Chief Medical Officer Directorate
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IMMEDIATE MESSAGE TO:

1. Directors of Pharmacy
2. Medical Directors NHS Boards

4 August 2022

Dear Healthcare Professional,

REVISED DRUG ALERT CLASS 1 – ACTION NOW INCLUDING OUT OF HOURS – CLINIGEN HEALTHCARE LTD – MEXILETINE HYDROCHLORIDE 50MG, 100MG AND 200MG HARD CAPSULES - NATIONAL PATIENT SAFETY ALERT 2022 007

Please see attached revised drug alert to reflect a correction by Clinigen Healthcare Ltd, an update to correct the expiry date to 02/2024 and National Patient Safety alert about the potential for over or under dosing of three batches of mexiletine hydrochloride for onward transmission as below .

Could all Directors of Pharmacy please forward this alert to:-

- Community Pharmacists
- Hospital Pharmacists
- Primary Care Pharmacists

Please could Medical Directors arrange to forward this alert on to:-

- General Practitioners
- Accident & Emergency Departments
- Ambulance and paramedic services
- Directors of Public Health
- Relevant Clinics
- Chief Executives of NHS Board

Thank you for your co-operation.

Yours sincerely

IRENE FAZAKERLEY
Medicines Policy Team

Medicines & Healthcare products Regulatory Agency

M E D I C I N E S R E C A L L

CLASS 1 MEDICINES RECALL

Action Now – including out of hours
Patient/Pharmacy/Wholesaler Level Recall

Date: 04 August 2022 NatPSA/2022/007/MHRA Our Ref: MDR 109-07/22

Dear Healthcare Professional,

Clinigen Healthcare Ltd

Mexiletine hydrochloride 50mg Hard Capsules PL 31644/0027

Batch Number	Expiry Date	Pack Size	First Distributed
2111216	02/2024*	84 capsules	10/02/2022

*Per correction by Clinigen Healthcare Ltd, an update was made to correct the expiry date to reflect 02/2024

Mexiletine hydrochloride 100mg Hard Capsules PL 31644/0028

Batch Number	Expiry Date	Pack Size	First Distributed
2111217	04/2024	84 capsules	10/02/2022

Mexiletine hydrochloride 200mg Hard Capsules PL 31644/0029

Batch Number	Expiry Date	Pack Size	First Distributed
2111218	04/2024	100 capsules	10/02/2022

Active Pharmaceutical Ingredients: mexiletine hydrochloride

Brief description of the problem
Clinigen Healthcare Ltd is initiating a recall of the above batches due to recent stability test results, which identified that some individual capsules on the market may fall outside the individual fill weight range. This issue means that there is the potential for some capsules to have too little active ingredient (mexiletine hydrochloride) in them and some capsules to contain too much active ingredient. Due to the error, there is a potential for underdosing and overdosing and experience of potentially serious adverse events

Clinigen Healthcare Ltd has confirmed that no alternative batches of mexiletine hydrochloride 50mg, 100mg or 200mg hard capsules will be available until later in the year, therefore the recall of these batches from patients should only be considered where patients have access to appropriate alternative products. Clinigen Healthcare Ltd has confirmed that these three strengths are all out of stock and not available for order. See below for more information on resupplying patients with alternative products.

Advice for healthcare professionals

- Stop supplying the above batches immediately. Quarantine all remaining stock and return it to your supplier using your supplier's approved process.

- Pharmacists involved in dispensing this product should immediately contact all patients who have been dispensed the impacted batches and ask them to confirm if they have remaining stock of the impacted batch within their possession. If batch traceability information is not available, all patients dispensed these products since 10 February 2022 should be contacted.

- **If the pharmacist identifies any patients with an impacted batch, they should, in the first instance, contact the patient's GP and discuss alternative mexiletine treatment for the patient. As this is a specialist use product and patients may require monitoring, other clinicians and healthcare professionals may need to be involved.**

- Patients should be advised not to stop any treatments without consulting their relevant healthcare professional. The risks of suddenly stopping medication for ventricular arrhythmias is higher than the potential risk presented by continuing to take capsules containing too much or too little of the active ingredient. This product should only be recalled from patients when it has been confirmed that the patient has access to an alternative mexiletine product.

- Healthcare professionals should be aware of the following clinical considerations related to the potential risk of either under- or overdosing.

