CHEMOTHERAPY INDUCED NAUSEA AND VOMITING: MANAGEMENT - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Nausea and vomiting are common but manageable adverse effects of chemotherapy.
- Management should be based on the emetogenicity of the chemotherapy and any contraindications present.
- Prevention and timely escalation of therapy can prevent further adverse events including dehydration.

CHANGE SUMMARY

- New Document
- **22/02/24**: Minor review. Amendment of aprepitant, fosaprepitant and dexamethasone dosing guidance and addition of Akynzeo® dosing

READ ACKNOWLEDGEMENT

Clinical staff caring for patients at risk of or experiencing chemotherapy-induced nausea and vomiting should read and understand this document, including

- Oncology medical staff
- Chemotherapy accredited nursing staff
- All nursing staff working in oncology inpatient and outpatient wards
- Oncology pharmacists

This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1 November 2022	**Review Period**: 3 years
Team Leader:	Oncology Pharmacist	**Area/Dept**: Oncology Pharmacy

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Aim

To provide guidance to clinical staff on the emetogenic potential of chemotherapeutic agents and appropriate prophylaxis and treatment of chemotherapy-induced nausea and vomiting.

Background

Chemotherapy–induced nausea and vomiting (CINV) is a common adverse event of chemotherapy. In addition to causing physical discomfort to patients, it can be emotionally and psychologically distressing to patients and carers and impact quality of life. When not adequately managed, CINV can also precipitate other adverse events, including dehydration and electrolyte disturbances and can prolong hospital admissions.

Anti-emetic therapy should be initiated prior to the first dose of chemotherapy; once symptoms have presented, regaining control becomes difficult.

Emetogenicity of Chemotherapeutic Agents

Unless otherwise specified, combination chemotherapy should be classed according to the highest risk single agent in the combination.

Contact pharmacy for advice regarding agents not classified below.

Table 1. Classification of emetogenic potential of chemotherapeutic agents

High Emetogenic Risk – Single Agent		
Carboplatin Carmustine >250mg/m2 Cisplatin Cyclophosphamide ≥ 1000mg/m2	Cytarabine ≥ 3g/m2/dose Dacarbazine Dactinomycin	Methotrexate ≥12g/m2 Procarbazine Thiotepa ≥ 300mg/m2 or 10mg/kg
High Emetogenic Risk – Combinations		
Cyclophosphamide + any anthracycline Cyclophosphamide + etoposide	Cytarabine 150-200mg/m2 + daunorubicin Cytarabine 300mg/m2 + etoposide	Doxorubicin + Ifosfamide Etoposide + Ifosfamide
Moderate Emetogenic Risk – Single Agent		
Aldesleukin > 12 million Units/m2 Arsenic trioxide Azacitidine Busulfan Carmustine ≤ 250mg/m2 Clofarabine Cyclophosphamide <1200mg/m2 (including oral)	Cytarabine 200-3000mg/m2 Daunorubicin Doxorubicin Epirubicin Etoposide Oral Idarubicin Ifosfamide Imatinib Intrathecal therapy	Irinotecan Lomustine Melphalan > 50mg/m2 Methotrexate 250mg/m2 – 12g/m2 Oxaliplatin >75mg/m2 Temozolamide Treosulfan Vinorelbine Oral

Low Emetogenic Risk – Single Agent		
Blinatumomab Brentuximab vedotin Capecitabine Carfilzomib Cytarabine ≤ 200mg/m2 Docetaxel Liposomal doxorubicin Etoposide IV	Fluorouracil Gemcitabine Ipilimumab Methotrexate 50-250mg/m2 Mitomycin Mitozantrone Nilotinib	Paclitaxel (inc. albumin bound) Pemetrexed Teniposide Thiotepa < 300mg/m2 or 10mg/kg Topotecan Vorinostat
Minimal Emetogenic Risk – Single Agent		
Alemtuzumab Asparaginase erwinia Bevacizumab Bleomycin Bortezomib Cetuximab Chlorambucil Cladribine Dasatinib Decitabine Dexrazoxane Erlotinib	Fludarabine Gemtuzumab ozogamicin Hydroxyurea Interferon alfa Mercaptopurine Methotrexate ≤ 50mg/m2 Nelarabine Nivolumab Pegaspagase Pembrolizumab Ramicirumab	Rituximab Sorafenib Sunitinib Temsirolimus Thalidomide Tioguanine Trastuzumab Vinblastine Vincristine Vindesine Vinorelbine IV

