**Best Practice Message**

**March 2025**

# **Focus on Ondansetron Dosing and Interactions**

## *Practice changing moments*

* Only short courses of ondansetron are required for any indication. Consider a maximum of 10 tablets.
* Consider medication interactions when prescribing ondansetron, particularly if the patient is on concomitant serotonergic medications or QT prolongating medicines.

## Introduction

Ondansetron is a widely used antiemetic. It reduces the vomiting reflex by blocking serotonin at 5HT3 receptors both peripherally in the gastro-intestinal tract and centrally in the chemoreceptor trigger zone. It is primarily indicated for the prevention and treatment of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy and post-operative nausea and vomiting. It is also often used for the acute severe vomiting, an unapproved indication in Aotearoa. Safe prescribing of ondansetron requires awareness of appropriate indications, dosing guidelines, and potential drug interactions, particularly the risk of serotonin syndrome.

The use of ondansetron has increased significantly in the last few years. However, the average amount of tablets (including 4 and 8mg oral and dispersible tablets) per prescription over this time period has been relatively stable.

In Hawke’s Bay patients received around 30 tablets of ondansetron per prescription. This is much more than would typically be required for short term treatment as indicated below.

## Dosing, duration and quantity prescribed

The duration of ondansetron therapy varies depending on the clinical scenario:

* **For chemotherapy and radiation-induced nausea and vomiting**: a dose of 8mg every 12 hours is typically continued for up to 5 days post treatment.
* **For postoperative nausea and vomiting**: a single dose of 8mg to 16mg may suffice.
* **For gastroenteritis:** HealthPathways does not recommend ondansetron for gastroenteritis symptom management in adults. In children a single dose can be considered in a dehydrated patient if ongoing vomiting is affecting the ability to tolerate oral rehydration therapy.
* **For other acute severe vomiting**: NZF recommends doses of 4mg – 8mg as a single dose, this can be repeated if clinically indicated with a maximum of 16mg in 24 hours.
* **For nausea and vomiting during pregnancy:** Ondansetron in not the first line antiemetic in pregnancy due to the small increased risk of oral cleft defects. For more information see [here](https://healthhb.co.nz/workforce-development/best-practice-messages/).

Prescribers should consider tailoring the quantity of ondansetron prescribed to the anticipated duration of symptoms, avoiding excessive quantities to minimise the risk of unnecessary prolonged use.

## Drug Interactions and Serotonin Syndrome

Serotonin syndrome is a potentially life-threatening condition characterized by symptoms such as agitation, confusion, hypermania, hyperreflexia, tremor, restlessness, rigidity, fever, tachycardia and other neuromuscular, autonomic and mental status changes. It can occur when there is excessive serotonin activity in the brain, often due to the interaction of multiple serotonergic drugs.

Ondansetron is a 5-HT3 receptor antagonist. While rare, serotonin syndrome has been seen in patients using 5-HT3 receptor antagonist when combined with other serotonergic drugs, such as [Selective Serotonin Reuptake Inhibitors](https://nzf.org.nz/nzf_2287) (SSRIs), [Serotonin-Noradrenaline Reuptake Inhibitors](https://nzf.org.nz/nzf_70526) (SNRIs), [Monoamine Oxidase Inhibitors](https://nzf.org.nz/nzf_2269) (MAOIs), or other 5-HT3 antagonists. Therefore, careful consideration should be given when co-prescribing ondansetron. Patients should be monitored for early signs of serotonin syndrome.

Ondansetron may also increase the risk of developing prolongation of the QT interval, which can lead to abnormal and potentially fatal heart rhythms, including Torsade de Pointes. This risk is increased when a patient is taking concomitant drugs that prolong QT interval. For more information on medicines with the potential to cause QT prolongation see [here](https://www.crediblemeds.org/healthcare-providers).

## CARM

Prescribers should continue to report adverse reactions to all medications to the Centre for Adverse Reactions Monitoring (CARM). This allows continued monitoring of the benefit-risk balance of the medicine. Healthcare professionals can report any suspected adverse reactions via [this form](https://pophealth.my.site.com/carmreportnz/s/).

