SUMMARY

H₂ antagonists aid the healing of gastric and duodenal ulcers, relieve the symptoms of gastro-oesophageal reflux and episodic dyspepsia, promote healing of (and help prevent) NSAID-associated ulcers and are, occasionally still, used in the treatment of Zollinger-Ellison syndrome¹.

As with proton pump inhibitors, H₂ antagonists are widely prescribed and account for a significant proportion of the prescribing budget expenditure. Ranitidine is the Dumfries and Galloway formulary choice.

This review will highlight patients eligible for switching to the formulary choice.

OBJECTIVE

To promote the D&G Formulary choice where this will provide equal or better clinical care.
To deliver cost-effective prescribing and clinical care.

RATIONALE

Various trials support the use of ranitidine 150mg bd or 300mg od for acid suppression, reduction of dyspepsia and for ulcer healing. Ranitidine appears to be of equal efficacy with famotidine and nizatidine and superior to cimetidine. It may provide longer-lasting acid suppression than nizatidine². It is NHS Dumfries and Galloway’s formulary 1st choice H₂ antagonist because of its clinical and cost-efficacy.

Cimetidine’s effect on liver enzymes causes it to interact with many other drugs (see later list and BNF). Some of these interactions can significantly
effect the clinical control of the patient’s other conditions. Ranitidine has fewer significant drug-drug interactions.

Dose equivalence Data
Ranitidine 150mg bd has been shown to be more effective in reducing day and nighttime stomach acid activity in patients with duodenal ulcer than cimetidine 200mg tds and 400mg n³. Healing rates of duodenal ulcer, following 4 weeks treatment, are similar when patients are given either ranitidine 150mg or cimetidine 200mg tds & 400mg n⁴. Head-to-head comparison of duodenal ulcer healing rates with famotidine 40mg od and ranitidine 300mg od treatment showed no statistical difference⁵. Both drugs produced satisfactory relief of pain and dyspeptic symptoms⁶. Similar results were found for gastric ulcer healing rates with these two drugs. In this comparison, both drugs were equally well tolerated and the need for antacids was similar in both treatment groups⁶.

In healthy volunteers, a placebo-controlled trial comparing ranitidine 300mg daily, famotidine 40mg daily and cimetidine 800mg daily showed ranitidine and famotidine provide similar acid reduction and are superior to cimetidine⁷. Ranitidine 150mg bd produces equal gastric and duodenal ulcer healing rates as Nizatidine 150mg bd or 300mg od⁸⁻¹¹.

Price Comparison & Dose Equivalencies

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Dose</th>
<th>Cost/30 days+</th>
<th>Equivalent Rantidine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranitidine</td>
<td>150mg bd</td>
<td>£1.76</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>300mg od</td>
<td>£1.95</td>
<td>-</td>
</tr>
<tr>
<td>Effervescent</td>
<td>150mg bd</td>
<td>£17.62</td>
<td>Change to regular tablets or consider orodispersible lansoprazole (15mg, £2.99, 30mg £5.50)</td>
</tr>
<tr>
<td>Effervescent</td>
<td>300mg od</td>
<td>£16.59</td>
<td></td>
</tr>
<tr>
<td>Famotidine</td>
<td>20mg od</td>
<td>£4.84</td>
<td>150mg od</td>
</tr>
<tr>
<td></td>
<td>40mg od</td>
<td>£6.11</td>
<td>150mg bd or 300mg od</td>
</tr>
<tr>
<td></td>
<td>20mg bd</td>
<td>£9.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40mg bd</td>
<td>£12.22</td>
<td>Review ongoing need for high dose</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>200mg bd</td>
<td>£8.39</td>
<td>Ranitidine 150mg bd</td>
</tr>
<tr>
<td></td>
<td>400mg od</td>
<td>£3.71</td>
<td></td>
</tr>
<tr>
<td></td>
<td>400mg bd</td>
<td>£7.41</td>
<td></td>
</tr>
<tr>
<td></td>
<td>800mg od</td>
<td>£22.21</td>
<td></td>
</tr>
<tr>
<td>Nizatidine</td>
<td>150mg od</td>
<td>£11.66</td>
<td>150mg od</td>
</tr>
<tr>
<td></td>
<td>150mg bd</td>
<td>£23.32</td>
<td>150mg bd or 300mg od</td>
</tr>
<tr>
<td></td>
<td>300mg od</td>
<td>£17.67</td>
<td></td>
</tr>
</tbody>
</table>
**METHOD**

A computer search will be used to identify patients currently receiving repeat prescriptions for Famotidine, Nizatidine, Cimetidine and effervescent Ranitidine.

