TAYSIDE PRIMARY CARE NHS TRUST

TAYSIDE PRESCRIBER

September 2000

Issue 78

CISAPRIDE (PREPULSID®) WITHDRAWAL - WHAT NOW?

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BACKGROUND

Prolongation of the QT-interval by cisapride, which predisposes to serious ventricular arrhythmias, was first highlighted by the Committee on Safety of Medicines (CSM) in February 1995 (*Current Problems* 1995*;* **21**: 1) and again in August 1998 (*Current Problems* 1998*;* **24**: 11). Advice was given on maximum recommended dose and the need to avoid concomitant use with other medicines which inhibit the liver metabolism of cisapride or which also prolong the QT-interval. Very recently the Scottish Executive (Health Department) confirmed the decision to suspend all product licences for Prepulsid® brand of cisapride from 28th July " . . . pending a European-wide review of its safety and benefits."

What now for those patients who have relied on cisapride in the past?

ACTION AND USES OF CISAPRIDE

The BNF (No 39, March 2000) describes cisapride as " . . . a motility stimulant believed to promote release of acetylcholine in the gut wall . . .". In fact, its action is mediated via 5-HT (serotonin) receptors - it is both an *antagonist* at the 5-HT_3 receptor and an *agonist* at the 5-HT_4 receptor, by which mechanisms it increases gut motility and stimulates gastric emptying. Stimulation of acetylcholine release occurs as an indirect consequence of its action at the 5-HT_3 receptor. Cisapride also increases lower oesophageal sphincter pressure by between 20% and 50% and the amplitude of oesophageal contractions and reduces the time during which the intragastric pH < 4.

Cisapride has been used in the following situations:

- Symptomatic treatment and maintenance of gastro-oesophageal reflux disease
- Treatment of non-ulcer dyspepsia
- Relief of symptoms associated with impaired gastric motility secondary to disturbed/delayed gastric emptying associated with diabetes, systemic sclerosis and autonomic neuropathy
- Relief of infantile gastro-oesophageal reflux. Note however that the CSM advises a contraindication to its use in premature infants of gestational age < 36 weeks for up to 3 months of age in whom unpredictable pharmacokinetics could result in accumulation of toxic blood levels.

ALTERNATIVES TO CISAPRIDE

Domperidone/Metoclopramide are dopamine D_2 receptor blockers and this (at least in part) explains their use as anti-emetics. Their GI prokinetic activity, however, probably results from an indirect effect on cholinergic transmission which is mediated via 5-HT receptors in the gut (ie they also possess cisapride-like activity). It is mainly by this mechanism that these agents increase lower oesophageal sphincter pressure and hasten gastric emptying. Domperidone may be preferred in younger and very old subjects who appear most susceptible to the acute dystonic reactions that are associated with metoclopramide.

Other measures e.g **ondansetron** or **erythromycin** may be considered, however such treatment is outwith licensed indications and should therefore be reserved for specialist use.

MEANWHILE CISAPRIDE IS STILL AVAILABLE - ON A NAMED PATIENT BASIS

Janssen-Cilag are willing to supply Prepulsid® brand of cisapride during the suspension of the product licence. They can only do so when treatment is requested for a named patient - such treatment is, of course, provided outwith licence and responsibility for the product rests solely with the prescriber. The stated indications for which a supply can be issued under these terms are:

- Gastro-oesophageal reflux disease: curative and maintenance treatment of gastro-oesophageal reflux disease, including oesophagitis, in patients not responding adequately to lifestyle modifications, antacids and gastric acid reducing agents.

- Severe forms of other gastrointestinal motility disorders:

  - Documented gastroparesis for patients who have failed or are unsuitable for other prokinetic treatment.
  - X-ray or endoscopy negative dyspepsia, persistent for at least three months, in patients not responding adequately to lifestyle modifications, antacids and gastric acid-reducing agents.

Janssen-Cilag further point out that the need for continued treatment should be re-evaluated periodically. A specialist gastroenterologist should confirm that the patient's condition is serious and that the patient's diagnosis satisfies the above indications. The specialist should review the patient at least every 3 months. A list of contraindications and drug interactions is provided.

Requests should be sent to the Medical Department, Janssen-Cilag Ltd, Saunderton, HIGH WYCOMBE, Buckinghamshire HP14 4HJ. Telephone 0800 679 7681. Fax 01494 567445.

FULL MARKS MOUSSE® FOR HEAD LICE INFECTION

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Full Marks Mousse® (Phenothrin 0.5%) has recently been widely promoted to the professional and lay press. The Policy for the Control of Head Louse Infection in Tayside produced by the Communicable Disease Department of Tayside Health Board was produced in August 1999 and makes the following recommendations regarding the use of Full Marks Mousse®.

- Only individuals with **proven head louse infection** should be treated.
- **First line** treatment for head louse infection remains **malathion alcoholic or aqueous solution.**
- Second line treatments should only be used if first line treatment fails to cure, having given due consideration to possible reasons for treatment failure e.g. incorrect application of product.
- Full Marks Mousse is considered as a second line treatment in Tayside along with Full Marks Lotion and Liquid.
- Any treatment for head louse infection should be repeated after 7 days in case some of the eggs have survived the first application.

Note that, as Full Marks Mousse® is formulated in an alcoholic base, it should not be used if skin or chest conditions are present.
Full details of the Tayside Policy for the Control of Head Louse Infection in Tayside are available from Shona Halley, Public Health Infection Control Nurse, Tel: 01382 596986.