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Dulaglutide

Updated: April 10, 2019.

OVERVIEW

Introduction

Dulaglutide is a recombinant DNA produced polypeptide analogue of human glucagon-like peptide-1 (GLP-1) which is used in combination with diet and exercise in the therapy of type 2 diabetes, either alone or in combination with other antidiabetic agents. There have been no published reports of hepatotoxicity attributed to dulaglutide therapy.

Background

Dulaglutide (doo" la gloo' tide) is a glucagon-like peptide-1 (GLP-1) analogue that acts like the native gastrointestinal hormone (incretin) to increase insulin secretion. Dulaglutide reproduces the activity of GLP-1, binding to specific receptors on pancreatic beta cells and increasing insulin secretion, which can lead to improvement of glycemic control in patients with type 2 diabetes. Dulaglutide, like other GLP-1 analogues, also causes weight loss which may contribute to its clinical effects. Dulaglutide is a recombinant DNA produced polypeptide that shares 97% homology to endogenous human GLP-1(7-37), but has an amino acid substitution which makes it resistant to DPP-4 degradation and thus extends its half-life in serum. In addition, the GLP-1 like polypeptide is linked to an Fc fragment of human IgG4 which further prolongs its serum half-life and duration of activity. Dulaglutide, like other GLP-1 analogues, must be given parenterally. Dulaglutide was approved for use in the United States in 2014 and current indications are for management of glycemic control in adults with type 2 diabetes in combination with diet and exercise, with or without other oral hypoglycemic agents. Dulaglutide is available under the brand name Trulicity in solution for subcutaneous injection in prefilled, single dose pens or syringes (0.75 and 1.5 mg/0.5 mL). The typical initial dose is 0.75 mg once weekly, which can be increased to 1.5 mg weekly. Dulaglutide is generally well tolerated, but side effects can be dose limiting and include nausea [~20%], vomiting [~5%], diarrhea [~12%], abdominal pain, decreased appetite, dyspepsia and fatigue. Rare side effects include pancreatitis [0.1-0.3%], hypoglycemia and hypersensitivity reactions.

Hepatotoxicity

In large clinical trials, serum enzyme elevations were no more common with dulaglutide therapy than with placebo or comparator agents, and no instances of clinically apparent liver injury were reported. Since licensure, there have been no published case reports of hepatotoxicity due to dulaglutide and the product label does not list liver injury as an adverse event. Thus, liver injury due to dulaglutide must be rare, if it occurs at all.

Mechanism of Injury

Dulaglutide is a polypeptide and is metabolized to amino acids by serum and tissue proteases, and is unlikely to have any direct hepatotoxic potential. Dulaglutide acts through the incretin pathway to affect glucose metabolism and, thus, is often grouped with other incretin-based antidiabetic mediations such as the DPP-4 inhibitors, sitagliptin, saxagliptin and linagliptin, and other GLP-1 analogues such as exenatide, liraglutide and albiglutide which are also discussed in LiverTox.

References regarding the hepatotoxicity and safety of dulaglutide are given with the Overview section of the GLP-1 Analogues.

Drug Class: Antidiabetic Agents

Other Drugs in the Subclass, Incretin-Based Drugs, Glucagon-Like Peptide-1 (GLP-1) Analogues: Albiglutide, Exenatide, Liraglutide, Lixisenatide, Semaglutide

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Dulaglutide – Trulicity®

DRUG CLASS

Antidiabetic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Dulaglutide	923950-08-7	Protein	Complex Polypeptide