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

PRODUCT LICENCE NO. 0055/0107 has been granted under and subject to the provisions of the Medicines Act 1968 to

Miles Laboratories Limited
T/A Cutter Laboratories
Division of Miles Laboratories Limited
Stoke Court
Stoke Poges
Slough
Berkshire
SL2 4LY

in respect of the products, particulars of which are set out in Part 1 of the attached Schedule. The Licence is subject to the further provisions set out or referred to in Part 2 of the said Schedule.

This Licence, unless previously suspended, revoked or varied as to the period of its validity, shall continue in force until the end of a period of five years from the date on which it was granted.

Date granted: 18 FEBRUARY 1985

GRO-C: L Lucas

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

18 FEBRUARY 1985

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

MEDICINES ACT 1968

Product Licence No. 0055/0107

SCHEDULE

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

1.	Name of Product:	KOATE-HT
2.	Pharmaceutical form:	Koate-HT is a white lyophilised powder presented in vials containing approximately 250, 500, 1000 and 1500 International Units of Factor VIII, for reconstitution with Water for Injection.
3.	Active constituents:	Coagulation Factor VIII - (Heat treated) NLT 0.8 i.u./mg protein.
4.	Uses:	The treatment of classical haemophilia (Haemophilia A) in which there is a demonstrated deficiency of Factor VIII activity.
5.	Recommended dose and dosage schedule:	The following formulae provide a guide for dosage calculations: Expected Factor VIII increase (in % of normal) = $\frac{\text{iu administered x 2.0}}{\text{bodyweight (in kg)}}$ iu required = bodyweight (kg) x desired Factor VIII (% normal) x 0.5 All efforts should be made to follow the course of therapy with Factor VIII level assays. It may be dangerous to assume any certain level has been reached unless direct evidence is obtained.
6.	Contra-indications, Precautions and Warnings:	There are no specific contraindications to the use of Koate-HT. Precautions 1. Koate-HT is intended for the treatment of bleeding disorders arising from a deficiency of Factor VIII. This deficiency should be proven prior to administering Koate-HT, since no benefit may be expected from its use in treating other causes of haemorrhage. 2. After reconstitution, administer as promptly as possible and within 3 hours. Do

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SCHEDULE

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

6. Contra-indications, Precautions and Warnings: (continued)

not refrigerate after reconstitution. Note: the recommendation to administer promptly after reconstitution is intended to avoid the ill effect of any possible bacterial contamination occurring during reconstitution. Koate-HT, in the vial unopened, is sterile. It is fully stable, without potency loss for at least 24 hours at room temperature after reconstitution.

3. Administer only by the intravenous route.

4. A filter needle should always be used for transfer to syringe prior to administering.

5. Koate-H contains levels of blood group isoagglutinins which are not clinically significant when controlling minor bleeding episodes. When large or frequently repeated doses are required in patients of blood groups A, B or AB. The possibility of the onset of intravascular haemolysis should be considered.

6. Administration equipment and any reconstituted Koate-HT not used should be discarded.

Warnings

1. Allergic reactions including chills, fever and hypersensitivity reactions, may result from the administration of Factor VIII preparations.

2. When large or frequently repeated doses are required in patients of blood groups A, B or AB, there is a possibility of intravascular haemolysis. Should this condition occur leading to progressive anaemia, administration of serologically compatible red blood cells should be considered. Also, the administration of type specific cryoprecipitate has been recommended for maintaining adequate Factor VIII levels.

3. Massive doses of Factor VIII preparations may result in hyperfibrogenaemia.

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

6.	Contra-indications, Precautions and Warnings: (continued)	4. Koate-HT concentrate is a purified dried fraction of pooled plasma obtained from many donors. The presence of hepatitis viruses should be assumed and the hazard of administering Koate-HT should be weighed against the medical consequence of withholding it, particularly in persons who have had few previous transfusions of blood or blood products.
7.	Legal Category:	Prescription Only Medicine
8.	Method of retail sale or supply:	To haemophilia centres as a prescription item
9.	Manufacturer of dosage form:	Cutter Biological Division of Miles Laboratories Inc USA - Berkeley, California, USA - Clayton, North Carolina, USA

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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.

6. This product may be sold or supplied only in accordance with a prescription given by an appropriate practitioner.