NHS Greater Glasgow & Clyde
Mental Health Services

-Protocol for the use of Unlicensed Pirenzepine

Indication

Pirenzepine is an unlicensed medicine indicated for use as an alternative treatment of hypersalivation secondary to clozapine treatment in patients for whom an adequate trial of hyoscine hydrobromide (both tablets and transdermal patches) and trihexyphenidyl have been unsuccessful either due to lack of efficacy or side effects. Pirenzepine was previously licensed in the UK for the management of duodenal ulcers but its use for this indication was superseded by the H2 antagonists and proton pump inhibitors. It was not withdrawn in the UK on safety grounds. It must not be used first line for clozapine-induced hypersalivation due to the unlicensed status.

Informed consent

Due to its unlicensed status, informed consent and explanation for the rationale of treatment choice must be obtained prior to treatment initiation.[1] Patient information explaining unlicensed medication in general terms is available via the Choice and Medication portal, as is a specific pirenzepine for hypersalivation leaflet.[2] Where there is a lack of capacity, adherence to the principles contained in the Adults with Incapacity (Scotland) Act, 2000 is mandatory.

Documentation

The consultant psychiatrist must make a clear record of the rationale for prescribing an unlicensed medication within the patient's case notes and document the discussion regarding consent.[1]

In-patient prescribing and administration

Nursing staff in the ward must be informed of the medicine's unlicensed status by the prescriber and ward clinical pharmacists must ensure that staff are aware of the unlicensed status.

When ordering pirenzepine, the patient's initials and CHI should be included on the requisition as well as the phrase "as per protocol" for the order to be processed. A record of administration of unlicensed medication must be kept (as per unlicensed medication policy).[3] When entering administration on HEPMA, the drug batch number and expiry date should be recorded when prompted. It is the responsibility of the nurse in charge to ensure this occurs.

When supplying pirenzepine from pharmacy, pharmacy staff must ensure that batch numbers are documented on the prescription or requisition.

Out-patient prescribing

The clozapine dispensary at Leverndale will supply pirenzepine prescriptions after discharge to outpatients. The standard clozapine out-patient prescription form will be used to prescribe pirenzepine in addition to the patient's regular clozapine dose.

Review

Need for ongoing prescription of an unlicensed medicine should be assessed on a 6 monthly basis

Monitoring

There is no requirement for any specific monitoring. Close monitoring of bowel function is mandatory with the combination of clozapine and pirenzepine and should be reflected within the clozapine side effect template on EMIS. Refer to the Guidelines for assessment and management of clozapine induced constipation for further information.

Approved by Prescribing Management Group (Mental Health)
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Dose range[4,5,6,7]
25-100mg/day (150mg in exceptional circumstances).

The limited published evidence available to support the use of pirenzepine for clozapine-induced hypersalivation has suggested a usual maximum of 100mg daily, although in practice 150mg daily is often used without issue. NB when pirenzepine had a product licence for duodenal ulcers, its maximum licensed dose was 150mg daily.

Evidence base
One randomised trial demonstrated no effect[4], however extensive clinical experience suggests efficacy in some individuals. The use of pirenzepine is recommended in both the Maudsley Guidelines & Psychotropic Drug Directory.[5,6]

Proposed mode of action
Selective anticholinergic at M_1, M_4 receptors

Side effects [7,8,9]

Very common	(> 1 in 10);	dry mouth
Common	(<1/10 and >1/100);	headache, blurred vision, constipation, diarrhoea, skin rash
Uncommon	(<1/100 and >1/1000);	urinary retention
Very rare	(<1/10,000):	confusional states
Not known		anaphylactic reactions, hypersensitivity reactions

If visual disturbance or urinary retention occurs the pirenzepine must be discontinued. [8]

Contraindications[8]
- Hypersensitivity to pirenzepine or any excipients
- Paralytic ileus
- Pregnancy

Cautions[8]
- Renal impairment (CrCl< 30ml/min)
- Glaucoma
- Prostatic hypertrophy
- Tachycardia

Interactions
May exacerbate the anticholinergic effects of other drugs including clozapine, especially constipation.

References:

1. GMC Good practice in prescribing and managing medicines and devices. Updated Dec14 http://www.gmc-uk.org/guidance/ethical_guidance/14316.asp

2. Choice and Medication. Handy Fact Sheets. Unlicensed medications and pirenzepine PIL http://www.choiceandmedication.org/nhs24/

3. NHS Greater Glasgow and Clyde Area Drug and Therapeutics Committee Policies Relating to the Management of Medicines Section 9.1 Acute Unlicensed Medicines Policy (ULM Policy)

4. UKMi Medicines Q&A. Drug-induced hypersalivation- what treatment options are available? May17

5. Bazire S. Psychotropic Drug Directory 2016; Lloyd Reinhold Publications

6. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry; 13th edition: Wiley Blackwell

7. Patient Information Leaflet Gastrozepin (Translation). Boehringer Ingelheim. January 2019

8. Summary of Product Characteristics Gastrozepin. Boehringer Ingelheim. July 2013. (obtained from Mawdsley Brooks & Co)

9. Martindale. The Complete Drug Reference. https://www.medicinescomplete.com/mc/martindale/2009/ Accessed 4/8/17.