Treatment Algorithms

Contraindications to dexamethasone

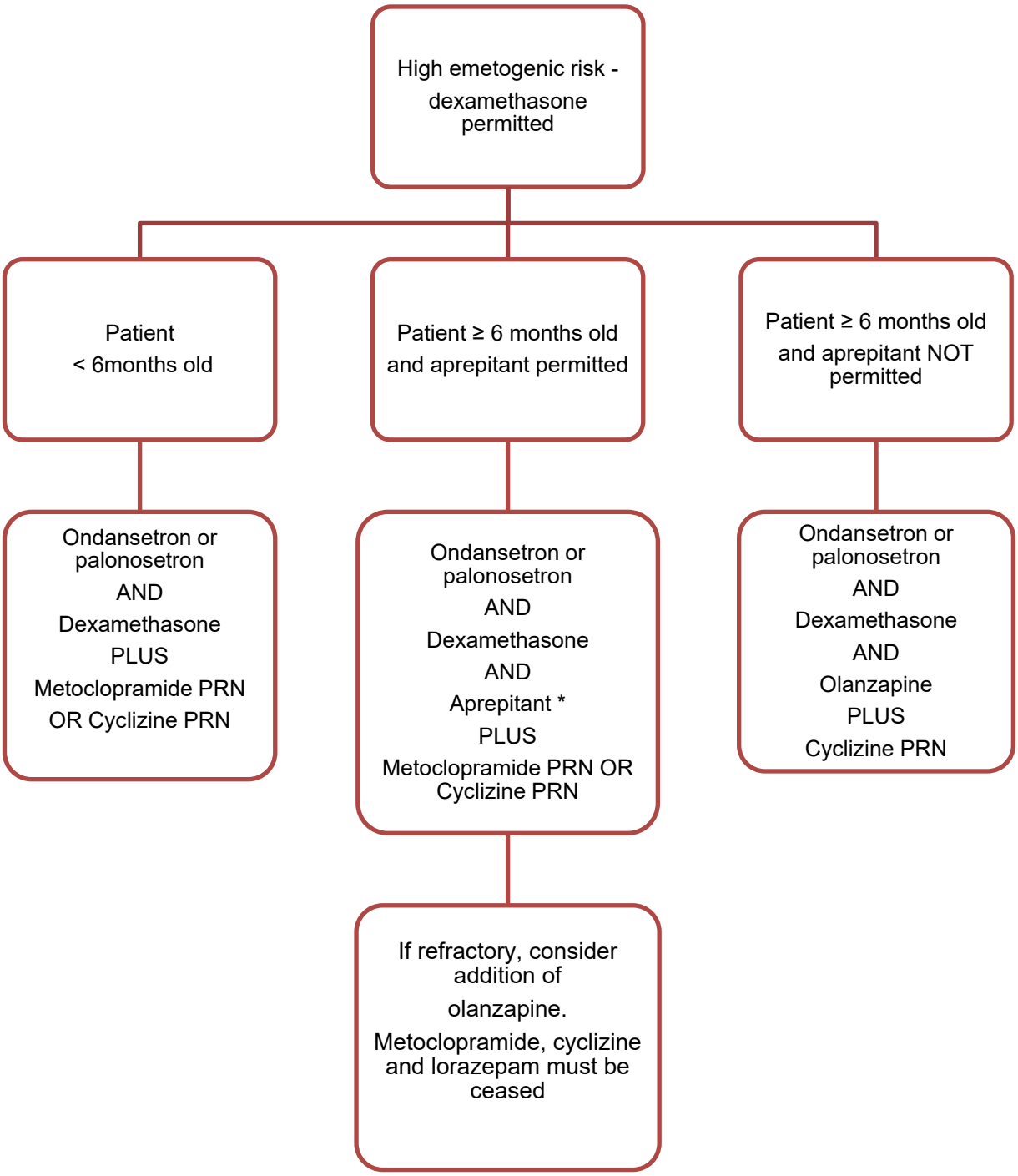
1. Patients receiving steroids as part of chemotherapy regimen (eg. leukaemia and lymphoma patients)
2. Patients with CNS tumours (unless on prescriber discretion; may be used for delayed emesis but must be ≥ 24 hours post completion of chemotherapy)

Contraindications for aprepitant (and fosaprepitant)

Aprepitant is not licensed for patients less than 6 months of age.

