

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

PRODUCT LICENCE No. 0055 / 0065 has been granted under and
subject to the provisions of the Medicines Act 1968 to

Miles Laboratories Ltd
T/A Cutter Laboratories (Division of Miles Laboratories Ltd)
Stoke Court
Stoke Poges
Slough
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: 16 August 1983

GRO-C: J Lucas

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

16 AUGUST 19 83

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

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

Product Licence No. 0055. / 0065

SCHEDULE

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

1. Name of Product: Antihæmophilic Factor (Human) KOATE
2. Pharmaceutical form: Sterile lyophilized powder for reconstitution with sterile water for injection.
3. Active constituents: Factor VIII concentrate which becomes the therapeutic agent upon reconstitution with the suitable volume of sterile water for injection.
4. Uses: Antihæmophilic Factor (Human) is indicated in the treatment of classical hæmophilia (hæmophilia 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) =
$$\frac{\text{IU administered} \times 2.0}{\text{bodyweight (in kg)}}$$

$$\text{IU required} = \text{bodyweight (kg)} \times \text{desired Factor VIII (\% normal)} \times 0.5$$
 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: Contraindications
 There are no specific contraindications to the use of Antihæmophilic Factor (Human).
Precautions
1. Antihæmophilic Factor (Human), Koate^R, is intended for treatment of bleeding disorders arising from a deficiency in Factor VIII. This deficiency should be proven prior to administering Koate, since no benefit may be expected from its use in treating other causes of hæmorrhage.
 2. After reconstitution, administer promptly (within 3 hours). Do not refrigerate after reconstitution.
 NOTE: The recommendation to administer promptly after reconstitution is intended to avoid the ill

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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.

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SCHEDULE

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

1. Name of Product: Antihaemophilic Factor (Human) KOATE
2. Pharmaceutical form: Sterile lyophilized powder for reconstitution with sterile water for injection.
3. Active constituents: Factor VIII concentrate which becomes the therapeutic agent upon reconstitution with the suitable volume of sterile water for injection.
4. Uses: Antihemophilic Factor (Human) is indicated in the treatment of classical hemophilia (hemophilia A) in which there is a demonstrated deficiency of Factor VIII activity.

The following formulae provide a guide for dosage calculations:

Expected Factor VIII increase (in % of normal) =
$$\frac{\text{IU administered} \times 2.0}{\text{bodyweight (in kg)}}$$

$$\text{IU required} = \text{bodyweight (kg)} \times \text{desired Factor VIII (\% normal)} \times 0.5$$

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:
Contraindications
There are no specific contraindications to the use of Antihaemophilic Factor (Human).
Precautions
 1. Antihaemophilic Factor (Human), Koate^R, is intended for treatment of bleeding disorders arising from a deficiency in Factor VIII. This deficiency should be proven prior to administering Koate, since no benefit may be expected from its use in treating other causes of haemorrhage.
 2. After reconstitution, administer promptly (within 3 hours). Do not refrigerate after reconstitution.
NOTE: The recommendation to administer promptly after reconstitution is intended to avoid the ill

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

6. Contra-indications
Precautions and Warnings:
- effect of any possible bacterial contamination occurring during reconstitution. Koate 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 be used prior to administering
5. Koate contains levels of blood group isoagglutinins which are not clinically significant when controlling relatively minor bleeding episodes. When large or frequently repeated doses are required in patients of blood groups A, B or AB, the possibility of intravascular haemolysis should be considered.
6. Administration equipment and any reconstituted Koate not used should be discarded.

Warning

Koate concentrate is a purified dried fraction of pooled plasma obtained from many paid donors. The presence of hepatitis viruses should be assumed and the hazard of administering Koate concentrate should be weighed against the medical consequence of withholding it, particularly in persons with 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 Laboratories Inc

A. Antihemophilic Factor (Human)
- Berkeley, California, USA
- Clayton, North Carolina, USA

B. Sterile Water for injection
- Chatanooga, Tennessee, USA