.

3. If more than one vial is to be administered to the same patient the infusion set may be transferred to a second vial.

4. When infusion of HIGH POTENCY FACTORATE is complete, the infusion set may be flushed with sterile isotonic saline to avoid loss of any of the reconstituted solution.

5. After use, discard infusion set, needles and vials together with any unused solution.

WARNING

Factor VIII is prepared from human plasma, each donation of which has been found negative for hepatitis B surface antigen (HBsAg) by the radioimmunoassay (RIA) method. In addition, each batch, after reconstitution as recommended, has been tested and found negative by the RIA method. However, since no completely reliable laboratory test is yet available to detect all potentially infectious plasma donations, the risk of transmitting viral hepatitis is still present.

SIDE EFFECTS

Products of this type are known to cause mild chills, nausea or stinging at the infusion site.

CONTRA-INDICATIONS

There are no known contra-indications to antihaemophilic fraction.

PRECAUTIONS

Factor VIII contains low levels of group A and B isohaemagglutinins. When large volumes are given to patients of blood groups A, B or AB, the possibility of intravascular haemolysis should be considered. Such patients should be monitored by means of haematocrit and direct Coombs test for signs of progressive anaemia.

PHARMACEUTICAL PRECAUTIONS

HIGH POTENCY FACTORATE is to be stored below 6°C. When stored as directed, it will maintain its labelled potency for the period indicated on the label.

LEGAL CATEGORY

P.O.M.

PACKAGE QUANTITIES

HIGH POTENCY FACTORATE is supplied in single dose vials (potency is stated on each vial label).

FURTHER INFORMATION

Haemophilia A, a hereditary disorder of blood coagulation occurring almost exclusively in males results in profuse bleeding in joints, muscles or internal organs as a result of minor trauma. The disease appears to be due to a deficiency of a specific plasma protein, antihaemophilic factor, Factor VIII: HIGH POTENCY FACTORATE provides temporary replacement of the missing clotting factor.

Affected individuals frequently require therapy following minor trauma. Surgery, when required in such individuals must be preceded by temporary correction of the clotting abnormality with fresh plasma transfusions, cryoprecipitate or by injections of Factor VIII concentrates. Advantages of the use of concentrates of Factor VIII are the avoidance of hyper-proteinaemia, overloading the circulatory system and possible kidney dysfunction resulting from large volume transfusions. Several different concentrations of Factor VIII have been used successfully. These range from Fraction I of Cohn to highly purified potent preparations. Dried Human Antihaemophilic Fraction-HIGH POTENCY FACTORATE is a purified preparation with lower levels of fibrinogen and other non-AHF proteins per international unit than "Intermediate Purity" AHF preparations.

PRODUCT LICENCE NUMBER
PL023I/0044