

Ranitidine Liquid Shortage: Barnsley Guidance on Alternatives to Ranitidine Liquid for Gastro-Oesophageal Reflux Disease in Babies and Children

MHRA Recall

On 8th October 2019 the MHRA issued a class 2 medicines recall for Zantac® Injection 50mg/2ml, Zantac® Syrup 150mg/10ml, Zantac® Tablets 150mg and Zantac® Tablets 300mg (EL (19)A 24).¹

GlaxoSmithKline recalled all unexpired stock of Zantac® (ranitidine hydrochloride) prescription only medicines (POM) from pharmacies due to possible contamination with an impurity N-nitrosodimethylamine (NDMA) which has genotoxic and carcinogenic potential.

The MHRA asked manufacturers to quarantine all ranitidine products which may contain the active pharmaceutical ingredient that is potentially affected by this issue.² Following advice from the EMA, the MHRA has now suspended all licenses for ranitidine products.³

The Department of Health and Social Care has previously issued a Supply Disruption Alert for all oral formulations of ranitidine:

<https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=102952>

All preparations of ranitidine are out of stock until further notice.

Guidance on Alternatives to Ranitidine Liquid for Gastro-Oesophageal Reflux Disease in Babies and Children

This guidance aims to suggest possible alternatives to ranitidine liquid for gastro-oesophageal reflux disease (GORD) in babies and children. If the indication for the ranitidine liquid is not gastro-oesophageal reflux disease (e.g. gastric/duodenal ulceration), then this lies outside the scope of this guidance and specialist advice should be sought.

NICE guidance: Gastro-oesophageal reflux disease in children and young people: diagnosis and management (NG1) ^{4,5} suggests **PPIs** as an alternative option to ranitidine in the pharmacological management of GORD. It should be noted that treatment of GORD in babies and children with ranitidine/PPIs should be reassessed after a four week trial and referral to a specialist (for possible endoscopy) should be considered if symptoms have not resolved or recur after stopping treatment. Treatment with ranitidine/PPIs should be continued in endoscopy proven reflux oesophagitis or under the recommendations of the specialist.^{4,5} For further information on diagnosis and management consult the NICE guidance at:

<https://www.nice.org.uk/guidance/ng1/chapter/1-Recommendations#initial-management-of-gor-and-gord>

It would seem appropriate to check whether the patient has previously tried an alginate and whether this was effective.

In **breast-fed infants** with frequent regurgitation associated with marked distress that continues despite a breastfeeding assessment and advice, NICE recommends to consider alginate therapy for a trial period of 1–2 weeks as initial management of GORD.^{4,5} If the alginate therapy is successful NICE recommends to continue with it, but try stopping it at intervals to see if the infant has recovered.

In **formula-fed infants** with frequent regurgitation associated with marked distress, NICE recommends that if the stepped-care approach is unsuccessful (see the full NICE guidance but includes the trial of a thickened formula), to stop the thickened formula and offer alginate therapy for

a trial period of 1–2 weeks as initial management of GORD.^{4,5} If the alginate therapy is successful NICE recommends to continue with it, but try stopping it at intervals to see if the infant has recovered.

For **older children**, pharmacological treatment of GORD with alginates is not mentioned within the NICE guidance or the BNF for children treatment summary for GORD⁶. However alginate preparations are included in the BNF for children which are indicated for GORD.⁶ Peptac® liquid, Acidex® Advance oral suspension and Gaviscon® Infant sachets are the preparations of choice on the Barnsley Formulary.⁷ Consult the relevant SPC for dosing information for the age of the child at: <https://www.medicines.org.uk/emc/>

Detailed Prescribing Information for PPIs in the treatment of GORD^{6,8}

For enteral feeding administration please consult the NEWT guidelines.⁹ Also note that a licensed omeprazole oral suspension (2mg/ml and 4mg/ml) is available (licensed for children over 1 month of age) and has a green classification on the Barnsley Formulary for administration via feeding tubes.

OMEPRAZOLE – First choice PPI for children in Barnsley

Available as 10mg, 20mg and 40mg gastro-resistant capsules, gastro-resistant tablets or gastro-resistant dispersible tablets (brands include Losec® MUPS). Note that the 40mg strength is not stocked at BHNFT. (Omeprazole capsules and tablets may be used for gastro-oesophageal reflux disease and acid-related dyspepsia in children aged under 1 year and under 10 kg but they are unlicensed⁶)

Dispersible tablets (MUPS) can be dispersed in a small amount of water (approx. 10ml) then mixed with fruit juice, apple sauce or yoghurt on a spoon.⁹ The mixture should be taken straight away. Milk or fizzy water/fizzy drinks should not be used. The dispersible tablets (MUPS) can be cut in half using a tablet cutter if the dose is half of the full tablet e.g. 5mg, before dispersing in water. Some guidance⁸ advises that the dispersible tablets (MUPS) can be quartered to achieve doses of 2.5mg and 7.5mg but the practicalities of this should be discussed with the parent/carer. The division must be done before mixing the tablet as the omeprazole granules do not produce a uniform mixture when dispersed in a liquid. MUPS should not be dispersed in water to draw off a proportion. Try to avoid use of an oral syringe where granules will remain deposited. The enteric coated pellets must not be chewed⁸

The capsules can be opened and the contents mixed with a small amount of soft food such as yogurt, honey or jam. The child should swallow it all straight away, without chewing the granules. Alternatively the capsule contents can be mixed with fruit juice, apple sauce or non-carbonated water.^{6,10} The mixture should be taken straight away and rinsed down with half a glass of water.¹⁰ Some capsules (e.g. Dexel®) have an enteric-coated tablet inside. These capsules should **not** be opened.