**Further reading:**

**Medsafe:** [**Advice about serotonin syndrome**](https://www.medsafe.govt.nz/safety/EWS/2015/SerotoninSyndrome.asp)

[**Opioids and serotonergic medicines**](https://medsafe.govt.nz/profs/PUArticles/September2022/Opioids-and-serotonergic%20medicines-risk-of-serotonin-syndrome.html)

**New Zealand Formulary:** [**Drugs used in nausea and vertigo**](https://nzf.org.nz/nzf_2346)

**HealthPathways:** [**Gastroenteritis in Children**](https://hawkesbay.communityhealthpathways.org/12652.htm)

[**Gastroenteritis in Adults**](https://hawkesbay.communityhealthpathways.org/77939.htm)

[**Pregnancy-related Nausea and Vomiting**](https://hawkesbay.communityhealthpathways.org/77939.htm)

**Patient information:**

**Healthify:** **[Serotonin syndrome](https://healthify.nz/health-a-z/s/serotonin-syndrome/)**

[**Ondansetron**](https://healthify.nz/medicines-a-z/o/ondansetron/)

**References:**

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6. Te Whatu Ora Health New Zealand, Te Matau a Māui Hawke’s Bay. (HBHNZ). IV Therapeutic Guidelines: Antiemetics Adults. TMMHB/IVTG/090. Reviewed January 2024.

**Authored by:** Riani Albertyn **Reviewed by:** Brendan Duck

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## Appendix 1: Antiemetic options considerations

| **Drug class/ Mechanism of action** | **Antiemetic** | **Effective for nausea and vomiting associated with:** | **Cautions/Contraindications** |
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| **Dopamine receptor antagonist** | [**Metolopramide**](https://nzf.org.nz/nzf_2384)[**Prochlorperazine**](https://nzf.org.nz/nzf_2147) | * Post operative state.
* Gastro-duodenal, hepatic, and biliary disease.
* Pregnancy (short term use only).
* Diffuse neoplastic disease, radiation sickness.
* Drugs such as opioids, general anaesthetics, and cytotoxic.
* Migraine.
 | * Risk of neurological effects such as Extrapyramidal Side Effects (**EPSE**) and tardive dyskinesia. Avoid long term high dose use.
* Due to the risk of dystonic side effects, metoclopramide use in **children and young adults** is limited to certain conditions and for second-line therapy.
* Should not be used in people with **Parkinson’s disease**.
* Avoid in severe **renal or hepatic impairment**.
* Avoid in cases where **increased gastric motility** is not desirable.
* Additive **sedative effect** with CNS depressants.
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| **Dopamine receptor antagonist** | [**Domperidone**](https://nzf.org.nz/nzf_2382) | * Chemotherapy.
* Dopaminergic drugs.
* Migraine.
 | * Concomitant use of drugs that **prolong QT interval.**
* Strong CYP3A4 inhibitors e.g. ketoconazole or erythromycin, can increase the plasma levels of domperidone which may lead to QT prolongation.
* Domperidone is associated with a small increased risk of **cardiac adverse effects**.
* Avoid in **hepatic impairment**.
* Avoid in cases where **increased gastric motility** is not desirable.
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| **Antihistamine** | [**Cyclizine**](https://nzf.org.nz/nzf_2359)[**Promethazine**](https://nzf.org.nz/nzf_1872) | * Motion sickness.
* Pregnancy (cyclizine).
* Post operative state.
* Meniere’s disease.
* Palliative care.
 | * Use with caution in patients with **glaucoma, obstructive disease of the GI tract** or males with possible **prostatic hypertrophy**.
* May enhance the side effects of **anticholinergic** drugs.
* Can lead to **decreased gut motility**.
* Additive **sedative effect** with alcohol and CNS depressants.

PROMETHAZINE:* **QT-interval prolongation** has been reported
* Do not use in **children under 6 years** due to risk of psychiatric and CNS side effects.
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| **5HT3-receptor antagonists** | [**Ondansetron**](https://nzf.org.nz/nzf_2392) | * Chemotherapy and radiotherapy.
* Post operative state.
* Pregnancy (SECOND LINE THERAPY).
 | * Contraindicated in congenital long QT syndrome. Avoid concomitant medicines that can **prolong the QT interval**.
* Rarely, potential to cause **serotonin syndrome** especially with concomitant administration of other serotonergic drugs.
* Can lead to **decreased gut motility**.
* Ondansetron has been associated with a **small increased risk of oral clefts** following use in the first trimester of pregnancy.
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| **Anticholinergic** | [**Hyoscine hydrobromide patch**](https://nzf.org.nz/nzf_6936) | * Motion sickness.
 | * Caution in patients with history of **psychotic disorders**.
* May enhance the side effects of **anticholinergic** drugs.
* Avoid in individuals susceptible to **angle-closure glaucoma.**
* Avoid in conditions characterised by **tachycardia.**
* Patients have experienced **withdrawal symptoms** on discontinuation if used for more than 3 days.
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