NHS
Barnsley
Clinical Commissioning Group

RANITIDINE tablets, effervescent tablets and oral solution out of stock long-term (See CAS Alert)

Licensed use for gastrointestinal conditions

- Oral ranitidine should not be initiated in new patients.
- Patients currently prescribed oral ranitidine should be identified and reviewed on an individual basis to establish if ongoing treatment is still required (e.g. ranitidine may no longer be required if NSAID has been stopped).
- If ongoing treatment is still required, then consider switching to an alternative oral treatment.
  The CAS Alert contains clinical advice on alternatives to oral ranitidine in adults and children which has been produced by UK Medicines Information. The UKMi has also provided updated clinical advice regarding alternatives of ranitidine preparations, which can be found in the tables in the **Medicines Supply Notification (12/6/20)** embedded below. Local guidance has also been produced on Alternatives to Ranitidine Liquid for Gastro-Oesophageal Reflux Disease in Babies and Children

1. MSN2020 025 U2 Ranitidine- all formula

Points to consider (adults):

- It is recommended that, where possible, patients are not switched to an alternative H2-receptor antagonist in the first instance as this may exacerbate a shortage of these products.
  There are short term supply issues affecting alternative H2-receptor antagonists. Prior to prescribing a H2-antagonist, prescribers should liaise with the clinical pharmacist / technician in the practice to understand local stock availability (including resupply dates) of clinical alternatives. Further information and updates on these shortages are regularly disseminated through primary and secondary care networks. The supplying community pharmacist can also confirm stock availability, as it is noted that the resupply dates given by the manufacturers do not always reflect the stock at the wholesalers.
- Formulary choices (see the Barnsley Formulary):
  - PPIs:
    - Omeprazole capsules are the first line choice of PPI in Barnsley (omeprazole tablets have a significantly higher cost).
    - Lansoprazole capsules are the second line choice.
    - Pantoprazole tablets can be used if the patient is on medication which interacts with either of the above.
    - Lansoprazole orodispersible tablets should be used **only** for patients with swallowing difficulties or enteral tubes.
    - Rabeprazole is non-formulary in Barnsley.
    - The use of **esomeprazole is restricted**. It can be used for patients who remain symptomatic on omeprazole 40mg, but the patient must be reviewed regularly. It is restricted for use in Savary-Miller Grade IV oesophagitis (Los Angeles Grade D) or above, or when complicated by GI bleeding.
  - H2-antagonists:
    - Cimetidine has a grey classification on the Barnsley Formulary (N.B. Cimetidine has multiple drug interactions).
    - Famotidine and nizatidine are non-formulary but use of these H2-antagonists can be considered where cimetidine is not appropriate.
    - See **Appendix 1** for costs of alternative H2-receptor antagonists.

- There are slight variations in licensed indications, drug interactions and cautions for individual PPIs and H2- antagonists. Consult the product SPC for further information (e.g. omeprazole and esomeprazole interact with clopidogrel).
- Local guidance has been produced on Safe and Effective use of Proton Pump Inhibitors (PPIs). PPIs should be used only where clearly indicated and for the shortest duration that is appropriate. The patient should be reviewed regularly and consideration given to 'stepping down' to the lowest effective dose required to control symptoms, using PPIs 'as required' or discontinuation of treatment. A Proton Pump inhibitors Patient Information Leaflet is also available.
    - An alginate-containing antacid can be used where required alongside 'as required' PPI use. They can also help reduce rebound acid hypersecretion when reducing PPI therapy. Peptac® Liquid (first line choice) and Acidex® Advance are green on the Barnsley Formulary.

- If a PPI has been used in the past, review the rationale for switching the PPI to ranitidine, taking into consideration the following:
    - was treatment stepped down to ranitidine?
    - did the patient experience side effects to the PPI?
    - is a PPI contraindicated? (did the patient suffer a serious long-term PPI side-effect such as hypomagnesaemia or hyponatraemia, or has the patient got current or a history of *Clostridium Difficile* infection).
      Further information on serious adverse effects associated with long-term use of PPIs can be found in the guidance on Safe and Effective use of Proton Pump Inhibitors (PPIs). Where side effects were experienced but the PPI is not contraindicated, an alternative PPI could be prescribed.
- Consider if an 'as required' alginate-containing antacid (Peptac® Liquid (first line choice) or Acidex® Advance) is an appropriate alternative to ranitidine.

