Product: Insulin Glargine + Lixisenatide (Soliqua)
Strengths: 3.64 mg (eq. to 100 Units of Insulin Glargine)/ 50 mcg/mL [BR-1270]; 3.64 mg (eq. to 100 Units of Insulin Glargine)/ 33 mcg/mL [BR-1271]
Presentation: Type I colorless glass cartridge x 3mL. Each cartridge is assembled into a disposable pen (Box of 1's, 3's, and 5's)
I: indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycemic control as an adjunct to diet and exercise in addition to metformin with or without SGLT-2 inhibitors.
D: Insulin Glargine + Lixisenatide (Soliqua) 100 units/mL + 50 mcg/mL pre-filled pen delivers dose steps from 10-40 units of insulin glargine in combination with 5-20 mcg lixisenatide [Soliqua (10-40) pen]. Insulin Glargine + Lixisenatide (Soliqua) 100 units/mL + 33 mcg/mL pre-filled pen delivers dose steps from 30-60 units of insulin glargine in combination with 10-20 mcg lixisenatide [Soliqua (30-60) pen]. Insulin Glargine + Lixisenatide (Soliqua) should be injected once a day within one hour prior to a meal. It is preferable that the prandial injection is performed before the same meal every day, when the most convenient meal has been chosen.
C: Hypersensitivity to the active substance or to any of the excipients listed.
W/P: Insulin Glargine + Lixisenatide (Soliqua) should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Hypoglycemia was the most frequently reported observed adverse reaction during treatment with Insulin Glargine + Lixisenatide (Soliqua). Hypoglycemia may occur if the dose of Insulin Glargine + Lixisenatide (Soliqua) is higher than required; Use of GLP-1 receptor agonists has been associated with a risk of developing acute pancreatitis and may be associated with gastrointestinal adverse reactions. Insulin Glargine + Lixisenatide (Soliqua) has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis and therefore, the use of Insulin Glargine + Lixisenatide (Soliqua) is not recommended in these patients; Insulin Glargine + Lixisenatide (Soliqua) is not recommended in patients with severe renal impairment or end-stage renal disease; Cases of pulmonary aspiration have been reported in patients receiving GLP-1 receptor agonists undergoing general anaesthesia or deep sedation. Therefore, the increased risk of residual gastric content due to delayed gastric emptying should be considered prior to performing procedures with general anaesthesia or deep sedation; Patients treated with Insulin Glargine + Lixisenatide (Soliqua) should be advised of the potential risk of dehydration. Insulin Glargine + Lixisenatide (Soliqua) is not recommended during pregnancy, in women of childbearing potential not using contraception and breast-feeding women.
Int: No interaction studies with Insulin Glargine + Lixisenatide (Soliqua) have been performed. The information given below is based on studies with the monocomponents.
AE: The most frequently reported adverse reactions during treatment with Insulin Glargine + Lixisenatide (Soliqua) were hypoglycemia and gastrointestinal adverse reactions.
Hypoglycemia (very common); Dizziness, Nausea, Diarrhea, Vomiting, and Injection site reactions (common); Nasopharyngitis, Upper respiratory tract infection, Urticaria, Headache, Dyspepsia, Abdominal Pain, Cholelithiasis, Cholecystitis, and Fatigue (uncommon); Delayed gastric emptying (rare); Cutaneous amyloidosis Lipodystrophy (not known).
PK: Absorption - The insulin glargine/lixisenatide ratio has no relevant impact on the PK of insulin glargine and lixisenatide in Insulin Glargine + Lixisenatide (Soliqua). There are no clinically relevant differences in the rate of absorption when lixisenatide as monotherapy is administered subcutaneously in the abdomen, deltoid, or thigh.
Distribution - The apparent volume of distribution of lixisenatide after subcutaneous administration of insulin glargine/lixisenatide combinations (Vz/F) is approximately 100 L. The apparent volume of distribution of insulin glargine after subcutaneous administration of the insulin glargine/lixisenatide combinations (Vss/F) is approximately 1700 L.
Biotransformation - A metabolism study in diabetic patients who received insulin glargine alone indicates that insulin glargine is rapidly metabolized at the carboxyl terminus of the B chain to form two active metabolites, M1 (21A-Gly-insulin) and M2 (21A-Gly-des-30B-Thrinsulin). In plasma, the principal circulating compound is the metabolite M1. The pharmacokinetic and pharmacodynamic findings indicate that the effect of the subcutaneous injection with insulin glargine is principally based on exposure to M1.
Elimination - As a peptide, lixisenatide is eliminated through glomerular filtration, followed by tubular reabsorption and subsequent metabolic degradation, resulting in smaller peptides and amino acids, which are reintroduced in the protein metabolism. After single subcutaneous administration of the insulin glargine/lixisenatide combination, the mean apparent clearance (CL/F) of insulin glargine was approximately 120 L/h. After multiple-dose subcutaneous administration of Lixisenatide in patients with type 2 diabetes, mean terminal half-life was approximately 3 hours and the mean apparent clearance (CL/F) about 35 L/h.
PD: Mechanism of Action - Insulin Glargine + Lixisenatide (Soliqua) combines two active substances with complementary mechanisms of action to improve glycemic control: insulin glargine, a basal insulin analogue (mainly targeting fasting plasma glucose), and lixisenatide, a GLP-1 receptor agonist (mainly targeting postprandial glucose).
Insulin glargine: The primary activity of insulin is regulation of glucose metabolism. Insulin and its analogues lower blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, and by inhibiting hepatic glucose production. Insulin inhibits lipolysis and proteolysis and enhances protein synthesis.
Lixisenatide: Lixisenatide is a GLP1 receptor agonist. The GLP-1 receptor is the target for native GLP-1, an endogenous incretin hormone that potentiates glucose dependent insulin secretion from beta cells and suppresses glucagon from alpha cells in the pancreas. Lixisenatide stimulates insulin secretion when blood glucose is increased but not at normoglycemia, which limits the risk of hypoglycemia. In case of hypoglycemia, the rescue mechanism of glucagon secretion is preserved. A preprandial injection of Lixisenatide also slows gastric emptying thereby reducing the rate at which meal derived glucose is absorbed and appears in the circulation.

Date of Revision: Oct 2024