    - Underdosing:
        - Underdose could lead to lack of efficacy, which could consequently result in a ventricular arrhythmia
        - There needs to be an increased vigilance for symptoms of arrhythmias (palpitation, chest pain, shortness of breath, light-headedness, and syncope) reported by a patient, which may be due to underdosing.
        - A patient alert card is supplied with the product in each pack. Advise patients to complete their and their doctor's name and contact details on the patient alert card and keep it with them at all times, for instance in a wallet or a purse.
        - Discuss the risk of cardiac arrhythmias with patients and tell them to seek urgent medical attention if they experience any new or worsening of symptoms of an arrhythmia including palpitations, angina pain, chest discomfort, dizziness and loss of consciousness
        - The HCP guide for management of risk of cardiac arrythmia is available here: Mexiletine Hydrochloride Healthcare Professional Guide.pdf (medicines.org.uk)

    - Overdosing:
        - The clinical features include nausea, hypotension, bradycardia, paraesthesia, left bundle branch block, asystole, convulsions, which may be life-threatening and can be fatal.
        - Refer to the approved Summary of Product Characteristics (SmPC) for treatment recommendations: Click here to access SmPC via eMC.

- Any patients experiencing any of the symptoms listed above should be advised to immediately contact their nearest accident and emergency centre.

- Healthcare professionals should note that some patients may have an implantable cardioverter-defibrillator (ICD) fitted and additional monitoring should be considered where appropriate.

- Additional monitoring should be considered for all patients due to the potential for under- and/or overdosing to have occurred and as per product literature to monitor electrolytes, full blood counts and liver function tests during treatment and where alternative products may be provided.

- Patients who have the impacted batch can be provided with a supplementary letter to explain any potential observations in relation to the issue and underdosing and/or overdosing. See more information in the Download Document section of the MHRA National Patient Safety Alert webpage.

Advice for healthcare professionals on recall and resupply

- **If the pharmacist identifies any patients with an impacted batch, they should, in the first instance, contact the patient's GP and discuss alternative mexiletine treatment for the patient. As this is a specialist use product and patients may require monitoring, other clinicians and healthcare professionals may need to be involved.**

- Healthcare professionals should be aware that other licensed preparations for mexiletine are available. Whilst licensed mexiletine products marketed by Clinigen Healthcare Ltd are out of stock, the only other licensed mexiletine product available is Namuscla 167mg (equivalent to 200mg mexiletine hydrochloride) hard capsules, Summary of Product Characteristics (SmPC): https://www.medicines.org.uk/emc/product/9838/smpc#gref

    - Namuscla 167mg hard capsules: Namuscla is indicated for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders and is not indicated for treatment of life-threatening ventricular arrhythmias and supply would be considered "off-label" use.
    - Although the MHRA does not recommend "off label" (outside of the licensed indications) use of products, if alternative UK licensed products can meet the patients clinical need, even "off-label", they should be used instead of an unlicensed product. Licensed products available in the UK have been assessed for quality, safety, and efficacy. It should be understood that the prescribing healthcare professional's responsibility and potential liability are increased when prescribing off-label.

- Healthcare professionals may consider that an unlicensed product (special) should be used as an alternative mexiletine product for patients requiring maintenance doses and any dose titrations in the absence of alternative licensed products.

- See **Department of Health and Social Care Guidance on ordering and prescribing unlicensed imports**:

    - Any decision to prescribe an unlicensed medicine must consider the relevant guidance and NHS Trust or local governance procedures. Please see the links below for further information:
        - The supply of unlicensed medicinal products, Medicines and Healthcare products Regulatory Agency (MHRA)
        - Professional Guidance for the Procurement and Supply of Specials, Royal Pharmaceutical Society
        - Prescribing unlicensed medicines, General Medical Council (GMC),

- When prescribing a product that is not licensed in the UK due to a supply issue with the licensed alternative, prescribers must indicate on the FP10 prescription that an unlicensed product is required. This can be done in one of the following two ways:
  - Electronic prescriptions – if the required unlicensed product is shown on electronic prescribing systems, GPs should select:
    - Mexiletine 50mg capsules (imported)
    - Mexiletine 100mg capsules (imported)
  - Paper prescriptions – where the unlicensed product is not shown on electronic prescribing systems, GPs should use a paper prescription and annotate with the following wording: "**special order**".

- Patients should be advised to report any side effects to their healthcare professional and via the MHRA's Yellow Card scheme.

Advice for patients

- Patients should not stop taking mexiletine without consulting your relevant healthcare professional. The risks of suddenly stopping medication for ventricular arrhythmias is higher than the potential risk presented by taking capsules containing too much or too little mexiletine.

- See further information in the supplementary letter explaining any potential observations relating to underdosing and/or overdosing. See more information in the Download Document section of the MHRA National Patient Safety Alert webpage.

- If you feel unwell or experience any of the symptoms mentioned relating to either underdose or overdose, please contact your doctor immediately or visit the nearest accident and emergency centre.

