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Alogliptin

Updated: January 3, 2018.

OVERVIEW

Introduction

Alogliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor which is used in combination with diet and exercise in the therapy of type 2 diabetes, either alone or in combination with other oral hypoglycemic agents. Alogliptin has been reported to cause liver injury, but the characteristics and details of the injury have not been defined in the published literature.

Background

Alogliptin (al" oh glip' tin) is an inhibitor of dipeptidyl peptidase-4, which is the major enzyme responsible for the degradation of glucagon-like peptide-1 (GLP-1), an important gastrointestinal hormone (incretin) that increases glucose dependent insulin secretion by the pancreas. By prolonging the effect of GLP-1, alogliptin increases insulin levels and lowers blood glucose and helps in glycemic control in patients with type 2 diabetes. Alogliptin was approved for use in the United States in 2013 and was the fourth DPP-4 inhibitor introduced into clinical practice. The current indications are for management of glycemic control in type 2 diabetes used in combination with diet and exercise, with or without other oral hypoglycemic agents or insulin. Alogliptin is available in tablets of 6.25, 12.5 and 25 mg under the brand name Nesina and in fixed combinations with metformin (12.5/500 mg and 12.5/1000 mg) under the name Kazano and with pioglitazone (various dose combinations) under the name Oseni. The typical dose of alogliptin in adults is 25 mg once daily. Adverse reactions to alogliptin are not common, but may include headache, nausea, rash and hypersensitivity reactions. Hypoglycemia is uncommon with alogliptin alone (<1%), but occurs in higher rates when it is combined with other oral hypoglycemic agents. Alogliptin has also been linked to rare instances of acute pancreatitis that can be severe and even fatal.

Hepatotoxicity

Liver injury due to alogliptin is rare. In large clinical trials, serum enzyme elevations were uncommon (1% to 3%) and no greater than with comparator arms or placebo. In these studies, no instances of clinically apparent liver injury with jaundice were reported. Since licensure, instances of serum enzyme elevations and acute hepatitis including acute liver failure attributed to alogliptin have been reported to the FDA and the sponsor. These cases have not been reported in the literature and the clinical features have not been defined. Cases of clinically apparent acute liver injury have been reported with other DPP-4 inhibitors such as sitagliptin and saxagliptin. The latency to onset was typically within 2 to 12 weeks of starting and the pattern of liver enzyme elevations was usually hepatocellular. Immunoallergic features were often present. Most cases were self-limited in course and rapidly reversed once the medication was stopped.

Likelihood score: E* (unproven but suspected cause of acute, idiosyncratic liver injury).

Mechanism of Injury

The cause of liver injury during alogliptin or other DPP-4 inhibitor therapy is not known. Alogliptin is mostly excreted unchanged and only a small proportion (<10%) is metabolized in the liver. Alogliptin has minimal drug-drug interactions.

Outcome and Management

The instances of liver injury associated with the DPP-4 inhibitors have ranged from mild self-limited serum enzyme elevations to clinically apparent hepatitis and acute liver failure. However, the details of cases with liver injury have not been published. Routine monitoring of serum aminotransferase levels is not recommended but prompt testing for liver test abnormalities is recommended for patients reporting symptoms that may indicate liver injury. The similarity in chemical structure among the DPP-4 inhibitors suggests that there may be cross sensitivity to hepatic injury among the different agents, but this has not been reported. However, the other common antidiabetic medications in use should be tolerated without increased risk of liver injury.

References regarding the hepatotoxicity and safety of the DPP-4 inhibitors are given in the Overview section of DPP-4 Inhibitors (updated 03 January 2018).

Drug Class: Antidiabetic Agents, Incretin-Based Drugs

Other Drugs in the Subclass, Dipeptidyl Peptidase-4 (DPP-4) Inhibitors: Linagliptin, Saxagliptin, Sitagliptin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Alogliptin – Nesina®

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
Alogliptin	850649-62-6	C18-H21-N5-O2.C7-H6-O2