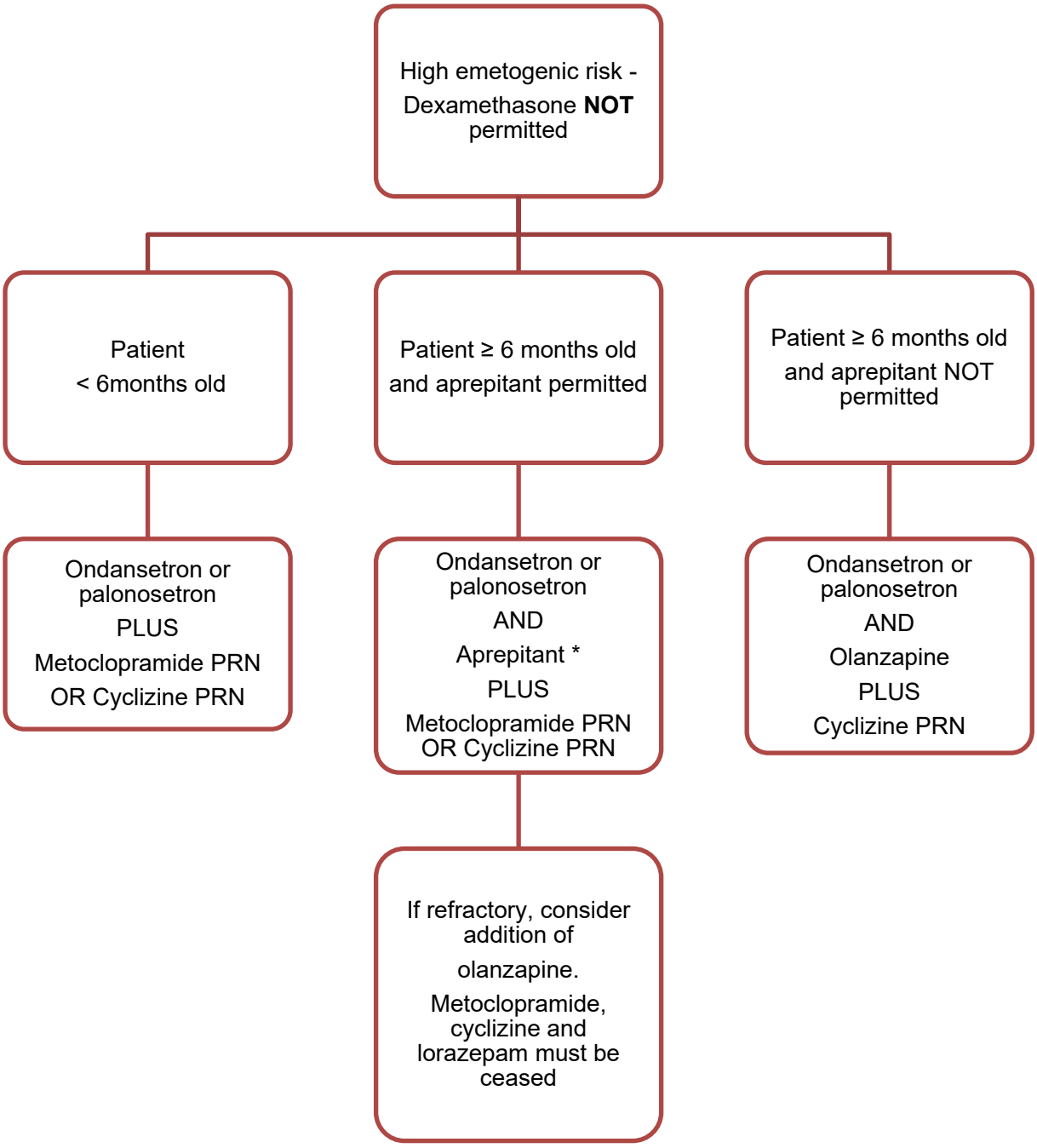
Aprepitant is a moderate CYP3A4 inhibitor, of which many chemotherapeutic agents are also substrates, inhibitors and inducers. The clinical significance of these interactions is debated. **Consultants should be contacted regarding use and dosage prior to prescribing using with interacting chemotherapy (eg ifosfamide).**