Further Information
For more information on licensed stock and resupply queries for the licensed presentation, please contact Quantum Pharmaceutical +44 (0) 1207 279 400 or email enquiries@quantumpharma.co.uk

For medical information queries, please contact Clinigen Medical Information on +44 (0) 1932 824026 or email medicalinformation@clinigengroup.com

For all other enquires place contact Clinigen Healthcare Ltd on +44 (0) 1283 494 340 or email medicineaccess@clinigengroup.com

Yours faithfully

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Medicines & Healthcare products Regulatory Agency

Mexiletine - recall of 50mg, 100mg and 200mg capsules due to filling error
Reference: NatPSA/2022/007/MHRA)

A manufacturing error has been detected for **all batches of Mexiletine hydrochloride Hard Capsules** made by Clinigen Healthcare Ltd. This problem could mean capsules of mexiletine may contain more or less medicine than they should.

Mexiletine hydrochloride 50mg Hard Capsules, PL 31644/0027

- Batch Number 2111216
- Expiry Date 02/2024*

*Per correction by Clinigen Healthcare Ltd, an update was made to correct the expiry date to reflect 02/2024

Mexiletine hydrochloride 100mg Hard Capsules, PL 31644/0028

- Batch Number 2111217
- Expiry Date 04/2024

Mexiletine hydrochloride 200mg Hard Capsules, PL 31644/0029

- Batch Number 2111218
- Expiry Date 04/2024

Advice for patients

- If you are taking mexiletine, check to see if you have any of the above batches at home. The batch number and expiry date can be found on the outer carton and also at the end of each blister strip. If you are unsure or unable to locate the batch number and expiry date, please contact your pharmacist for further advice.

- **Do not to stop taking mexiletine without consulting your healthcare professional. The risks of suddenly stopping medication for ventricular arrhythmias is higher than the potential risk presented by taking capsules containing too much or too little mexiletine.**

- Your pharmacist, GP/doctor, or other healthcare professional will contact you to make sure you get a new prescription for an alternative product before you need to take your medicine back. You can contact them directly if you are worried.

- There has been no reported harm associated with this issue, but patients should be aware of possible symptoms of too much or too little mexiletine (below).

A smaller dose than you need could result in worsening control of cardiac arrhythmia (irregular heartbeat). The patient alert card supplied with your medication provides important information on the symptoms of arrhythmia. These symptoms can include feeling like your heart is beating too hard or too fast (palpitations), chest pain, shortness of breath, light-headedness, dizziness or fainting.

A larger dose than you need could increase side effects. The symptoms of overdose include feeling sick, hypotension (low blood pressure), paraesthesia (tingling of the extremities), hallucinations (seeing or hearing something that is not present), convulsions (fits) or, feeling like your heart is beating irregularly (slower or faster).

Seek urgent medical attention if you experience any of the symptoms suggestive of an underdose or overdose.

- Additionally, you may need closer monitoring particularly after changes in your mexiletine treatment. Please follow your doctor's instructions.

- If you are in any doubt, please contact your pharmacist, GP/doctor, or other healthcare professionals for advice as to whether you are in possession of an affected batch.

Patients are advised to complete your name and your doctors name and contact details on the patient alert card supplied with the medication and keep it at all times, for instance in a wallet or a purse.

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National Patient Safety Alert

Medicines & Healthcare products Regulatory Agency

Recall of Mexiletine hydrochloride 50mg, 100mg and 200 mg Hard Capsules, Clinigen Healthcare Ltd due to a potential for underdosing and/or overdosing

Date of Issue:	04-Aug-22	**Reference No:**	NatPSA/2022/007/MHRA

This alert is for action by: primary and secondary care, specifically those involved in pharmacy services, including dispensing general practices.

This is a safety critical and complex National Patient Safety Alert. Implementation should be coordinated by an executive leader (or equivalent role in organisations without executive boards) supported by Chief Pharmacists and the clinical lead for cardiology, as well as leaders in general practice and community pharmacy

DMRC Medicines Defect Classification	NatPSA equivalent to Class 1 Recall Notification

Explanation of identified safety issue:

Clinigen Healthcare Ltd is initiating a recall of three batches of Mexiletine hydrochloride hard capsules due to a potential risk of underdose or overdose, which could have consequences for the safety of patients.

Stability testing identified that some individual capsules on the market may fall outside the individual fill-weight range. This means that there is the potential for some capsules to contain too little active ingredient and for some to contain too much active ingredient. This could result in potential underdosing and overdosing.

Page 2 lists potential clinical consequences, noting the need for vigilance of symptoms of arrhythmias.

Clinigen Healthcare Ltd has confirmed that no alternative batches of mexiletine hydrochloride 50mg, 100mg or 200mg hard capsules will be available until later in the year, therefore the recall of these batches from patients should only be considered where patients have access to appropriate alternative products. See below for more information on resupplying patients with alternative products.

Patients should be advised not to stop any treatments without consulting their relevant healthcare professional. The risks of suddenly stopping medication for ventricular arrhythmias is higher than the potential risk presented by too much or too little of the active ingredient in the capsule.

