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PUBLIC HEALTH COMMITTEE

EUROPEAN PHARMACOPOEIA COMMISSION

GROUP OF EXPERTS NO. 6B

(HUMAN BLOOD AND BLOOD PRODUCTS)

CONCENTRATUM ANTI-HAEMOPHILICUM HUMANUM CRYODESICCATUM

Human Antihaemophilic Factor Concentrate Freeze-dried

Distribution

For action:

- Members of Group of Experts No. 6B (Human Blood and Blood Products)

Strasbourg

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* *Under the aegis of the Public Health Committee (Partial Agreement)*

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CONCENTRATUM ANTI-HAEMOPHILICUM HUMANUM CRYODESICCATUM

Human Antihaemophilic Factor Concentrate Freeze-dried

Human antihaemophilic factor concentrate is a freeze-dried preparation containing the coagulation factor VIII obtained from human plasma or from human antihaemophilic cryoprecipitate from donors satisfying the requirements prescribed in the monograph on Sanguis Humanus (Vol. III, page 344).

It may be prepared for example by extraction of the cryoprecipitate or the cryethanol-precipitate with buffer and fractionation by a non denaturing precipitate- or chromatographic-system.

After sterilisation by filtration the final solution is distributed into its final sterile glass containers in a manner so as to ensure freedom from microbiological contamination and immediately frozen. It is subsequently freeze-dried and the containers are sealed in vacuo or under nitrogen. No preservative is added during or after preparation.

When dissolved in the volume of water for injections stated on the label, the solution contains not less than 10 International Units of factor VIII activity per ml. The specific activity of the preparation is not less than 0,5 International Units per mg of protein.

CHARACTERS

A white or very pale yellow powder or friable solid.

IDENTIFICATION

Precipitation tests with species-specific antisera carried out on a freshly prepared solution in the volume of water for injections stated on the label show that the preparation contains only plasma proteins of human origin.

The assay for factor VIII serves also to identify the product.

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TESTS

Solubility It dissolves completely under gentle swirling within not more than 10 minutes in the volume of water for injections stated on the label at 20° to 25° C forming an almost colourless clear or slightly turbid solution. No clot forms within 3 hours of reconstitution when the solution is kept at 20° to 25° C.

pH (Vol. I, page 63) The pH of the reconstituted preparation is 6,9 ± 0,3.

HBs antigen When tested by radio-immunoassay it is shown to be free from hepatitis B surface antigen.

Abnormal toxicity (Vol. II, page 61) It complies with the test of abnormal toxicity of vaccines and sera. Use of the reconstituted preparation a volume equivalent to at least 6 International Units for each mouse and 60 International Units for each guinea-pig.

Sterility (Vol. II, page 53) It complies with the test for sterility.

Pyrogens (Vol. II, page 58) It complies with the test for pyrogens. Inject per kg of body weight a volume of the reconstituted preparation equivalent to at least 10 International Units.

Loss on drying (Vol. I, page 93) Not more than 2 % by drying for 24 hours at a pressure not exceeding 0.02 Torr.

Haemagglutinins anti-A and anti-B The reconstituted preparation diluted 1 in 256 does not show the presence of anti-A or anti-B haemagglutinins as determined by an indirect method such as that shown in the Annex (Vol. , page).

Total protein Dilute, if necessary, an accurately measured volume of the preparation to be examined, with water to obtain a solution containing about 100 mg of protein in 2 ml. To 2 ml of this solution in a round-bottomed centrifuge tube add 2 ml of a 7.5 per cent m/V solution of sodium molybdate R and 2 ml of a mixture containing one volume of nitrogen-free sulphuric acid R and 30 volumes of water. Shake, centrifuge for 5 min. decant the supernatant liquid and allow the inverted tube to drain on filter paper. Determine the nitrogen in the residue by the method of sulphuric digestion (Vol. I, page 117) and calculate the content of protein by multiplying by 6.25.

Specific activity Not less than 0,5 International Units of coagulation factor VIII activity per mg of protein.

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ASSAY

Estimate the factor VIII activity using the two-stage method (Vol. , page). A single-stage method may be used if it has been shown to give identical results to those obtained using the two-stage method, using the International Standard for Blood Coagulation Factor VIII (1) Concentrate as the standard.

STORAGE

Store protected from light at a temperature below 10° under vacuum or in an atmosphere of nitrogen in sterile containers sealed so as to exclude micro-organisms and moisture.

Expiry date When stored under the prescribed conditions it may be used up to 2 years from the date of the estimation of activity.

LABELLING

The labelling complies with the relevant national legislation and international agreements.

In addition the label on the container and the label on the package indicate:

- the amount of factor VIII in International Units in the container
- the volume of water for injections to be used to reconstitute the preparation
- that the preparation must be used immediately after reconstitution
- that the reconstituted solution should not be used if solution is incomplete or if a clot forms.

The label on the container or a leaflet included in the package indicates:

- that the contents must be used on one occasion only
- the name and quantity of any added substance

(1) The equivalence in International Units of factor VIII of the International Standard is stated from time to time by the World Health Organisation.