Veriton Pharma Limited, Unit 16, Trade City, Avro Way,
Brooklands Business Park, Weybridge, Surrey KT13 OYF

Direct Healthcare Professional Communication

13/11/2020

Midazolam maleate (Epistatus 10mg in 1 ml Oromucosal Solution, Multidose bottle), unlicensed, emergency use medication for prolonged, acute, convulsive seizures: potential risk of faulty and incorrectly engaged child-resistant container closure

Dear Healthcare Professional,

The manufacturers and product distributor of Epistatus 10mg in 1 ml Oromucosal Solution (Multidose bottle), in agreement with the MHRA, would like to inform you of the following:

Summary

- There is a very low incidence rate where unsecured bottle tops (caps) have been reported for Epistatus 10mg in 1 ml Oromucosal Solution, (Multidose bottle), and can be removed without unscrewing.
- Loose caps have potential consequences, including evaporation of ethanol, and subsequent crystallisation and formulation viscosity changes. Where crystallisation or particles are present, the concentration of midazolam in the product may be reduced and potentially lead to a lower dose being administered.
- Only healthcare professionals with expertise* in using buccal midazolam maleate medicines should prescribe them, with their use being in line with patient treatment protocols and Patient Information Leaflet (PIL).
- Where healthcare professionals prescribe or dispense Epistatus 10mg in 1 ml Oromucosal Solution (Multidose bottle), they should:
    - provide to the patient/carer, full and clear dosing instructions according to patient treatment protocols.
    - ensure the medicine has been stored upright, in its carton, below 25°C, out of direct sunlight, and not refrigerated or frozen.
    - check carefully at every **new** prescription/dispensing that:
        - the cap is secure, and tamper-proof seal is present.
        - the solution is clear, and no particles or crystals are present.
    - ask users to check carefully at **every use** of the multidose bottle that:
        - the cap has been previously replaced securely to prevent ethanol evaporation.
        - the solution is clear, and no particles or crystals are present.
        - ensure the cap is replaced correctly and securely after use to prevent ethanol evaporation.
- Healthcare professionals and patient/carers should not use the product if the solution is not clear or contains particles or crystals. (Ref. Epistatus MDB- patient information leaflet).

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*Prescribers should be aware of the benefits and risks of midazolam maleate products and have the necessary competence to prescribe them safely. Healthcare professionals should be trained in the use of specific emergency medications associated with patient protocols.

Further information on the safety concern

Epistatus (Midazolam) is used for the treatment of prolonged, acute convulsive seizures. The child-resistant container closure for Epistatus 10mg in 1 ml Oromucosal Solution (Multidose bottle), may be faulty and incorrectly engaged. The child-resistant closure can potentially be removed without unscrewing the cap closure. Removal of an incorrectly engaged cap closure will result in the yellow tamper-evident band not being retained on the neck of the bottle.

The following batches of Epistatus (Midazolam) 10mg/mL Oromucosal Solution (Multidose bottles) potentially contain products with the identified defect:

Batch Number	Expiry Date	Pack Size	Manufacture Date
200224B1	02-2022	5mL in 30mL bottle	24 Feb 2020
200420C1	04-2022	5mL in 30mL bottle	20 Apr 2020
200420C2	04-2022	5mL in 30mL bottle	20 Apr 2020
200511C1	05-2022	5mL in 30mL bottle	11 May 2020
200511C2	05-2022	5mL in 30mL bottle	11 May 2020
200423C1	04-2022	5mL in 30mL bottle	23 Apr 2020

Future batches of Epistatus (Midazolam) 10mg/mL Oromucosal Solution (Multi-Dose Bottle) manufactured after November 2020 will have a reduced expiry date, being limited to 12 months. The shortened shelf-life will be applied until data allows a justification for a longer shelf-life.

Recommendations

To minimise the risk of administering a faulty medicine, healthcare professionals and patient/carers should not use the product if the tamper-evident seal is not retained on the neck of the bottle or the solution is not clear or contains particles or crystals.

Healthcare professionals should advise patients/carers on the following upon supply of the medicine:

- The cap may be faulty and incorrectly fixed on the bottle; Healthcare professionals should demonstrate to the patient/carer the cap is securely fitted to the bottle and the tamper seal is present when handing the medicine over.
- The solution is clear, and no particles or crystals can be seen on receipt and at every use.
- **After first opening** ensure the tamper seal is retained on the neck of the bottle.
- The bottle should be stored upright, in its carton, below 25°C, out of direct sunlight, and not refrigerated or frozen.
- Re-cap the bottle securely after each use.
- Do not use and return to the dispensing pharmacy, if:
    - The solution is not clear, or particles or crystals can be seen.
    - The tamper seal is not retained on the neck of the bottle after first opening.

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- If they have concerns about their treatment to contact their specialist.

Pharmacy Professionals: Any defect products identified should not be used and be returned to your supplier using your supplier's approved process.

Call for reporting

Please report any suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

It is easiest and quickest to report ADRs online via the Yellow Card website: www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- via the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- by downloading and printing a form from the Yellow Card section of the MHRA website.

Suspected adverse drug reactions may also be reported to Veriton Pharma Ltd., Telephone +44 (0)1932 690325 or email info@veritonpharma.com

For reporting of identified defects or queries, please contact Veriton Pharma Ltd., Telephone +44 (0)1932 690325 or email info@veritonpharma.com

With many thanks in advance for your understanding and cooperation

Yours sincerely
Veriton Pharma Limited

Chris Grimes

Chief Executive Officer