Prescribing information:

Oral mexiletine for ventricular arrhythmias

Mexiletine is a class Ib antiarrhythmic agent with cardiac actions similar to those of lidocaine. It should only be initiated by consultant cardiologists, when other antiarrhythmics have not worked.

Indication:

Mexiletine is used for life-threatening ventricular arrhythmias.

Dose & Administration:

Mexiletine hydrochloride is given orally at a usual loading dose of 400mg, followed by 200 to 300mg three times daily, starting 2 to 8 hours after the loading dose.
The dose can be adjusted in 50 or 100mg increments, no more frequently than every 2 to 3 days.
The usual maintenance dosage is 200 to 300mg every 8 hours. The maximum dose is 1.2 g daily.
Mexiletine should be taken with food and swallowed with plenty of liquid to avoid oesophageal ulceration.

Renal impairment: No dosage adjustment necessary.

Hepatic impairment: Consider a dose reduction, as half-life is approximately doubled in patients with hepatic impairment.

Adverse Effects:

Mexiletine has a narrow therapeutic ratio; although many of its adverse effects are dose-related and will respond to dosage reduction, they may be severe enough to force treatment to be stopped. Toxicity is common with loading doses, when plasma concentrations are high.

The most common adverse effects involve the gastrointestinal tract and central nervous system.

Effects on the gastrointestinal tract include nausea, vomiting, constipation, and diarrhoea; oesophageal ulceration has also been reported.

Effects on the nervous system include tremor, confusion, light-headedness, dizziness, blurred vision and other visual disturbances, sleep disturbances, and speech difficulties.

The most frequent cardiovascular effects are hypotension, sinus bradycardia, heart block and AV dissociation, and atrial fibrillation. As with other antiarrhythmics, mexiletine may exacerbate arrhythmias.

Other reported adverse effects include rashes, abnormal liver function tests, thrombocytopenia, positive antinuclear factor titres and convulsions. The Stevens-Johnson syndrome has been reported rarely.

Contraindications and cautions:

Mexiletine is contra-indicated in cardiogenic shock and in second- or third-degree AV block (unless the patient has a pacemaker).

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It should be used with caution in patients with sinus node dysfunction, other conduction disorders, bradycardia, hypotension, heart failure, or hepatic impairment. ECG and blood pressure monitoring should be carried out during treatment.

Absorption of oral mexiletine may be delayed in situations where gastric emptying is slowed, such as acute myocardial infarction.

Drug Interactions:

Mexiletine undergoes extensive metabolism in the liver, particularly by the cytochrome P450 isoenzymes CYP1A2 and CYP2D6, and possibly CYP3A4, and interactions may occur with other drugs metabolised by the same enzymes.
Plasma concentrations of mexiletine may be reduced by hepatic enzyme inducers such as phenytoin and rifampicin. Increased plasma concentrations may occur with enzyme inhibitors (fluvoxamine, propafenone).

Absorption of mexiletine may be delayed by drugs that slow gastric emptying such as opioid analgesics, atropine, and magnesium- and aluminum-containing antacids. The rate of absorption may be increased by metoclopramide. The extent of absorption is unaffected.

Concomitant administration of cimetidine with mexiletine may result in increased, decreased, or unchanged plasma concentrations of mexiletine. Plasma concentrations of mexiletine should be closely monitored during such concurrent use.

Drugs that acidify or alkalinise the urine enhance or reduce the rate of elimination of mexiletine, respectively.

There may be an increased risk of arrhythmias if mexiletine is used with other antiarrhythmics or with arrhythmogenic drugs.

Mexiletine has been reported to increase theophylline concentrations and to precipitate lidocaine toxicity.

Monitoring Requirements:

Liver function tests.
ECG is recommended to determine whether the desired antiarrhythmic effect has been achieved and to guide dosage titration and adjustment.
Therapeutic range: 0.5 to 2 mcg/ml; potentially toxic: >2 mcg/ml

Availability:

Mexiletine comes as 50mg and 200mg capsules. It is not actively marketed in the UK; it is available from 'special-order' manufacturers or specialist importing companies.

Ref.
1. Martindale, Mexiletine, accessed November 2017.
2. Lexicomp, Mexiletine Drug Information, accessed November 2017.
3. AHFS, Mexiletine, accessed November 2017.

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