

# Memo – shortage of supply

8<sup>th</sup> December 2015

## **Re: Cyclizine lactate 50 mg/ml Injection**

### **Description of product affected**

Cyclizine is licensed for the prevention and treatment of nausea and vomiting in adults including:

- Motion sickness when the oral route cannot be used.
- Nausea and vomiting caused by narcotic analgesics and by general anaesthetics in the post-operative period.
- Vomiting associated with radiotherapy especially for breast cancer since cyclizine does not elevate prolactin levels.
- Pre-operative use in patients undergoing emergency surgery in order to reduce the hazard of regurgitation and aspiration of gastric contents during induction of general anaesthesia.

The SPC also mentions that cyclizine may be of value in relieving vomiting and attacks of vertigo associated with Menière's disease and other forms of vestibular disturbance when the oral route cannot be used. The injection is administered by the intramuscular or intravenous route up to three times daily.<sup>1</sup>

### **Background**

There is a delay to the delivery of cyclizine injection and stock is now expected in Jan 2016. The company anticipates being out of stock for between 2 to 4 weeks.<sup>2</sup>

### **Current usage**

- There is a well defined role for cyclizine injection in the palliative care setting.<sup>3,4</sup> Because of its antimuscarinic properties, the use of cyclizine tends to be restricted to situations where metoclopramide and/ or other more specific antiemetics (e.g. haloperidol, 5HT<sub>3</sub> antagonists) have failed to provide relief e.g. some patients with mechanical bowel obstruction or as the antiemetic of choice for raised intracranial pressure. In the UK, cyclizine is generally the antihistaminic antimuscarinic anti-emetic of choice.<sup>5</sup>
- Cyclizine is commonly used for the prevention and management of postoperative nausea and vomiting.
- Cyclizine can be administered by midwives in the course of their professional practice under the Medicines Act exemptions i.e. without the need for a prescription from an authorised prescriber or without the need for a specific Patient Group Direction.<sup>6,7</sup>

### **Alternative agents and management options**

Drugs used for postoperative nausea and vomiting include 5HT<sub>3</sub>-receptor antagonist, some phenothiazines, and antihistamines. A combination of two or more antiemetic drugs that have different mechanisms of action is often indicated in those at high risk of postoperative nausea and vomiting (PONV) or where postoperative vomiting presents a particular danger (e.g. in some types of surgery). When a prophylactic antiemetic drug has failed, PONV is treated with one or more drugs from a different class. Other antipsychotic drugs including haloperidol and levomepromazine are used for the relief of nausea and vomiting in terminal illness.<sup>8</sup>

The only other antiemetic midwives can administer under the Medicines Act exemptions is prochlorperazine injection.<sup>6</sup> Alternative agents would be ondansetron or metoclopramide injection but a prescription would be required. In practice, ondansetron would be used postnatally and not during delivery. Metoclopramide is usually avoided in this patient group as some may not tolerate it. However there may be more experience in this area with use of the latter agent.<sup>7</sup>

Due to the large cost increase in cyclizine, there has been a move in some areas towards use of ondansetron, but there may be a small number of patients who will need cyclizine if other antiemetics are unsuitable or ineffective<sup>9</sup> as it tends to have fewer interactions with other medications or additive side effects.<sup>3</sup>

In order to preserve existing stock for critical areas, cyclizine may need to be restricted for palliative care use and no longer used as a first line antiemetic in areas where alternatives antiemetics are available, such as using ondansetron for post operative N&V. Advice should be sought from the relevant specialist team in the event of a shortage. Importers are currently investigating availability of cyclizine from outside the UK.

The table below outlines some of the treatment alternatives:

<b>Antiemetic</b>	<b>Type</b>	<b>Antiemesis indication</b>	<b>Notes/cautions</b>
Ondansetron <sup>10</sup>	5HT <sub>3</sub> antagonists	Management of N&V induced by cytotoxic chemotherapy and radiotherapy; and prevention and treatment of post-operative nausea and vomiting (PONV) <sup>10</sup>	<p>It can cause dose-dependent prolongation of ECG corrected QT interval (QTc), which can lead to Torsade de Pointes, It should be avoided in patients with congenital long QT syndrome and caution must be used if administering to patients with risk factors for QT interval prolongation or cardiac arrhythmias and with concomitant use of drugs that prolong the QT interval.<sup>11</sup></p> <p>Ondansetron is known to increase large bowel transit time so patients with signs of sub-acute intestinal obstruction should be monitored after administration of dose.<sup>11</sup></p> <p>Constipation is a common adverse effect.<sup>11</sup></p> <p>It has a relatively short half life so administered towards the end of surgery.<sup>12</sup></p>
Dexamethasone <sup>13</sup>	Glucocorticoid	Off label use	

Prochlorperazine <sup>14</sup>	Phenothiazine neuroleptic.	N&V from whatever cause <sup>14</sup>	Only licensed for IM use
Haloperidol <sup>15</sup>	Butyrophenone neuroleptic	Treatment of N&V <sup>15</sup>	Intermittent supply problems
Droperidol <sup>16</sup>	Butyrophenone neuroleptic	Prevention and treatment of PONV in adults and, as second line, in children  Prevention of N&V induced by morphine and derivatives during post-operative patient controlled analgesia (PCA) in adults <sup>16</sup>	Contraindication in patients with known or suspected prolonged QT and those treated with medicinal products known to prolong the QT interval
Metoclopramide <sup>17</sup>	Structurally related to phenothiazines	Treatment N&V associated with: GI disorders, cyclical vomiting, intolerance to cytotoxic drugs, congestive heart failure, deep x-ray or cobalt therapy, and post-anaesthetic vomitin <sup>17</sup>	Not suitable for patients with bowel obstruction <sup>15</sup>  Prefer to avoid for 3-4 days after surgery involving gut anastomosis <sup>18</sup>
Levomepromazine <sup>19</sup>	Possesses pharmacological actions similar to chlorpromazine and promethazine	Off label use (palliative care)	As with other neuroleptics, cases of QT interval prolongation have been reported

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