The auditor will record on the data collection form, the following information regarding each patient identified by the search;

- the indication for the H₂ antagonist
- the dosage, frequency and strength of tablets issued
- the apparent compliance
- treatment duration
- intended treatment duration (from endoscopy reports etc.)
- any interacting drugs and any action required regards this
- whether the Formulary choice has been used before
- any significant drug allergies/intolerances
- whether a specific product has been recommended for a special reason

Where information is not available in the patient’s electronic records, the paper notes will be checked and missing information recorded on the data collection form. This information will be verified by the GP and added to the electronic notes by administrative staff where appropriate.

The Prescribing Support Technician will then identify which patients are suitable for a switch to ranitidine and recommend an equivalent dose to their current therapy. The recommendations will be presented to the GP for authorisation that the change can take place.

Where it does not seem appropriate to switch the patient to ranitidine, the preferred treatment should be prescribed in the most cost-efficient regimen (see table above).

Patients who are prescribed an H₂ antagonist and a Proton Pump Inhibitor should be referred to the GP to query if both are required.

Non-compliant patients can be brought to the attention of the GP. Where the patient has not requested the H₂ antagonist in the last 12 months, and it is not prescribed as GI-protection (e.g. secondary to steroid or NSAID use) or for Zollinger-ellison or Barret’s oesophagus, the item will be removed from the repeat list in accordance with the house-keeping protocol unless the practice advise otherwise.

The Prescriber will be informed of any drug interactions if these are felt to be of significance.

A note will be made in the patient’s computer record detailing the action taken and letters will be sent out to explain any changes.
The local community pharmacy/pharmacies will be informed about the activity

**EXCLUSION CRITERIA**
Children under the age of 16yrs or those under the care of a paediatrician. Patients prescribed cimetidine for opioid-induced sweating (unlicensed use).

**LIMITATIONS**
This audit is NOT aimed at identifying patients for whom an H$_2$ antagonist may be appropriate but who are not currently prescribed one. It will not primarily identify those patients for whom the clinical need for long-term treatment with H$_2$ antagonist should be reviewed or assess the appropriateness of stepping up or down treatment. Some referrals of this nature may be made to the Prescriber where the Prescribing Support Team has a query. However, the number of patients on long-term therapy will be recorded for information and reported in the work summary. It will not identify those patients for whom a Proton Pump Inhibitor may be a more appropriate treatment than an H$_2$ antagonist.

**SUGGESTED CRITERIA FOR REFERRAL TO PRACTICE**
Those described in the Method section and any specified by the practice.
CHANGES TO REPEAT PRESCRIBING

1. The audit must be checked and agreed with a GP in the practice prior to work being undertaken by the Prescribing Support Team.

2. Agreement is made between the Practice and the Prescribing Support Technician on a suitable date for implementation.

3. It is recommended that the prescribing support technician notify local community pharmacies of the impending change in prescribing.

4. The Prescribing Support Technician conducts a search of the Practice Clinical System to identify patients currently prescribed an H₂-antagonist.

5. The patient list is checked to ensure that all patients are still undergoing treatment and are compliant.

6. Patients are assessed, with respect to potential referral to GP or who require documentation of clinical information held on paper notes only.

7. No patient may be changed beyond the scope of the SPC unless authorised by the prescriber.

8. All changes to prescribing must be recorded within the prescribing field and, wherever possible, an indication recorded for the medication added.

9. Each patient should be informed of any changes made in accordance with the Practice’s preferred mode of communication. The Prescribing Support Team recommends personalised written communication sent from the Practice. Additional information e.g. patient leaflets may be included wherever possible.

10. If the patient is in residential care or has their medication otherwise supervised, e.g. Dosette dispensing, information regarding any changes should also be communicated to the relevant service providers.

11. The Prescribing Support technician will communicate information about the review to relevant personnel within the practice e.g. receptionists, nurses and will, if appropriate, create on-screen reminders on the Clinical System.

12. A project file is retained by the Practice containing a list of patients involved, patient letter templates and any individual information sent, a copy of the protocol and prescribing review form and contact details for the Prescribing Support Team.

13. The Prescribing Support Technician may record statistics of the review for report purposes and analysis of the review. No information regarding individual patients leaves the practice.
**Interacting Medication**

NB. This is not an exhaustive list; for more detailed information, please refer to individual SPC’s and BNF.

