Ondansetron
for diarrhoea predominant Irritable Bowel Syndrome

Traffic light classification: Amber 2
Information sheet for Primary Care Prescribers

Indication
Ondansetron is indicated off-label for the management of diarrhoea predominant Irritable Bowel Syndrome (IBS-D) as a second line therapy following initiation within Secondary Care by a Specialist.

Therapeutic summary
Ondansetron is a specific 5HT3-receptor antagonist which blocks 5HT3 receptors in the gastro-intestinal tract and in the central nervous system. The most common side effect is constipation. Therefore, low dose ondansetron has been used off-label with good evidence for effective management of frequent loose stools with urgency characteristic of IBS-D. However, ondansetron is not currently licensed for this indication.

Irritable bowel syndrome with diarrhoea is characterised by loose stools, diarrhoea, and sudden urges to have bowel movements often with loss of bowel control which has significant negative impact on daily life. Clinical trials have demonstrated that ondansetron slows the accelerated colonic transit associated with IBS-D, and therefore, reduces urgency, and improves symptoms providing effective treatment option.

Ondansetron is recommended as a second line therapy in the management of IBS-D by the British Society of Gastroenterology in the IBS guidelines. Locally, it may be initiated by a Specialist for IBS-D symptoms, which are not effectively controlled by the conventional therapy with dietary exclusions, loperamide, or amitriptyline. The ongoing prescribing may be requested from Primary Care once efficacy has been demonstrated.

NICE guidelines on diagnosis and management of IBS in adults (CG61) last updated in April 2017 does not make any recommendation on ondansetron.

Products available
- 4mg tablets – cost £1.67 per pack of 10 tablets
- 8mg tablets – cost £3.09 per pack of 10 tablets

Other formulations are significantly more expensive – see formulary for details.

Dose and route of administration
Ondansetron for the treatment of IBS with diarrhoea is initiated at dose of 4mg once daily for two days and can be increased by 4mg every two days to a maximum dose of 8mg three times a day. If there is no satisfactory response within the first 2 weeks, it should be discontinued.

Monitoring requirements
No clinical monitoring is required. Patients should be advised to observe their stool consistency and to stop ondansetron if excessively hard stools, no bowel movement, or if rectal bleeding occurs.

Contraindications and precautions

Ondansetron is contraindicated in patients with known hypersensitivity to the active substance or to any of the excipients and should not be concomitantly used with apomorphine.

Ondansetron prolongs the QT interval in a dose-dependent manner and post marketing cases of Torsade de Pointes have been reported in patients using high intravenous dose of ondansetron. It should be avoided in patients with congenital long QT syndrome. Ondansetron should be administered with caution to patients who have or may develop prolongation of QTc or cardiac arrythmias, including patients with electrolyte abnormalities, congestive heart failure, bradyarrhythmias or patients taking other medications that lead to QT prolongation or electrolyte abnormalities.

Hypokalaemia and hypomagnesaemia should be corrected prior to ondansetron administration.

As ondansetron is known to increase large bowel transit time, patients with signs of sub-acute intestinal obstruction should be monitored following administration.

Ondansetron should not be used during the first trimester of pregnancy and female patients should be advised to stop ondansetron during this time. MHRA has issued warning on small increased risk of oral clefts associated with ondansetron use in the first 12 weeks of pregnancy. To reduce the inadvertent exposures, female patients of childbearing potential should be advised on the need to use effective contraception.

Clinically relevant medicine interactions and their management

- Serotonergic drugs (e.g. selective serotonin reuptake inhibitors (SSRI) and serotonin noradrenaline reuptake inhibitors (SNRIs)) – there have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability, and neuromuscular abnormalities) following the concomitant use with ondansetron. If concomitant treatment with ondansetron and other serotonergic drugs is clinically warranted, appropriate observation of the patient is advised.
- Apomorphine - reports of profound hypotension and loss of consciousness when administered with ondansetron. Concomitant use is contraindicated.
- Potent inducers of CYP3A4 (e.g. phenytoin, carbamazepine, and rifampicin) may reduce the effectiveness of ondansetron by increasing its oral clearance and reducing the blood concentrations of ondansetron.
- Tramadol - the analgesic effect of tramadol may be reduced by ondansetron (data from small studies).
- Caution should be exercised when ondansetron is co-administered with drugs that prolong the QT interval and/or cause electrolyte abnormalities. Concomitant use of ondansetron with cardio toxic drugs, antibiotics (e.g. erythromycin), antifungals (e.g. ketoconazole), antiarrhythmics (e.g. amiodarone) and beta blockers (e.g. atenolol or timolol) may increase the risk of arrhythmias.

Side effects

- Very common: headache.
- Common: constipation and sensation of warmth or flushing.
- Uncommon: arrhythmias, chest pain with or without ST segment depression, bradycardia, seizures, movement disorders (including extrapyramidal reactions such as dystonic reactions, oculogyric crisis and dyskinesia), hypotension, hiccups, asymptomatic increases in liver function tests.
- Rare: dizziness predominantly during rapid IV administration, transient visual disturbances (e.g. blurred vision), predominantly during IV administration, QTc prolongation (including Torsade de Pointes).
- Very rare: transient blindness, predominantly during IV administration.

For a full list of side effects and information on incidence of ADRs, refer to the BNF or Summary of Product Characteristics (SPC).

Information given to patient

Lifestyle and dietary advice should be provided. Useful resources include:
Irritable bowel syndrome (IBS) - Diet, lifestyle and medicines - NHS (www.nhs.uk)
Irritable bowel syndrome (IBS) and diet - British Dietetic Association (BDA)
Diarrhoea | Causes, Symptoms, Treatment & Support | Guts UK (gutscharity.org.uk)

References

1. Vasant DH, Paine PA, Black CJ, Houghton LA, Everitt HA, Corsetti M, Agrawal A, Aziz I, Farmer AD, Eugenicos MP, Moss-Morris R, Yiannakou Y, Ford AC. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut. 2021 Jul;70(7):1214-1240. https://doi.org/10.1136/gutjnl-2021-324598.
2. Gunn D, Topan R, Barnard L, Fried R, Holloway I, Brindle R, et al. Randomised, placebo-controlled trial and meta-analysis show benefit of ondansetron for irritable bowel syndrome with diarrhoea: The TRITON trial. Aliment Pharmacol Ther. 2023; 57: 1258–1271. https://doi.org/10.1111/apt.17426