



Medicine Supply Notification

MSN/2021/045

Metformin 500mg/5ml oral solution

Tier 2 – medium impact*

Date of issue: 13/09/2021

Summary

- Advanz Pharma have discontinued metformin 500mg/5ml oral solution due to further testing requirements necessitated by the potential presence of N-nitrosodiethylamine (NDMA) impurities.
- Rosemont Pharmaceuticals have recalled one batch of metformin 500mg/5ml oral solution due to the presence of NDMA impurities and are therefore out of stock due to further testing requirements.
- Limited supplies of metformin 500mg/5ml oral solution are expected to be made available week commencing 4th Oct 2021, however, this is unable to support full demand.
- Long term supply issues of metformin 500mg/5ml oral solution are expected.
- Metformin 850mg/5ml and 1000mg/5ml oral solutions remain available but cannot support an increased demand.
- Metformin 500mg powder for oral solution sugar free is available but cannot fully support an uplift in potential demand.
- Supplies of metformin 500mg/5ml oral solution specials can be sourced. However, the presence of NDMA within Specials is unknown. Therefore, it is imperative that Specials are only prescribed where all other options have been exhausted.

Actions Required

All clinicians in primary and secondary care who prescribe metformin 500mg in 5ml oral solution should consider:

- reviewing if patients can swallow solid dosage forms and switching to metformin tablets, where appropriate;
- working with local pharmacy teams to understand the availability of metformin 500mg powder for oral solution and where appropriate issue a prescription to make up the required dose, ensuring that the patient is not intolerant to any of the excipients and is counselled on the appropriate dose and volume required to reconstitute the powder (see supporting information below);
- **prioritising remaining oral solution for patients with enteral feeding tubes or swallowing difficulties** (see supporting information below);
- assessing patient's ability to crush metformin tablets and mix with water, and recommending to do so, if appropriate (see supporting information below);
- prescribing unlicensed products from Specials manufacturers, in the event of above options being exhausted and where metformin is still required.

*Classification of Tiers can be found at the following link:

<https://www.england.nhs.uk/publication/a-guide-to-managing-medicines-supply-and-shortages/>

Supporting information

Clinical Information

Please refer to the following links for further information on the risks of nitrosamine impurities:

- [Batch of metformin oral solution recalled by MHRA due to nitrosamine impurity \(GOV.UK\)](#)
- [Nitrosamines EMEA-H-A5\(3\)-1490 - Assessment Report \(europa.eu\)](#)

Please refer to the BNF and SPCs for further information on alternative preparations:

- [Metformin BNF](#)
- [Metformin 500mg/5ml oral solution SmPC](#)
- [Metformin 500mg powder for oral solution sugar free \(Morningside\) SmPC](#)

Administration via enteral feeding tubes

- Resources on administration of medication to patients with enteral feeding tubes states that metformin tablets do not disperse well in water, however, they can be crushed and mixed with water to form a fine suspension, which flushes easily via an 8Fr NG tube.
- There is currently no data available on the use of Metformin 500mg powder for oral solution sugar free sachets (Morningside) in enteral tubes, however, the formulation is based on Glucophage (metformin) 500 mg powder for oral solution in sachets, with similar excipients. Glucophage powder is reported to dissolve completely in 20 mL of water to give a cloudy solution, with a pH of 4.5, which flushes easily via an 8Fr feeding tube without blockage.

Guidance on ordering and prescribing Specials

- Specials manufacturers are not required to monitor NMDA levels when releasing unlicensed supplies, therefore Specials should only be used where all other options have been considered but are unsuitable and where metformin is still required. It is the prescriber's responsibility to ensure that the benefits from using the Specials outweighs the risks of potential exposure to NMDA (see clinical information above).
- The following manufacturers have confirmed they can source unlicensed metformin 500mg/5ml oral solution (please note there may be other companies that can also source supplies):
 - Ascot Labs
 - Eaststone Specials
 - Nova Laboratories
 - Quantam Pharmaceuticals
 - Target Healthcare
- 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:
 - metformin 500mg/5ml oral solution (special order)
 - 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”**.

Enquiries

If you have any queries, please contact DHSCmedicinesupplyteam@dhsc.gov.uk.