* denotes interactions that are potentially hazardous and should be avoided.

**H₂ antagonist interactions**
- Atazanavir* (possible reduces plasma concentration)
- Itraconazole* (reduces absorption)
- Ketoconazole* (reduces absorption)
- Posaconazole* (reduces plasma concentration)
- Tolazoline* (effects antagonised)

**Cimetidine-specific Interactions**
- Amiodarone* (increases plasma concentration)
- Amitriptyline (increases plasma concentration)
- Benzodiazepines (increases plasma concentration)
- Calcium Channel Blockers (possibly increases plasma concentration)
- Carbamazepine* (increases plasma concentration)
- Chloroquine* (increases plasma concentration)
- Chlorpromazine* (possibly enhances effects)
- Ciclosporin* (possibly increases plasma concentration)
- Cilostazol* (possibly increases plasma concentration; AVOID)
- Citalopram (increases plasma concentration)
- Clomethiazole (increases plasma concentration)
- Clozapine* (possibly enhances effects)
- Coumarins* (including Warfarin, enhances anticoagulant effect)

**CYTOTOXICS*; see BNF**
- Doxepin (increases plasma concentration)
- Ergotamine* (increases risk of ergotism; AVOID)
- Erythromycin (increases risk of toxicity)
- Escitalopram (increases plasma concentration)
- Flecainide* (increases plasma concentration)
- Hydroxychloroquine* (increases plasma concentration)
- Imipramine (increases plasma concentration)
- Labetolol (increases plasma concentration)
- Lidocaine/Lignocaine* (increases risk of toxicity)
- Loratadine (may increase plasma concentration)
- Mebendazole (increases plasma concentration)
- Melatonin (increases plasma concentration)
- Methysergide* (increases risk or ergotism; AVOID)
- Metoprolol (increases plasma concentration)
- Metformin (increases plasma concentration)
- Metronidazole (increases plasma concentration)
- Moclobemide (dose should be halved)
Mirtazapine (increases plasma concentration)
Nortriptyline (increases plasma concentration)
Octreotide (absorption of cimetidine possibly delayed)
Opioid analgesics (increases plasma concentrations)
Phenytoin* (increases plasma concentration)
Pramipexole (increases plasma concentration)
Propafenone* (increases plasma concentration)
Propranolol (increases plasma concentration)
Quinine* (increases plasma concentration)
Rifampicin (reduces plasma concentration)
Sertraline (increases plasma concentration)
Sertindole (increases risk of ventricular arrhythmias; AVOID)
Sildenafil (increases plasma concentration; reduce initial dose)
Sulphonylureas (Gliclazide, Glipizide, Glimepiride, Glibenclamide, Tolbutamide; enhances hypoglycaemic effect)
Theophylline* (increases plasma concentration)
Thyroxine (reduces absorption)
Terbinafine* (increases plasma concentration)
Tricyclic Antidepressants (possibly increases plasma concentration)
Zolmitriptan (inhibits metabolism; reduce dose of zolmitriptan)
Valproate* (increases plasma concentration)
Warfarin* (enhances anticoagulant effect)
REFERENCES

## H2-antagonist Formulary Adherence: Data Collection

|----------------------|-------------|-----------------------------------------------------------------------|-----------------|-----------------------------------------------|----------------------|--------------|----------------|
Dear Mr x

(Anywhere St
DOB)

H₂ -Antagonists

We are currently reviewing all patients prescribed an H₂ Antagonist (Cimetidine, Nizatidine or Famotidine)

We would like to change your current treatment to Ranitidine xmg daily/twice daily. Ranitidine is similar to your previous medicine but more cost-effective than your current medicine. It is proven to reduce the acidity of your stomach, helping to prevent or treat indigestion and ulcers.

Other measures that can help, with indigestion, are;

- Avoiding spicy food
- Stopping smoking.
- Eating less fatty food
- Reducing the intake of caffeine, alcohol, fizzy and citrus fruit drinks
- Reducing portion sizes
- Avoiding eating before bedtime
- Losing weight (if applicable)

Care has been taken to select only those patients for whom this change seems appropriate. If you feel that Ranitidine will not be suitable for you or does not agree with you, please contact the Prescribing Support Team at the number above or contact the Practice directly.

Please continue to use your current medicine until your supply is finished. Ranitidine will be available the next time you request your repeat medications.

If you would like any more information on medicines for the stomach, or the change to your medication, please get in touch.

Prescribing Support Team