Mexiletine Cardiology Shared Care Guideline

Specialist Details	Patient Identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

This shared care guideline does not cover the use of mexiletine for treatment of myotonia in neurology.
Mexiletine is a class Ib antiarrhythmic, supported by current European Society of Cardiology Guidelines for ventricular arrhythmia.
Licensed indications: ventricular arrhythmias.

Adult Dosage and Administration

Treatment with mexiletine should be initiated by a specialist.
The optimal dosage should be determined individually based on the patient's response and tolerance.
A maintenance dose of 150 mg to 300 mg, two to three times daily is recommended.
If necessary, the dose may be adjusted in 50 or 100 mg increments. A minimum of two to three days between dose adjustments is recommended. The dose should not exceed 1200 mg per day.
Available as: Licensed mexiletine (non-proprietary) preparations are available as 50mg, 100mg and 200mg capsules. NB the brand NaMuscla® should not be used for cardiology indications.

Hospital Specialist Responsibilities

- Assess patient's suitability for treatment with mexiletine, including that there are no significant drug interactions with the patient's other medicines.
- Agree shared care with patient's GP.
- Advise GP on dose of mexiletine to be prescribed.
- Provide the patient/carer with relevant (written) information on use, side effects and need for monitoring of medication.
- Undertake baseline tests:
  - ECG
  - FBC
  - LFTs
  - U&Es
- Review results of safety monitoring and request additional tests e.g. ECG as required.
- Monitor disease response to treatment and annually the need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.

GP Responsibilities

- Prescribe mexiletine as specified by the hospital specialist.
- Arrange and record ongoing monitoring as advised by specialist, ensuring practice systems are in place to recall patients for monitoring blood tests.
- Arrange ongoing monitoring
  - Annual FBC,
  - Annual U&Es.
- Report any adverse drug reactions to initiating specialist and the usual bodies (e.g. MHRA/CHM).
- Ensure there are no significant drug interactions with other medicines.

Adverse Effects, Precautions and Contraindications

- **Contraindications**:
  - Sinus node dysfunction (unless a pacemaker is present), severe atrioventricular (AV) conduction disturbances (unless a pacemaker is present), severe heart failure, cardiogenic shock.
  - Reduced left ventricular ejection fraction (LVEF): Note that the specialist will advise when appropriate to use in patients with reduced LVEF. In clinical use, patients with ventricular arrhythmia commonly have reduced LVEF and the European Society of Cardiology guidelines and other sources advise there are no negative effects on LVEF.
  - Inherited Long QT syndrome (LQTS) (other than LQTS3) or concomitant treatment with medicines associated with QT-interval prolongation.
  - Renal function: eGFR < 30ml/min/1.73m^2
- **Cautions:**
  - in patients with **hypotension or congestive heart failure** because of its potential for depressing myocardial contractility.
  - in patients with **first degree AV block or intraventricular conduction abnormalities**. If a ventricular pacemaker is operative, patients with second- or third-degree AV block may be treated with mexiletine if continuously monitored.
  - in electrolyte disturbances: correct electrolyte disturbances, liaising with specialist if required.
  - in **hepatic dysfunction**: mexiletine should be used with caution in patients with mild or moderate hepatic dysfunction and should not be used in severe hepatic impairment. If persistent or worsening elevation of hepatic enzymes is detected, contact the specialist for advice on possible discontinuation.
  - In patients with a **history of seizures.**
  - Poor metabolisers of **CYP2D6** may exhibit higher mexiletine plasma levels, slower dose titration is recommended.
- **Cardiovascular side effects** may include: hypotension tachycardia, palpitations, angina pain, atrial fibrillation.
- **Leukopenia and thrombocytopenia** have been reported. Contact the specialist for advice if suspected.
- **Insomnia, dizziness, tremor, abdominal pain and dyspepsia** are commonly reported.
- **Fatigue, confusion and blurred vision:** May effect driving and performance of skilled tasks.
- **Pregnancy / Contraception**: As a precautionary measure, it is advised to avoid the use of mexiletine during pregnancy, but the specialist should be contacted for advice.
- **Breast Feeding**: mexiletine is excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from mexiletine therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Common Drug Interactions

Other anti-arrhythmics: Co-administration of mexiletine and any other antiarrhythmics (Class Ia: quinidine, procainamide, disopyramide, ajmaline; Class Ic: encainide, flecainide, propafenone, moricizine; Class III: amiodarone, sotalol, ibutilide, dofetilide, dronedarone, vernakalant, Class Ib: lidocaine, phenytoin, tocainide; Class II: propranolol, esmolol, timolol, metoprolol, atenolol, carvedilol, bisoprolol, nebivolol; Class IV: verapamil, diltiazem) increase the risk of adverse cardiac reactions.

Medicinal products metabolised by CYP1A2: Co-administration of mexiletine with medicinal products metabolised by CYP1A2 such as aminophylline, theophylline, lidocaine or tizanidine, may increase plasma concentrations of the concomitant medicine.

CYP1A2 inhibitors or CYP2D6 inhibitors: Co-administration of mexiletine with CYP1A2 inhibitors such as ciprofloxacin, fluvoxamine and propafenone or CYP2D6 inhibitor such as propafenone and quinidine significantly increases mexiletine levels. Slower dose titration is recommended.

CYP1A2 inducers or CYP2D6 inducers: Co-administration of mexiletine with CYP1A2 inducers such as omeprazole or CYP2D6 inducers such as phenytoin and rifampicin may decrease levels and the half-life of mexiletine.

Other interactions include:

Clozapine: Mexiletine increases the concentration of clozapine. Manufacturer advises monitoring for adverse effects and adjusting dose.

Fluvoxamine, cinacalcet or buproprion: Co-administration may increase the exposure to mexiletine. Manufacturer advises monitoring ECG.

Warfarin: Concomitant administration may increase the risk of bleeding.

Communication

For any queries relating to this patient's treatment with mexiletine, please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC at www.medicines.org.uk or the BNF

Date Prepared: June 2024 **Date of review: June 2029**