glargine. This formulation would allow patients to inject the same number of units of insulin glargine at one third the volume of injection.
Both insulin glargine formulations, U100 and U300, were expected to provide the same insulin exposure and the same effectiveness, i.e. time profiles.

SUMMARY OF THE INVENTION

In one aspect, there is provided an aqueous pharmaceutical formulation comprising 300 U/mL of insulin glargine being equimolar to 300 IU human insulin.

In one aspect, there is provided the use of an aqueous pharmaceutical composition comprising insulin glargine in a concentration of 300 U/ml in the manufacture of a medicament for treating Type I and Type II Diabetes Mellitus.

In one aspect, there is provided the use of an aqueous pharmaceutical composition comprising insulin glargine in a concentration of 300 U/ml in the manufacture of a medicament for extending the duration of exposure of a long acting insulin in the treatment of Type I and Type II Diabetes Mellitus.

In one aspect, there is provided the use of an aqueous pharmaceutical composition comprising insulin glargine in a concentration of 300 U/ml in the manufacture of a medicament for reducing the incidence of hypoglycaemia in the treatment of Type I and Type II Diabetes Mellitus in a patient with a long acting insulin.

In one aspect, there is provided the use of an aqueous pharmaceutical composition comprising insulin glargine in a concentration of 300 U/ml in the manufacture of a medicament for providing a peakless long acting basal insulin in the treatment of Type I and Type II Diabetes Mellitus.

In one aspect, there is provided the use of an aqueous pharmaceutical formulation as defined herein in the manufacture of a medicament for treating Type 1 Diabetes Mellitus or Type 2 Diabetes Mellitus.

DETAILED DESCRIPTION

Exposure and activity of insulin glargine U300, the test (T) medication, was tested in non-diabetic healthy subjects in euglycemic clamps for equivalence in exposure and activity to Lantus U100, the approved reference (R) product. To account for the long duration of action of insulin glargine after subcutaneous administration 30 hours were selected. Exposure was assessed from insulin glargine concentration time profiles after subcutaneous administration while activity was simultaneously assessed as glucose utilization per unit insulin.

A replicate design allowed limiting the number of subjects for assessing bioequivalence and variability as recommended by the FDA guideline "Guidance for Industry, Statistical Approaches to Establishing Bioequivalence".

The respective clinical study was expected to establish equivalence in exposure and activity.

A dose of 0.4 U/kg was selected for this study; it corresponds to the average basal insulin dose in patients. In non-diabetic healthy subjects this dose produces a sizeable elevation in plasma insulin concentration and a lasting glucose lowering effect that can be quantified in euglycemic clamp settings.

The replicate design favoured by guidelines requires two replicate single dose injections of either IP (R: Lantus® U100, T: insulin glargine U300) in predefined four way cross-over sequences (RTTR or TRRT) as allotted by the randomization plan. This was executed in Periods (P) 1 - 4 at four different days. As a result, each subject received two replicate single subcutaneous doses of 0.4 U/kg Lantus® U100 (R) and