Additional points to consider for patients taking a combination of a PPI and ranitidine (adults):

- **NICE CKS Dyspepsia - proven GORD** contains some information on the combined use of both a PPI and ranitidine and considers it as **one of a number of options** for people with **persistent or recurrent symptoms and confirmed oesophagitis.** It states:

  Add in a histamine H2-receptor antagonist at bedtime, such as ranitidine, particularly if there are nocturnal symptoms. Prescribe a H2-receptor antagonist for short-term use (for example for a 2-week course intermittently).

  The recommendation is based on the opinion that adding a H2-receptor antagonist at bedtime may improve symptoms in people who have nocturnal acid breakthrough in the short-term, however tachyphylaxis (rebound symptoms) may occur after 1 week, and ongoing H2-receptor therapy is likely to become increasingly ineffective.

  Due to tachyphylaxis, local specialists usually advise to take the H2-receptor antagonist continuously for a period of 2 weeks, then miss for a week, and then keep repeating this cycle.

- Consider the patient's compliance with the PPI treatment.
- Consider reviewing the PPI to ensure the correct PPI is being used, at an appropriate dose, with the correct administration (doses should be given 30 minutes before breakfast and (if twice daily dose) 30 minutes before the evening meal, to provide optimal control of gastric pH).[1] See NICE CG184: Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management | Guidance | NICE for further information.

- **Alternative treatment options to ranitidine where the patient is on a PPI and ranitidine include:**
  - A 'trial without' ranitidine, followed by a review of the patient's symptoms (e.g. after 2 weeks). Consider use of an 'as required' alginate-containing antacid (Peptac® Liquid (first line choice) or Acidex® Advance) for breakthrough symptoms where clinically appropriate.
    Peptac® and Acidex® Advance contain sodium and are cautioned in patients on a sodium restricted diet (e.g. patients with hypertension/ heart failure/renal impairment).[2,3] *Acidex® Advance also contains potassium which should be taken into consideration for patients with reduced kidney function or patients on a controlled potassium diet.*[3]
  - Amend the choice of PPI and/or dose as appropriate.
  - If a H2-receptor antagonist is deemed necessary after trialling without ranitidine, using an 'as required' alginate-containing antacid where appropriate and amending the choice of PPI and/or dose where appropriate, OR after reviewing the patient's history, severity and duration of disease, then an alternative H2-antagonist can be considered (see above for more information on stock availability and formulary choices).

Specialist / unlicensed indications (e.g. chronic urticaria and angioedema)

- Oral ranitidine should not be initiated in new patients.
- Local specialists should be consulted for advice on alternatives to ranitidine for specialist / unlicensed indications and high-risk cohorts of patients.

References

1. NICE CKS Dyspepsia – proven GORD. Available at: https://cks.nice.org.uk/dyspepsia-proven-gord#!management Accessed 04.08.20
2. Peptac® Summary of Product Characteristics. Available at: https://mhraproductsproduction.blob.core.windows.net/docs/43e0355deb2f7ec87293c44708f4908edd9558ab Accessed 05.08.20
3. Acidex® Advance Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/9998/smpc Accessed 05.08.20

Acknowledgements

Adapted from Sheffield CCG 'Ranitidine tablets, effervescent tablets and oral solution out of stock long-term' guidance available at:
https://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/Practice%20resources%20and%20PGDs/Meds%20Supply%20Issues/Flowchart_reviewing_ranitidine.pdf

Development Process

This guidance has been developed by the CCG Medicines Management Team and has been subject to consultation and endorsement by the gastroenterologists in Barnsley and was approved at the Area Prescribing Committee on 14th October 2020.

Appendix 1: Costs of alternative H2-receptor antagonists (Drug Tariff August 2020)

H2-receptor antagonist	**Cost (£) for 28 tablets/capsules or 28x5ml dose oral solution** (N.B. There are differences in the recommended frequencies of administration of different H2-receptor antagonists depending on the indication)
Cimetidine 200mg tablets	£8.65
Cimetidine 200mg/5ml oral solution	£6.65
Cimetidine 200mg/5ml oral solution sugar free	£15.95
Cimetidine 400mg tablets	£7.42
Cimetidine 800mg tablets	£19.83
Nizatidine 150mg capsules	£4.69
Nizatidine 300mg capsules	£14.40
Famotidine 20mg tablets	£21.99
Famotidine 40mg tablets	£38.99