

Anti-emetic agents

Following the recent MHRA alert on metoclopramide, and a previous alert relating to domperidone safety concerns in certain patients groups, this document has been produced as an aid to help prescribers choose the most suitable agent.

It is obviously not possible to provide in-depth information on each drug in a document of this style, prescribers should also refer to the BNF and SPC for more details, and assess each patient on an individual basis prior to making a decision on the most appropriate agent. Prescribers are encouraged to use this new advice as an opportunity to review their patients' ongoing need for an anti-emetic

Other anti-emetic agents are available, however, when possible drugs from the NHS Gateshead CCG formulary should be considered prior to non-formulary options. To encourage prescribers to use formulary agents this document only considers formulary anti-emetic agents. The table below illustrates the licensed indications for each of the respective agents

Drug	Indications							
	Nausea & vomiting	Motion sickness	Vertigo	Dyspepsia	GORD	CINV	N& V in Meniere's disease	Delayed gastric emptying or poor gastric motility
Betahistine							x	
Cinnarizine		x	x				x	
Cyclizine	x	x	x				x	
Domperidone	x			x	x			x
Metoclopramide	x			x	x			x
Ondansetron						x		
Prochlorperazine	x		x					
Promethazine	x	x	x					

GORD = Gastro-Oesophageal Reflux Disease CINV= Chemotherapy-Induced Nausea & Vomiting

The tables on the subsequent pages give details on the cautions, contra-indications, side effects, MHRA advice and significant interactions of these agents.

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Drug	Contra- Indications	Cautions	MHRA advice	Side Effects	Significant interactions
Betahistine	Phaeochromocytoma	<ul style="list-style-type: none"> • Asthma • History of peptic ulcer • Not recommended for children 		<ul style="list-style-type: none"> • Nausea • Dyspepsia • Headache 	<ul style="list-style-type: none"> • Antihistamines • Caution is recommended with MAO inhibitors
Cinnarizine		<ul style="list-style-type: none"> • Parkinson's disease 		<ul style="list-style-type: none"> • Nausea • Dyspepsia • Somnolence • Weight increased 	<ul style="list-style-type: none"> • Alcohol • CNS depressants • TCAs
Cyclizine		<ul style="list-style-type: none"> • Severe heart failure • Porphyria • Glaucoma • GI obstruction • Hepatic disease • Epilepsy • Prostatic hypertrophy 			<p>Additive effects with alcohol and other central nervous system depressants e.g. hypnotics, tranquillisers, anaesthetics.</p> <p>Note: <u>Reports of abuse of cyclizine for its euphoric or hallucinatory effects have been noted.</u></p> <p>Prescribers should exercise caution in prescribing to those with a history of addiction or abuse.</p>
Domperidone	<ul style="list-style-type: none"> • Prolactinoma • If gastric motility is harmful • Hepatic or Renal impairment 	<ul style="list-style-type: none"> • Not recommended for children • QT prolongation • Electrolyte disturbances • Cardiac disease 	<p>There is a small increased risk of serious ventricular arrhythmia or sudden cardiac death with domperidone. These risks may be higher in patients older than 60 years and in those receiving daily doses of more than 30 mg.</p>	<ul style="list-style-type: none"> • GI disturbances • Galactorrhoea • Gynaecomastia • Hyperprolactinaemia 	<p>Erthromycin, Citalopram and other drugs known to prolong the QT interval.</p> <p>Ketonconazole should be avoided due to risk of ventricular arrhythmias.</p>

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Metoclopramide	<ul style="list-style-type: none"> • GI obstruction, perforation or haemorrhage • Phaeochromocytoma • Children younger than 1 year 	<ul style="list-style-type: none"> • Elderly • Young adults and children (those under 20 years of age) • Atopic allergy (including asthma) • Epilepsy 	<p>A review demonstrated that in long term or high dose treatment the risks of extrapyramidal and cardiovascular effects outweighed the benefits. It was noted that the risk of these adverse effects is higher in children than in adults. Metoclopramide should not be used for longer than 5 days and new lower maximum doses are recommended. See recent email circulation for further details.</p>	<p>Extrapyramidal effects (particularly in those under 20 years of age) Hyperprolactinaemia</p>	<p>Ciclosporin</p>
Ondansetron	<p>Congenital long QT syndrome</p>	<ul style="list-style-type: none"> • Risk of QT prolongation • GI obstruction • Adenotonsillar surgery 	<p>Caution must be used if administering ondansetron to patients at risk of QT prolongation or arrhythmias. Hypokalaemia and hypomagnesaemia should be corrected before ondansetron administration</p>	<ul style="list-style-type: none"> • Constipation • Headache • Flushing 	<p>Phenytoin, Carbamazepine and Rifampicin reduce the effectiveness of ondansetron.</p> <p>Erthromycin, Domperidone, Citalopram and other drugs known to prolong the QT interval.</p>

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Drug	Contra- Indications	Cautions	MHRA advice	Side Effects	Significant interactions
Prochlorperazine	Avoid in children under 10kg	<ul style="list-style-type: none"> Elderly Epileptics- due to lower seizure threshold Cardiovascular disease or family history of QT prolongation 		Extrapyramidal symptoms	Acute withdrawal symptoms including nausea, vomiting, sweating and insomnia have been described after abrupt cessation.
Promethazine	Contraindicated for use in children less than 2 years of age because of the potential for fatal respiratory depression	<ul style="list-style-type: none"> Asthma Bronchitis Bronchiectasis Bladder neck or pyloro-duodenal obstruction Severe coronary artery disease Narrow angle glaucoma Epilepsy Hepatic and renal insufficiency Children and adolescents with signs and symptoms suggestive of Reye's Syndrome 		Drowsiness, Dizziness, Restlessness, Headaches, Nightmares, Tiredness, Disorientation	Action of anticholinergic agents, tricyclic antidepressants, sedatives or hypnotics is enhanced. Alcohol should be avoided. Urine pregnancy tests can produce false-positive or false-negative results whilst taking promethazine.

Information from BNF 65, www.medicines.org.uk/emc and www.mhra.gov.uk accessed 12.09.2013