INSULIN INJECTION, ISOPHANE

Insulinum isophanum inyectabile

Isophane insulin injection complies with the monograph on Insulin preparations, injectable (0854) with the modifications prescribed below.

DEFINITION
Isophane insulin injection is a sterile suspension of bovine, porcine or human insulin, complexed with protamine sulphate or another suitable protamine.

PRODUCTION
Isophane insulin injection is prepared by carrying out the procedures described in the monograph on Insulin preparations, injectable (0854).

The amount of protamine is based on the known isophane ratio and is not less than the equivalent of 0.3 mg and not more than the equivalent of 0.6 mg of protamine sulphate for each 100 IU of insulin in the insulin-protamine complex.

CHARACTERS
A white or almost white suspension which on standing deposits a white or almost white sediment and leaves a colourless or almost colourless supernatant liquid; the sediment is readily resuspended by gently shaking. When examined under a microscope, the particles are seen to be rod-shaped crystals, the majority with a maximum dimension greater than 1 µm but rarely exceeding 60 µm, free from large aggregates.

IDENTIFICATION
Examine the chromatograms obtained in the Assay. The position of the peak due to insulin in the chromatogram obtained with the test solution corresponds to that of the principal peak obtained with the appropriate reference solution.

TESTS
Total zinc. Not more than 40.0 µg per 100 IU of insulin.

Determine by the method described in the monograph on Insulin preparations, injectable (0854).

Use the following test solution.

Test solution. Dilute a volume of the gently shaken preparation containing 200 IU to 25.0 ml with water R. Dilute if necessary to a suitable concentration (for example, 0.4 µg to 1.6 µg of Zn per millilitre) with water R.

INSULIN LISPLO

Insulinum lisprum

C_{257}H_{383}N_{65}O_{77}S_{6} \quad M_r 5808

DEFINITION
28^{b}-L-Lysine-29^{b}-L-proline insulin (human).

Insulin lispro is a 2-chain peptide containing 51 amino acids. The A-chain is composed of 21 amino acids and the B-chain is composed of 30 amino acids. It is identical in primary structure to human insulin, only differing in amino acid sequence at positions 28 and 29 of the B-chain. Human insulin is Pro(B28), Lys(B29), whereas insulin lispro is Lys(B28), Pro(B29). As in human insulin, insulin lispro contains 2 interchain disulphide bonds and 1 intrachain disulphide bond.

Content: 94.0 per cent to 104.0 per cent (dried substance).

By convention, for the purpose of labelling insulin lispro preparations, 0.0347 mg of insulin lispro is equivalent to 1 unit.

PRODUCTION
Insulin lispro is produced by a method based on recombinant DNA (rDNA) technology under conditions designed to minimise the degree of microbial contamination.

Prior to release the following tests are carried out on each batch of final bulk product, unless exemption has been granted by the competent authority.

Host-cell-derived proteins. The limit is approved by the competent authority.

Single-chain precursor. The limit is approved by the competent authority. Use a suitably sensitive method.