U.S. National Library of Medicine
National Center for Biotechnology Information

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-. Irbesartan. [Updated 2017 Jan 13].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Irbesartan

Updated: January 13, 2017.

OVERVIEW

Introduction

Irbesartan is an angiotensin II receptor blocker used alone or in combination with other agents in the therapy of hypertension and diabetic nephropathy. Irbesartan is associated with a low rate of transient serum aminotransferase elevations and has been linked to rare instances of acute liver injury.

Background

Irbesartan (ir" be sar' tan) was the third angiotensin II receptor blocker (ARB) to be approved for use in the United States and is still widely used for therapy of hypertension. Irbesartan inhibits the renin-angiotensin system by blocking the angiotensin II type 1 receptor (AT1), which prevents the vasoconstriction and volume expansion induced by circulating angiotensin II and which accounts of its antihypertensive activity. Irbesartan was approved for use in the United States in 1997 for hypertension and indications were subsequently expanded to include diabetic nephropathy. Ibresartan is available in 75, 150 and 300 mg tablets generically and under the trade name Avapro. Fixed combinations of irbesartan with hydrochorothiazide are also available (Avalide and others). The typical dose of irbesartan in adults in 150 or 300 mg once daily, and it is used long term. Irbesartan is also available in fixed combinations with hydrochlorothiazide (Avalide). Side effects are uncommon, but can include headache, dizziness, fatigue, cough and gastrointestinal upset. Many ARBs, but not specifically ibresartan, have been implicated in rare instances of a severe sprue-like enteropathy that presents with chronic diarrhea and weight loss with villous flattening and atrophy on intestinal biopsy. This syndrome does not improve to corticosteroids or to a gluetn-free diet, but does resolve promptly with stopping the angiotensin receptor blocker. This side effect is most common with olmesartan.

Hepatotoxicity

Irbesartan has been associated with a low rate of serum aminotransferase elevations (<2%) that in controlled trials was no higher than with placebo therapy. These elevations were transient and rarely required dose modification. Rare instances of clinically apparent acute liver injury have been reported in associated with irbesartan therapy. The onset is usually within 1 to 8 weeks of starting therapy and the serum enzyme pattern is typically hepatocellular with an acute hepatitis-like clinical syndrome. In some instances, cholestasis has developed which can be prolonged and relapsing, but irbesartan therapy has not been associated with vanishing bile duct syndrome or chronic liver injury. Immunoallergic manifestations (rash, fever, eosinophilia) are not common, nor is autoantibody formation. Serum aminotransferase levels may also be raised during ARB therapy due to fatty liver and steatohepatitis in patients who develop the severe ARB-related enteropathy.

Likelihood score: C (Probable rare cause of clinically apparent liver injury).

Mechanism of Injury

The cause of the minor serum aminotransferase elevations and the acute liver injury associated with irbesartan is not known, but resembles idiosyncratic liver injury due to a hypersensitivity reaction. Irbesartan is metabolized by the liver via the cytochrome P450 system, predominantly by CYP 2C9.

Outcome and Management

The instances of acute liver injury reported with irbesartan use have been self limited and have not resulted in acute liver failure or chronic liver injury. While corticosteroids have been used in cases of severe cholestasis due to ARBs, their efficacy has not been shown and their use is best avoided. Patients with irbesartan induced acute liver injury should probably avoid use of other ARBs, although cross sensitivity to liver injury among the members of this class of agents has not been shown.

References on the safety and potential hepatotoxicity of irbesartan are given in the Overview section on the angiotensin II receptor antagonists.

Drug Class: Antihypertensive Agents, Angiotensin II Receptor Antagonists

Other Drugs in the Subclass, Angiotensin II Receptor Antagonists: Azilsartan, Candesartan, Eprosartan, Losartan, Olmesartan, Telmisartan, Valsartan

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Irbesartan – Avapro®

DRUG CLASS

Angiotensin II Receptor Antagonists

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Irbesartan	138402-11-6	C25-H28-N6-O