Figure 1. High Emetogenic Risk – Dexamethasone Permitted



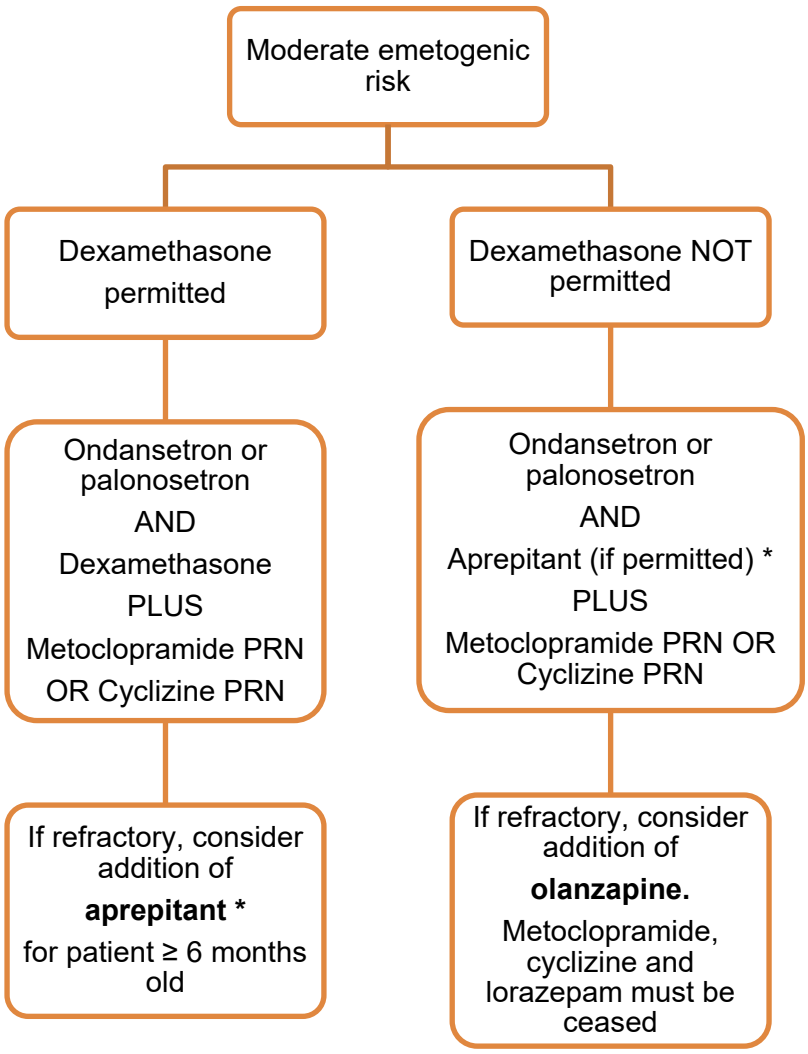
* Fosaprepitant IV may be substituted for oral aprepitant on Day 1. Dosing is not equivalent, refer to Table 2 for dosing.

Figure 2. High Emetogenic Risk – Dexamethasone NOT Permitted



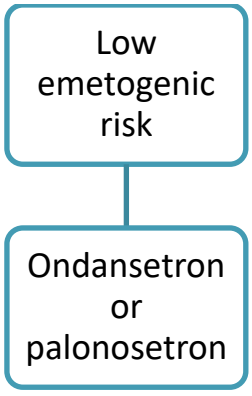
* Fosaprepitant IV may be substituted for oral aprepitant on Day 1. Dosing is not equivalent, refer to Table 2 for dosing.

Figure 3. Moderate Emetogenic Risk



* Fosaprepitant IV may be substituted for oral aprepitant on Day 1. Dosing is not equivalent, refer to Table 2 for dosing.

Figure 4. Minimal and Low Emetogenic Risk



Anti-emetic Drug Information and Dosing

Table 2.

Drug	Age, Weight or BSA	Route	Dose	Interval	Dose Limit/Comments
Ondansetron	< 6 months[1]	PO/IV	0.15mg/kg/dose	8 hourly	Max 8mg/dose
	≥ 6 months	PO/IV	5mg/m2/dose OR 0.15mg/kg/dose	6-8 hourly	Max 8mg/dose **and** 32mg/day
Palonosetron	1 month – 17 years	IV	0.02mg/kg 30 minutes prior to chemotherapy	48-72 hourly	Max 1.5mg/dose
	> 17 years	IV	0.25mg 30 minutes prior to chemotherapy	48-72 hourly	
	Do NOT administer palonosetron and ondansetron concurrently due to risk of serotonin syndrome and QT prolongation[2]. If required, ondansetron should be resumed no earlier than 48 hours post the last dose of palonosetron.				
Dexamethasone[3]	**Moderate and High Emetogenic Risk Patients**				
	≤ 0.6m^2	PO/IV	2mg/**dose**	BD given morning and midday	DO NOT halve dose if used with aprepitant
	> 0.6m^2	PO/IV	4mg/**dose**	BD given morning and midday	DO NOT halve dose if used with aprepitant
	High Emetogenic Risk patients may have dose escalated to TDS or QID if required; in these instances, consider halving dexamethasone dose.				
Aprepitant	≥6 months	PO	**Day 1**: 3 mg/kg/dose **Day 2 onwards** : 2 mg/kg/dose	24 hourly	**Day 1:** 120 mg/dose **Day 2 onwards:** 80 mg/dose Give 60 minutes prior to chemotherapy
	Alternative dosing regimen for patients ≥ 12 years and ≥ 30kg. Patient must be able to swallow capsule.				
	≥ 12 years and ≥ 30 kg	PO	**Day 1:** 165 mg/dose (**NOT/kg**) **Day 4 :** 165 mg/dose (**NOT/kg**) for multi-day chemotherapy	72 hourly	**Day 1:** 165 mg/dose **Day 4:** 165 mg/dose Give 60 minutes prior to chemotherapy

