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NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Lixisenatide. [Updated 2019 Apr 10].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Lixisenatide

Updated: April 10, 2019.

OVERVIEW

Introduction

Lixisenatide 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. Therapy with lixisenatide has not been associated with serum enzyme elevations or with episodes of clinically apparent liver injury.

Background

Lixisenatide (lix" i sen' a tide) is a glucagon-like peptide-1 (GLP-1) analogue (also called a GLP-1 receptor agonist) that acts like the native gastrointestinal hormone (incretin) to increase insulin secretion. Lixisenatide, like other GLP-1 analogues, also suppress glucagon production and slows gastric emptying, features that may increase the beneficial effects in type 2 diabetes. Lixisenatide is a recombinant DNA-produced polypeptide that is 44 amino acids in length with a single proline substitution and a modified C-terminus of six lysine molecules that makes it relatively resistant to degradation by dipeptidyl peptidase 4 (DPP4) and extends its half-life allowing for once daily dosing. In multiple preregistration clinical trials, lixisenatide was shown to improve glycemic control and lower HbA1c levels in patients with inadequately controlled type 2 diabetes. Lixisenatide was approved in the United States in 2016 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 or insulin. Lixisenatide is available under the brand name Adlyxin in multiuse prefilled pens (50 and 100 μg/mL). The recommended starting dose is 10 μg once daily which after 2 weeks can be increased to 20 μg once daily. A fixed combination of lixisenatide (33 μg/mL) with insulin glargine (100 units/mL) is also available under the brand name Soliqua (100/33). Lixisenatide is generally well tolerated, but side effects can be dose limiting and include injection site reactions, diarrhea, nausea, vomiting, dizziness, headache, fatigue and hypoglycemia. Rare adverse events include pancreatitis, severe hypoglycemia, acute renal injury and hypersensitivity reactions.

Hepatotoxicity

In large clinical trials, serum enzyme elevations were no more common with lixisenatide therapy than with placebo or comparator agents. In pooled safety analyses of more than 5000 patients, ALT elevations above 3 times the upper limit of normal occurred in 0.6% of both lixisenatide and placebo groups and no instances of treatment related clinically apparent liver injury were reported. Since licensure, there have been no published case reports of hepatotoxicity due to lixisenatide and the product label does not list liver injury as an adverse event. Thus, liver injury due to lixisenatide, as with other GLP-1 analogues, must be rare, if it occurs at all.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

Lixisenatide is a polypeptide and is metabolized to amino acids by serum and tissue proteases, and is unlikely to have any direct hepatotoxic potential. Lixisenatide 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, dulaglutide and albiglutide which are also discussed in LiverTox.

References regarding the hepatotoxicity and safety of lixisenatide 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, Dulaglutide, Exenatide, Liraglutide, Semaglutide

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Lixisenatide – Adlyxin®

DRUG CLASS

Antidiabetic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Lixisenatide	320367-13-3	Protein	Complex Polypeptide