Another licensed mexiletine product is available as Namuscla 167mg (equivalent to 200mg mexiletine hydrochloride) hard capsules, however, this is indicated for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders and is not indicated for treatment of life-threatening ventricular arrhythmias and supply would be considered “off-label" use (i.e. use outside of its licensed indication).

Actions required

Actions to complete by 12-Aug-22:

The action to recall should be coordinated by the Chief Pharmacist/Superintendent Pharmacist/Responsible Pharmacist and Dispensing GPs in the first instance.

1. Stop supplying the impacted batch immediately. Quarantine all remaining stock and return it to your supplier/MAH using your supplier’s approved process.

2. Identify and immediately contact all patients who have been dispensed the impacted batch and ask them to confirm if they have remaining stock within their possession. If batch traceability information is not available, all patients dispensed this product since 10 February 2022 should be contacted.

3. If the pharmacist identifies any patients with an impacted batch, they should, in the first instance, contact the patient’s GP and discuss alternative mexiletine treatment of the patient. As this is a specialist use product and patients may require monitoring, other clinicians and healthcare professionals may need to be involved.

4. Discuss the risk of cardiac arrhythmias with patients and advise them to seek urgent medical attention if they experience any new or worsening of symptoms of an arrhythmia including palpitations, angina pain, chest discomfort, dizziness and loss of consciousness.

Healthcare professionals may also consider the use of unlicensed medicines where appropriate. See the MHRA recall notice for more information.

Additional information:

For further detail, resources and supporting materials see: www.gov.uk/drug-device-alerts

Product Information: Clinigen Healthcare Ltd.

	Mexiletine hydrochloride 50mg Hard Capsules PL 31644/0027	Mexiletine hydrochloride 100mg Hard Capsules PL 31644/0028	Mexiletine hydrochloride 200mg Hard Capsules PL 31644/0029
Batch Number	2111216	2111217	2111218
Expiry Date	02/2024*	04/2024	04/2024
Pack Size	84 capsules	84 capsules	100 capsules
First Distributed	10/02/2022	10/02/2022	10/02/2022

*Per correction by Clinigen Healthcare Ltd, an update was made to correct the expiry date to reflect 02/2024

Defective Medicines Report Centre Reference: MDR 109-07/22

Healthcare professionals should be aware of the following clinical considerations related to the potential risk of either under- or overdosing.

Underdosing:

- Underdose could lead to lack of efficacy, which could consequently result in a ventricular arrhythmia
- There needs to be an increased vigilance for symptoms of arrhythmias (palpitation, chest pain, shortness of breath, light-headedness, and syncope) reported by a patient, which may be due to underdosing.
- A patient alert card is supplied with the product in each pack. Advise patients to complete their and their doctor's name and contact details on the patient alert card and keep it with them at all times, for instance in a wallet or a purse.
- Discuss the risk of cardiac arrhythmias with patients and tell them to seek urgent medical attention if they experience any new or worsening of symptoms of an arrhythmia including palpitations, angina pain, chest discomfort, dizziness and loss of consciousness. The HCP guide for management of risk of cardiac arrythmia is available here: https://www.medicines.org.uk/emc/product/13306/rmms

Overdosing:

- The clinical features include nausea, hypotension, bradycardia, paraesthesia, left bundle branch block, asystole, convulsions, which may be life-threatening and can be fatal.
- Refer to the approved Summary of Product Characteristics (SmPC) for treatment recommendations: https://www.medicines.org.uk/emc/product/13306/smpc.

Any patients experiencing any of the symptoms listed above should be advised to immediately contact their nearest accident and emergency centre. Healthcare professionals should note that some patients may have an implantable cardioverter-defibrillator (ICD) fitted and additional monitoring should be considered where appropriate.

Additional monitoring should be considered for all patients due to the potential for under- and/or overdosing to have occurred and as per product literature to monitor electrolytes, full blood counts and liver function tests during treatment and where alternative products may be provided.

Patients who have the impacted batch can be provided with a supplementary letter to explain any potential observations relating to under- and/or overdosing. See more information in the accompanying PDFs with this NatPSA.

Advice to provide to patients

Patients should not stop taking mexiletine hydrochloride hard capsules without consulting their relevant healthcare professional. The risks of suddenly stopping medication for ventricular arrhythmias is higher than the potential risk presented by taking capsules containing too much or too little of the active ingredient. Patients need to be aware of possible symptoms of having taken too much or too little of the active ingredient in the capsule.

This alert includes the more relevant critical information, however, please see further guidance in the MHRA notice in relation to this recall.

Reference Information:

1. Class 1 Medicines Recall Notification including patient specific information – Click Here

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Please check website www.gov.uk/drug-device-alerts for when actions should be ceased or advice to check for date restriction are lifted.