Drug	Age, Weight or BSA	Route	Dose	Interval	Dose Limit/Comments
Fosaprepitant	6 months–12 years; 6-30kg	IV	**Day 1:** 3 mg/kg/dose **Day 2 onwards : Oral aprepitant** 2mg/kg/dose	Single dose (24 hour interval with oral aprepitant)	**Day 1:** 115mg **Day 2 onwards :** 80 mg/dose of oral aprepitant Give 90 minutes prior to chemotherapy Fosaprepitant infused over 60 minutes, to be completed at least 30 minutes prior to chemotherapy
	>12 years; >30 kg	IV	**Day 1:** 150mg **Reassess and repeat on Day 4 if required**	Single dose (24 hour interval with oral aprepitant)	150mg/dose Give 60 mins prior to chemotherapy Fosaprepitant infused over 30 minutes, to be completed at least 30 minutes prior to chemotherapy
Netupitant 300mg and palonosetron 500microg (Akynzeo) capsule	>12 years; >30 kg	PO	**Day 1:** One capsule **Reassess and repeat on Day 4 if required**	Single dose	One capsule/dose
Olanzapine[4]	10-18kg and ≥ 3 years	PO	1.25mg	Night	Start with this dose in the evening; an additional half dose in the morning may be beneficial. Cease metoclopramide and benzodiazepines prior to commencement.
	19-31kg and ≥ 3 years	PO	2.5mg	Night	
	32-43kg	PO	3.75mg	Night	
	≥44kg	PO	5mg	Night	
Metoclopramide	≤28 days (at term)	PO/IV/IM	0.15 mg/kg/**dose**	6 hourly	0.6 mg/kg/**DAY**
	>28 days	PO/IV/IM	0.1–0.15 mg/kg/**dose**	6-8 hourly	30 mg/**DAY**

Cyclizine	≥ 1 month	PO/IV	0.5 – 1mg/kg/dose	8 hourly	<12 years: 25mg/dose ≥12 years: 50mg/dose
Lorazepam	≥ 1 month	PO	0.02-0.05mg/kg/**dose**	24, 12 or 6 hourly prn	Max 2mg/dose

Adverse Effects of Anti-emetics and Precautions for Use

Table 3.

Drug	Common or Serious Adverse Effects	Precautions
Ondansetron Palonosetron	Common: Constipation, headache Serious: QT prolongation	Concurrent use of other QT prolonging drugs (eg. olanzapine)
Dexamethasone	Common: GI side effects, behavioural/mood changes, increased appetite, increased BGLs, hypertension, neuromuscular and skeletal effects	Diabetes
Aprepitant Fosaprepitant	Common: Diarrhoea, headache, hiccups	Potential for drug interactions – consult pharmacy
Olanzapine	Common: Hyperglycaemia, sedation, peripheral oedema, postural hypotension Serious: Extrapyramidal symptoms, hepatic failure, rhabdomyolysis, venous thromboembolism, metabolic syndrome, blood dyscrasias	Cease metoclopramide and benzodiazepines prior to commencement. Use caution with other drugs with anticholinergic effects
Metoclopramide	Common: Restlessness, drowsiness, fatigue Serious: Extrapyramidal symptoms	Do not use with olanzapine
Cyclizine	Common: Tachycardia, hypertension blurred vision, dry eyes, constipation, dry mouth, urinary tension, sedation Serious: Hypotension, paradoxical stimulation	Use caution with other drugs with anticholinergic effects
Lorazepam	Common: Drowsiness, dizziness, sedation	Potential for tolerance, dependence and abuse

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