Product: Insulin Glulisine (Apidra SoloStar); Insulin Glulisine (Apidra)
Strengths: 100 Units/mL Solution for Injection (SC) [BRP- 030]; 100 Units/mL Solution for Subcutaneous / Continuous SC Pump Infusion / Intravenous Injection (BR-1046)
Presentation: Insulin Glulisine (Apidra SoloStar) – Pre-filled Pen in 3mL Cartridge (Box of 5's); Insulin Glulisine (Apidra) – 10mL Type I Colorless Glass Vial (Box of 1's)
I: Treatment of adults, adolescents and children 6 years or older, with diabetes mellitus, where treatment with insulin is required.
D: The potency of this preparation is stated in units. These units are exclusive to Insulin Glulisine (Apidra) and are not the same as IU or the units used to express the potency of other insulin analogues. Insulin Glulisine (Apidra) should be used in regimens that include an intermediate or long-acting insulin or basal insulin analogue and can be used with oral hypoglycemic agents. The dose of Insulin Glulisine (Apidra) should be individually adjusted.
C: Hypersensitivity to the active substance or to any of the excipients listed. Hypoglycemia.
P: Transferring a patient to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (regular, neutral protamine Hagedorn [NPH], lente, long-acting, etc.), origin (animal, human, human insulin analogue) and/or method of manufacture may result in the need for a change in dose. Concomitant oral antidiabetic treatment may need to be adjusted.
Hyperglycemia: The use of inadequate doses or discontinuation of treatment, especially in insulin-dependent diabetic, may lead to hyperglycemia and diabetic ketoacidosis; conditions which are potentially lethal.
Hypoglycemia: The time of occurrence of hypoglycemia depends on the action profile of the insulins used and may, therefore, change when the treatment regimen is changed.
Medication errors: Medication errors have been reported in which other insulins, particularly long-acting insulins, have been accidentally administered instead of insulin glulisine. Insulin label must always be checked before each injection to avoid medication errors between insulin glulisine and other insulins.
Excipients: This medicinal product contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially 'sodium-free'. Insulin Glulisine (Apidra) contains metacresol, which may cause allergic reactions.
Int: Substances that may enhance the blood-glucose-lowering activity and increase susceptibility to hypoglycaemia include oral antidiabetic medicinal products, angiotensin converting enzyme (ACE) inhibitors, disopyramide, fibrates, fluoxetine, monoamine oxidase inhibitors (MAOIs), pentoxifylline, propoxyphene, salicylates and sulfonamide antibiotics.
Substances that may reduce the blood-glucose-lowering activity include corticosteroids, danazol, diazoxide, diuretics, glucagon, isoniazid, phenothiazine derivatives, somatropin, sympathomimetic medicinal products (e.g. epinephrine [adrenaline], salbutamol, terbutaline), thyroid hormones, estrogens, progestins (e.g. in oral contraceptives), protease inhibitors and atypical antipsychotic medicinal products (e.g. olanzapine and clozapine).
Beta-blockers, clonidine, lithium salts or alcohol may either potentiate or weaken the blood-glucose-lowering activity of insulin. Pentamidine may cause hypoglycaemia, which may sometimes be followed by hyperglycemia.
AE: Hypoglycemia (very common); Injection site reactions, Local hypersensitivity reactions (common); systemic hypersensitivity reactions (uncommon); Lipodystrophy (rare); Hyperglycemia (potentially leading to Diabetic ketoacidosis) [unknown].
Metabolism and nutrition disorders: Symptoms of hypoglycemia usually occur suddenly. They may include cold sweats, cool pale skin, fatigue, nervousness or tremor, anxiousness, unusual tiredness or weakness, confusion, difficulty in concentration, drowsiness, excessive hunger, vision changes, headache, nausea and palpitation. Hypoglycemia can become severe and may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or even death.
PK: Absorption and bioavailability - Pharmacokinetic profiles in healthy volunteers and diabetes patients (type 1 or 2) demonstrated that absorption of insulin glulisine was about twice as fast with a peak concentration approximately twice as high as compared to regular human insulin.
Obesity
Another phase I study with insulin glulisine and insulin lispro in a non-diabetic population in 80 subjects with a wide range of body mass indices (18-46 kg/m²) has demonstrated that rapid absorption and total exposure is generally maintained across a wide range of body mass indices. The time to 10% of total INS exposure was reached earlier by approximately 5-6 min with insulin glulisine.

PK: Distribution and elimination - The distribution and elimination of insulin glulisine and regular human insulin after intravenous administration is similar with volumes of distribution of 13 l and 22 l and half-lives of 13 and 18 minutes, respectively.
After subcutaneous administration, insulin glulisine is eliminated more rapidly than regular human insulin with an apparent half-life of 42 minutes compared to 86 minutes. In an across study analysis of insulin glulisine in either healthy subjects or subjects with type 1 or type 2 diabetes mellitus the apparent half-life ranged from 37 to 75 minutes (interquartile range). Insulin glulisine shows low plasma protein binding, similar to human insulin.
Special populations - *Renal impairment*
In a clinical study performed in non-diabetic subjects covering a wide range of renal function (CrCl >80 ml/min, 30-50 ml/min, <30 ml/min), the rapid-acting properties of insulin glulisine were generally maintained. However, insulin requirements may be reduced in the presence of renal impairment.
Hepatic impairment - The pharmacokinetic properties have not been investigated in patients with impaired liver function.
Elderly - Very limited pharmacokinetic data are available for elderly patients with diabetes mellitus.
Children and adolescents - The pharmacokinetic and pharmacodynamic properties of insulin glulisine were investigated in children (7-11 years) and adolescents (12-16 years) with type 1 diabetes mellitus. Insulin glulisine was rapidly absorbed in both age groups, with similar Tmax and Cmax as in adults (see section 4.2). Administered immediately before a test meal, insulin glulisine provided better postprandial control than regular human insulin, as in adults (see section 5.1). The glucose excursion (AUC0-6h) was 641 mg.h.dl-1 for insulin glulisine and 801 mg.h.dl-1 for regular human insulin.
PD: Mechanism of action - Insulin glulisine is a recombinant human insulin analogue that is equipotent to regular human insulin. Insulin glulisine has a more rapid onset of action and a shorter duration of action than regular human insulin. The primary activity of insulins and insulin analogues, including insulin glulisine, is regulation of glucose metabolism. Insulins lower blood glucose levels by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis in the adipocyte, inhibits proteolysis and enhances protein synthesis. Studies in healthy volunteers and patients with diabetes demonstrated that insulin glulisine is more rapid in onset of action and of shorter duration of action than regular human insulin when given subcutaneously. When insulin glulisine is injected subcutaneously, the glucose lowering activity will begin within 10-20 minutes. After intravenous administration, a faster onset and shorter duration of action, as well as a greater peak response were observed as compared with subcutaneous administration. The glucose-lowering activities of insulin glulisine and regular human insulin are equipotent when administered by intravenous route. One unit of insulin glulisine has the same glucose-lowering activity as one unit of regular human insulin.