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Saxagliptin

Updated: January 3, 2018.

OVERVIEW

Introduction

Saxagliptin 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. Saxagliptin is a relatively new medication and has yet to be implicated in causing clinically apparent liver injury.

Background

Saxagliptin (sax' a 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, saxagliptin increases insulin levels and lowers blood glucose, thereby improving glycemic control in patients with type 2 diabetes. Saxagliptin was approved for use in the United States in 2009 and was the second DPP-4 inhibitor introduced into clinical practice. Its 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. Saxagliptin is available in tablets of 2.5 and 5 mg under the brand name Onglyza and as a fixed dose combination with metformin under the name Kombiglyze and with dapagliflozin under the name Qtern. The typical dose of saxagliptin in adults is 2.5 to 5 mg once daily. Adverse reactions to saxagliptin are not common, but may include headache, nausea, allergic reactions and rash. Hypoglycemia is uncommon with saxagliptin alone (<1%), but occurs in higher rates when it is combined with other oral hypoglycemic agents. Rare side effects reported with saxagliptin as with other DPP-4 inhibitors include bullous pemphigoid, severe arthralgias, acute pancreatitis and hypersensitivity reactions.

Hepatotoxicity

In large clinical trials, rates of serum enzyme elevations were similar with saxagliptin therapy (<1%) as with placebo, and no instances of clinically apparent liver injury were reported. Nevertheless, postmarketing experience suggests that some DPP-4 inhibitors can cause hepatic enzyme elevations and rare instances of clinically apparent acute liver injury. However, instances of hepatotoxicity due to saxagliptin have yet to be published.

Likelihood score: E* (unproven but suspected rare cause of clinically apparent liver injury).

Mechanism of Injury

The cause of possible liver injury during saxagliptin therapy is not known. The drug is metabolized by the liver, largely by the cytochrome P450 system (CYP 3A4), and a toxic or immunogenic intermediate of metabolism might be produced that could cause liver injury.

Outcome and Management

The instances of liver injury associated with the DPP-4 inhibitors have been rare and self-limited, and have resolved rapidly and completely with stopping the medication. The similarity in activity 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: Alogliptin, Linagliptin, Sitagliptin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Saxagliptin – Onglyza®

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
Saxagliptin	945667-22-1	C18-H25-N3-O2.H2O