M E D I C I N E S A C T 1 9 6 8

AI000137/1

RENEWAL OF PRODUCT LICENCE

PRODUCT LICENCE No. 0231/0044

Granted to: Armour Pharmaceuticals Company Ltd
St Leonards House
St Leonards Road
Eastbourne, East Sussex
BN21 3YG

Date of grant 13 June 1979

The Licence granted under the above reference number in respect of the product, particulars of which are set out in Part 1 of the attached Schedule, is hereby renewed, subject to the further provisions set out or referred to in Part 2 of the said Schedule.

The Licence, as now renewed, will, unless previously suspended, revoked or varied as to the period of its validity, continue in force until the end of a period of five years from the date of renewal given below.

Date of renewal: 13 JUNE 1984

GRO-C

A person authorised to
sign on behalf of the
Secretary of State for
Social Services

11 October 1984

Department of Health and Social Security
Medicines Division
Market Towers
1 Nine Elms Lane
LONDON SW8 5NQ

AI000137/2

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Product Licence No. 0231/0044

SCHEDULE

Part 1 - PARTICULARS OF THE PRODUCTS TO WHICH THE LICENCE RELATES

1.	Name of Product:	High Potency Factorate
2.	Pharmaceutical form:	Lyophilised cake in a vial with vacuum for intravenous administration to human beings after reconstitution.
3.	Active constituents:	Dried Human Antihaemophilic Fraction BP 250 iu " " " " " 500 iu " " " " " 1000 iu " " " " " 2000 iu
4.	Uses:	Indications For use in therapy of classical haemophilia. Route of administration Intravenous
5.	Recommended dose and dosage schedule:	(a) Standard Dose 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. 1. Overt Bleeding Initially 20 units per kg of body weight followed by 10 units per kg every eight hours for the first 24 hours and the same dose every 12 hours for 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: 10 units per kg once a day for 2 or 3 days. (b) Massive haemorrhages in non-vital areas: 10 units per kg by infusion at 12 hour intervals for 2 days and then once a day for 2 more days.

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SCHEDULE

Part 1 - PARTICULARS OF THE PRODUCTS TO WHICH THE LICENCE RELATES

5. Recommended dose and dosage schedule:

(c) Haemorrhages near vital organs (neck, throat, subperitoneal): 20 units per kg initially; then 10 units per kg every 8 hours. After 2 days the dose may be reduced by one half.

3. Joint Haemorrhages

10 units per kg every 8 hours for a day; then twice daily for 1 or 2 days. If aspiration is carried out, 10 units per kg just prior to aspiration with additional infusions of 10 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.

(b) Children

It was demonstrated in a study using 8 month to 14 year old boys that 1 unit of AHF per kg body weight consistently produced an increase of 2% (of normal), which is of the same magnitudes as in adults.

(c) Other Special Groups

Patients with inhibitors to Factor VIII receiving treatment with HIGH POTENCY FACTORATE may require doses in excess of those usually recommended for specific types of haemorrhage and/or bleed.

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SCHEDULE

Part 1 - PARTICULARS OF THE PRODUCTS TO WHICH THE LICENCE RELATES

5. Recommended dose and dosage schedule cont'd:

(d) Administration

HIGH POTENCY FACTORATE is for intravenous administration only and should be reconstituted using Water for Injections BP as recommended under Dilution (see Pharmaceutical Particulars) using standard aseptic precautions.

Standard aseptic techniques should be used at all times.

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 HIGH POTENCY FACTORATE 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/minute.

(e) 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 Dilution.

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.

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SCHEDULE

Part 1 - PARTICULARS OF THE PRODUCTS TO WHICH THE LICENCE RELATES

5.	Recommended dose and dosage schedule: cont'd:	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.
6.	Contra-indications, Precautions and Warnings:	USE IN PREGNANCY As the disease occurs almost exclusively in males, the eventuality of a pregnant woman requiring treatment with Factor VIII is extremely rare. There is, therefore, very little experience of the use of Factor VIII in pregnant women. Consequently, there is no evidence either in human pregnancy or in animal work that administration of Factor VIII is free from hazard. CONTRAINDICATIONS There are no known contraindiations to antihaemophilic fraction. PRECAUTIONS Factor VIII contains low levels of group A and B isohaemaglutinins. 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.
7.	Legal Category:	PRESCRIPTION ONLY MEDICINE
8.	Method of retail sale or supply:	FOR HOSPITAL SUPPLY ONLY
9.	Manufacturer of dosage form:	Armour Pharmaceutical Company P O Box 511 Kankakee Illinois 60901 USA
10.	Dates of letters of variation to original licence:	16 April 1980, 31 July 1980, 31 July 1980 (2 variations), 14 October 1980, 8 August 1981 (2 variations), 5 April 1982, 6 April 1982, 15 August 1983.

DMC/15

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SCHEDULE

Part 2 - FURTHER PROVISIONS SUBJECT TO WHICH THE LICENCE HAS BEEN GRANTED

1. All the provisions of Part I of Schedule 1 of the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971 (SI 1971 No 972) as amended by the Medicines (Standard Provisions for Licences and Certificates) Amendment Regulations 1972 (SI 1972 No 1226), the Medicines (Standard Provisions for Licences and Certificates) Amendment Regulations 1974 (SI 1974 No 1523). The Medicines (Standard Provisions for Licences and Certificates) Amendment Regulations 1977 (SI 1977 No 675) and the Medicines (Standard Provisions for Licences and Certificates) Amendment (No 2) Regulations 1977 (SI 1977 No 1039) shall apply.

2. Leaflets issued with proprietary medicinal products shall comply with the requirements of the Medicines (Leaflets) Regulations 1977 (SI 1977 No 1055). Labels of medicinal products shall comply with the Medicines (Labelling) Regulations 1976 (SI 1976 No 1726) as amended by the Medicines (Labelling) Amendment Regulations 1977 (SI 1977 No 996).

3. The product(s) shall not be recommended to be used for any purposes other than those specified in Part 1 of this Schedule as Uses.

4. The specification of the constituent and of the finished product shall be in accordance with the information contained in the application for this product licence.

5. The product shall be manufactured only in accordance with the method given in the application for this product licence.