Description

Aqueous Insulin preparations containing methionine

The invention relates to an aqueous pharmaceutical formulation with an insulin, insulin analog or insulin derivative, and methionine; and also to its preparation, use for treating diabetes mellitus, and to a medicament for treating diabetes mellitus.

An increasing number of people around the world suffer from diabetes mellitus. Many of them are what are called type I diabetics, for whom replacement of the deficient endocrine insulin secretion is the only possible therapy at present. Those affected are dependent on insulin injections for life, usually several times a day. Type II diabetes contrasts with type I diabetes in that there is not always a deficiency of insulin, but in a large number of cases, especially at the advanced stage, treatment with insulin, where appropriate in combination with an oral antidiabetic, is considered the most advantageous form of therapy.

In healthy individuals, release of insulin by the pancreas is strictly coupled to the blood glucose concentration. Elevated blood glucose levels, like those occurring after meals, are quickly compensated by a corresponding rise in insulin secretion. In the fasting state, the plasma insulin level falls to a base line value which is sufficient to ensure a continuous supply of glucose to insulin-sensitive organs and tissues, and to keep hepatic glucose production low in the night. The replacement of the endogenous insulin secretion by exogenous, usually subcutaneous administration of insulin does not in general come close to the above-described quality of the physiological regulation of blood glucose. Frequently there are instances of blood glucose being thrown off-track, either upwardly or downwardly, and in their most severe forms these instances may be life-threatening. In addition, however, blood glucose levels which are elevated over years, without initial symptoms, constitute a considerable health risk. The large-scale DCCT study in the USA (The Diabetes Control and Complications Trial Research Group (1993), N. Engl. J. Med. 329, 977-986) showed unambiguously that chronically elevated blood glucose levels are responsible for the development of late diabetic complications. Late diabetic complications are microvascular and macrovascular