A licensed (for children over 1 month of age) omeprazole oral suspension is available (2mg/ml and 4mg/ml) but this has a grey classification on the Barnsley Formulary for all indications apart from administration via feeding tubes (see above). It can be used ONLY when dispersible tablets (MUPS) have been tried and not tolerated or in cases where doses cannot be safely rounded to the nearest quarter dispersible tablet (MUPS).

Medicines for Children leaflet: Omeprazole for gastro-oesophageal reflux disease (GORD):
https://www.medicinesforchildren.org.uk/sites/default/files/content-type/leaflet/pdf/MfC_Omeprazole_for_GORD_PV2_2015-03-20.pdf

| Age/weight | Omeprazole Dosing | Notes |
|-------------------|--|--------------|
| Neonate | 700mcg/kg once daily, increased if necessary after 7-14 days to 1.4mg/kg once daily. Some neonates may require up to 2.8mg/kg once daily | |

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|---|--|-----------------------------|
| Child 1 month- 1 year | 700mcg /kg once daily, increased if necessary to 3mg/kg (max 20mg) once daily. (round dose to the nearest quarter omeprazole MUPS tablet (e.g. 2.5mg) where appropriate) | |
| Child 2-17 years (body-weight 10-19kg) | 10mg once daily, increased if necessary to 20mg once daily (in severe ulcerating reflux oesophagitis) | Max 12 weeks at higher dose |
| Child 2-17 years (body-weight ≥ 20kg) | 20mg once daily, increased if necessary to 40mg once daily (in severe ulcerating reflux oesophagitis) | Max 12 weeks at higher dose |

LANSOPRAZOLE

Available as 15mg and 30mg capsules and orodispersible tablets.
(Lansoprazole is **not licensed** for use in children)

Orodispersible tablets should be placed on the tongue, allowed to disperse and swallowed, or may be swallowed whole with a glass of water. Alternatively, tablets can be dispersed in a small amount of water and administered by an oral syringe.⁶ Some guidance⁸ advises that for doses less than 15mg, the dose can be rounded to the nearest quarter/half tablet (a tablet cutter should be used) **before** dispersing in water. The practicalities of this method should be discussed with the parent/carer.

Medicines for Children leaflet: Lansoprazole for gastro-oesophageal reflux disease (GORD) and ulcers:
https://www.medicinesforchildren.org.uk/sites/default/files/content-type/leaflet/pdf/20140530174723_0.pdf

| Age/weight | Lansoprazole Dosing | Notes |
|--------------------------------|--|--|
| Child (body-weight up to 30kg) | 0.5mg-1mg/kg (max 15mg) once daily in the morning (round dose to the nearest quarter tablet (e.g. 3.75mg) where appropriate) | Best given on an empty stomach, at least 30 minutes before a feed/food |
| Child (body-weight ≥ 30kg) | 15-30mg once daily in the morning | |

References

- MHRA Class 2 Medicines recall: Zantac Injection 50mg/2ml, Zantac Syrup 150mg/10ml, Zantac Tablets 150mg, Zantac Tablets 300mg (EL (19)A 24). Available at: <https://www.gov.uk/drug-device-alerts/class-2-medicines-recall-zantac-injection-50mg-2ml-zantac-syrup-150mg-10ml-zantac-tablets-150mg-zantac-tablets-300mg-el-19-a-24> Accessed <01.09.21>
- Press release: Zantac – MHRA drug alert issued as GlaxoSmithKline recalls all unexpired stock. 8.10.19. Available at: <https://www.gov.uk/government/news/zantac-mhra-drug-alert-issued-as-glaxosmithkline-recalls-all-unexpired-stock> Accessed <01.09.21>
- EMA confirms recommendation to suspend all ranitidine medicines in the EU, 24th November 2020. Available at: https://www.ema.europa.eu/en/documents/referral/ranitidine-article-31-referral-ema-confirms-recommendation-suspend-all-ranitidine-medicines-eu_en.pdf Accessed <01.09.21>
- NICE guidance: Gastro-oesophageal reflux disease in children and young people: diagnosis and management (NG1). Available at: <https://www.nice.org.uk/guidance/ng1> Accessed <01.09.21>
- NICE CKS. GORD in children. Available at: <https://cks.nice.org.uk/gord-in-children#!scenario> Accessed <15.10.19>
- BNF for Children. Available at: <https://www.medicinescomplete.com/#/> Accessed <01.09.21>
- Barnsley Joint Formulary. Available at: <http://www.barnsleyformulary.nhs.uk/default.asp> Accessed <01.09.21>
- Derbyshire JAPC. Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people April 2019. Available at: http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/Formulary_by_BNF_chap

[ter_prescribing_guidelines/BNF_chapter_1/GORD_in_children_and_young_people.pdf](#) Accessed <01.09.21>

9. NEWT guidelines. Available at: <https://access.newtguidelines.com/index.html> Accessed <01.09.21>
10. EMC. Losec 10mg capsules. Available at: <https://www.medicines.org.uk/emc/product/1495/smpc> Accessed <20.09.21>

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Detailed prescribing information for PPIs adapted from Derbyshire JAPC Guidance on Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people April 2019.

Development Process

This guideline has been subject to consultation and endorsement by the consultant pediatricians in Barnsley and was ratified by the Area Prescribing Committee on 10th November 2021.