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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-. Carvedilol. [Updated 2017 Jan 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Carvedilol

Updated: January 15, 2017.

OVERVIEW

Introduction

Carvedilol is a unique antihypertensive medication with activity against both alpha- and beta-adrenergic receptors. Carvedilol has been linked to at least one instance of clinically apparent liver injury.

Background

Carvedilol (kar' ve dil" ol) is a unique beta-blocker and antihypertensive agent that has both alpha- and beta-adrenergic receptor blocking activity. The beta-blockade is nonselective, acting on both beta-1 and beta-2 adrenergic receptors. Beta-1 adrenergic blockade reduces the heart rate and myocardial contractility by slowing the AV conduction and suppressing automaticity. Beta-2 blockade affects peripheral vascular resistance and can cause bronchospasm and hypoglycemia. The alpha-adrenergic blockade acts on alpha-1 receptors which results in relaxation of arterial smooth muscle and vasodilation. Carvedilol was approved for use in the United States in 1995 and is still in wide use with more than 2.5 million prescriptions filled yearly. Current indications include hypertension and heart failure. Carvedilol is also approved for use after myocardial infarction to reduce cardiovascular mortality. Carvedilol is also used off label to treat migraine and vascular headaches. Carvedilol is available in tablets of 3.125, 6.25, 12.5 and 25 mg in generic forms and under the trade name Coreg. The typical initial oral dose in adults is 6.25 mg twice daily, with subsequent dose modification based upon clinical response and tolerance, the average total daily maintenance dose being 25 to 50 mg. Extended release capsules of 10, 20, 40 and 80 mg capsules which can be given once daily are also available. Common side effects of carvedilol include bradycardia, hypotension, fatigue, dizziness, depression, memory loss, impotence, cold limbs and less commonly severe hypotension, heart failure and bronchospasm. Sudden withdrawal can trigger rebound hypertension. Beta-blockers are contraindicated in patients with asthma, bradycardia and heart failure and should be used cautiously in the elderly and in patients with diabetes.

Hepatotoxicity

Mild-to-moderate elevations in serum aminotransferase levels occur in less than 2% of patients on carvedilol and are usually transient and asymptomatic, resolving even with continuation of therapy. Despite its wide spread use, carvedilol has been linked to only a single case of clinically apparent liver injury, with injury arising 6 months after starting therapy and a mixed pattern of enzyme elevations without jaundice or signs of hypersensitivity or autoimmunity, and rapid recovery on stopping. Thus, clinically apparent liver injury from carvediol is exceeding rare.

Likelihood score: D (Possible rare cause of clinically apparent liver injury).

Mechanism of Injury

Carvedilol undergoes extensive metabolism by the liver into both active and inactive metabolites and its excretion is largely biliary. The mechanism of liver injury due to carvedilol is unknown but is likely to be an idiosyncratic reaction to the drug or a metabolite.

References to the safety and potential hepatotoxicity of carvedilol are provided in the overview on Beta-Adrenergic Receptor Antagonists, last updated in June 2019.

Drug Class: Beta-Adrenergic Receptor Antagonists

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Carvedilol – Generic, Coreg®

DRUG CLASS

Beta-Adrenergic Receptor Antagonists

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Carvedilol	72956-09-3	C24-H26-N2-O4