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Plazomicin

Updated: April 12, 2019.

OVERVIEW

Introduction

Plazomicin is a parenterally administered, broad spectrum aminoglycoside antibiotic typically used for moderate-to-severe urinary tract infections or pyelonephritis. Plazomicin has had limited clinical use but has not been linked to serum enzyme elevations during therapy or to instances of clinically apparent liver injury.

Background

Plazomicin (pla" zoe mye' sin) is a semi-synthetic aminoglycoside with broad bacteriocidal activity against many aerobic gram negative and some aerobic gram positive organisms including strains resistant to conventional aminoglycosides. Plazomicin was prepared from sisomicin and modified to evade the most common forms of aminoglycoside resistance. Like other aminoglycosides, plazomicin is thought to act by binding to bacterial ribosomes and inhibiting protein synthesis and is considered bacteriocidal as well as bacteriostatic. Plazomicin is most commonly used for complicated urinary tract infections including pyelonephritis, particularly when drug resistance to conventional aminoglycosides is suspected. Plazomicin was approved for use in the United States in 2018 and is available in solution in 10 mL single-dose vials of 500 mg (50 mg/mL) under the brand name Zemdri. The typical adult dose is 15 mg/kg every 24 hours by intravenous infusion for 4 to 7 days. Doses must be modified based upon renal function, which should be assessed before starting therapy. Common side effects include diarrhea, hypertension, headache, nausea, vomiting and hypotension. Important, dose related adverse effects include oto- and nephrotoxicity, which are shared by all aminoglycosides but are uncommon with short courses of plazomicin. Rare, but potentially severe adverse events also shared with other aminoglycosides include hypersensitivity reactions and Clostridium difficile associated diarrhea.

Hepatotoxicity

Intravenous therapy with plazomicin has been linked to only rare instances of serum enzyme elevations (<1%), which were largely mild and asymptomatic and which resolved rapidly once the antibiotic course was completed. There have been no reports of acute liver injury with jaundice associated with plazomicin therapy, and despite many years of widespread use, the other aminoglycosides have rarely been linked to instances of clinically apparent liver injury. The cases of suspected aminoglycoside associated liver injury were characterized by a short latency to onset (within 1 to 3 weeks), a mixed or cholestatic pattern of injury and self-limited course. The liver injury was typically accompanied by skin rash, fever and sometimes eosinophilia, suggesting an immunoallergic cause. Chronic liver injury from aminoglycoside toxicity has not been described. Aminoglycosides are not listed or mentioned in large case series of drug induced liver disease and acute liver failure. Thus, hepatic injury due to plazomicin is rare if it occurs at all.

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

Mechanism of Injury

The possible cause of hepatic injury from plazomicin is not known. Uptake of aminoglycosides into hepatocytes is limited, and they are rapidly excreted in the urine; high concentrations are found mainly in renal tubular cells and hair cells of the inner ear, perhaps explaining why they are more likely to cause nephro- or oto- rather than hepato-toxicity. Liver injury may accompany the rare hypersensitivity reactions to aminoglycosides.

Outcome and Management

The outcome of hepatic injury due to aminoglycosides is usually benign. Acute liver failure has not been associated with aminoglycoside use and nor has chronic bile duct vanishing syndrome. Patients with clinical apparent reactions to one aminoglycoside should probably avoid use of other systemic aminoglycosides.

An annotated bibliography on the safety and potential hepatotoxicity of plazomicin is provided in the Overview section on the Aminoglycosides (Last updated: December 2018).

Drug Class: Aminoglycosides

Other Drugs in the Class: Amikacin, Gentamicin, Neomycin, Streptomycin, Tobramycin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Plazomicin – Zemdri®

DRUG CLASS

Aminoglycosides

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Plazomicin	1154757-24-0	C25-H48-N6-O10