6. Toren P, *et al.* Ondansetron treatment in Tourette's disorder: a 3-week, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry* 2005; **66:** 499–503.
7. Hewlett WA, *et al.* Pilot trial of ondansetron in the treatment of 8 patients with obsessive-compulsive disorder. *J Clin Psychiatry* 2003; **64:** 1025–30.

Substance dependence. Ondansetron is being studied in the management of alcohol dependence (p.1626). However, in one study[1] a significant reduction in alcohol consumption was found only in lighter drinkers after subgroup analysis. Another study[2] found a reduction in alcohol consumption by patients with early-onset alcoholism (onset before age 25) who took ondansetron compared with placebo. No such effect was seen, however, in patients with late-onset alcoholism. Further study found that ondansetron also effectively ameliorated mood disturbances including symptoms of depression, anxiety, and hostility, in early-onset alcoholics.[3] Self-reported alcohol consumption also reduced in adolescents (between ages 14 and 20) with alcohol dependence who were given ondansetron in an open study.[4]

1. Sellers EM, *et al.* Clinical efficacy of the 5-HT antagonist ondansetron in alcohol abuse and dependence. *Alcohol Clin Exp Res* 1994; **18:** 879–85.
2. Johnson BA, *et al.* Ondansetron for reduction of drinking among biologically predisposed alcoholic patients. *JAMA* 2000; **284:** 963–71.
3. Johnson BA, *et al.* Ondansetron reduces mood disturbance among biologically predisposed, alcohol-dependent individuals. *Alcohol Clin Exp Res* 2003; **27:** 1773–9.
4. Dawes MA, *et al.* A prospective, open-label trial of ondansetron in adolescents with alcohol dependence. *Addict Behav* 2005; **30:** 1077–85.

Preparations

USP 31: Ondansetron Hydrochloride Oral Suspension; Ondansetron Injection; Ondansetron Oral Solution; Ondansetron Orally Disintegrating Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Cetron; Dantenk; Dismolan; Emivox†; Espasevit; Finaber; Finoxi; Tiosalis; Zofran; ***Austral.:*** Ondaz; Onsetron; Zofran; ***Austria:*** Glaxosetron; Ondanoglax; Ondensan; Zofran; ***Belg.:*** Zofran; ***Braz.:*** Ansentron; Injectrax; Modifical; Nausedron; Ontrax; Vonau; Zofran; ***Canad.:*** Zofran; ***Chile:*** Amilene; Gardoton; Izofran; Odanex; Oncoemet; Trorix; ***Cz.:*** Danemet; Emeset; Emetron†; Novetron; Ondemet; Setron†; Setronon; Zofran; ***Denm.:*** Hexatron; Zofran; ***Fin.:*** Zofran; ***Fr.:*** Zophren; ***Ger.:*** Zofran; ***Gr.:*** Biosetron; Cruzafen; Dentron; Fedral; Odnatron; Onda; Ondameton; Ondaren; Ondaseprol; Setrodan; Vefron; Zetron; Zodatron; Zofron; Zophralen; ***Hong Kong:*** Zofran; ***Hung.:*** Antivom; Emetron; Ondagen; Zofran; ***India:*** Emeset; Periset; Vomiof; ***Indon.:*** Cedantron; Dantroxal; Entron; Frazon; Invomit; Narfoz; Ondavell; Onetic 4; Vomceran; Zantron; Zofran; ***Irl.:*** Emital; Zofran; ***Israel:*** Zofran; ***Ital.:*** Zofran; ***Malaysia:*** Osetron; Zofran; ***Mex.:*** Danac; Modifical; Precirux; Zofran; ***Neth.:*** Zofran; ***Norw.:*** Zofran; ***NZ:*** Onsetron; Zofran; ***Philipp.:*** Emodan; Zofran; ***Pol.:*** Atossa; Emetron; Setronon; Zofran; ***Port.:*** Nausiend; Otobrol; Zofran; ***Rus.:*** Emetron (Эметрон); Setronon (Сетронон); Zofran (Зофран); ***S.Afr.:*** Dantron; Nausetron; Zofran; ***Singapore:*** Zofran; ***Spain:*** Fixca†; Yatrox; Zofran; ***Swed.:*** Zofran; ***Switz.:*** Zofran; ***Thai.:*** Dantron; Emeset; Onsia; Vomitron†; Zetron; Zofran; ***Turk.:*** Zofer; Zofran; Zoltem; ***UK:*** Ondemet; Zofran; ***USA:*** Zofran; ***Venez.:*** Dismolan; Emeset; Tructum; Zofran.

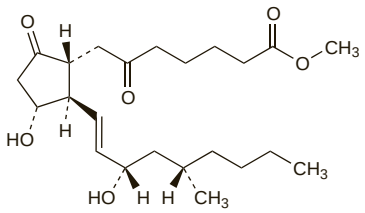
Ornoprostil *(rINN)*

Ornoprostilo; Ornoprostilum; OU-1308. Methyl (–)-(1*R*,2*R*,3*R*)-3-hydroxy-2-[(*E*)-(3*S*,5*S*)-3-hydroxy-5-methyl-1-nonenyl]-ε,5-dioxocyclopentaneheptanoate.

Орнопростил

$C_{23}H_{38}O_6$ = 410.5.

CAS — 70667-26-4.



Profile

Ornoprostil is a synthetic prostaglandin analogue that has been used in the treatment of peptic ulcer disease.

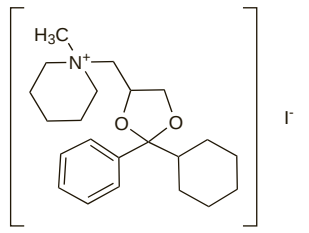
Oxapium Iodide *(rINN)*

Ciclonium Iodide; Cyclonium Iodide; Ioduro de oxapio; Oxapii Iodidum; Oxapium, Iodure d'; SH-100. 1-(2-Cyclohexyl-2-phenyl-1,3-dioxolan-4-ylmethyl)-1-methylpiperidinium iodide.

Оксапия Йодид

$C_{22}H_{34}INO_2$ = 471.4.

CAS — 6577-41-9.



NOTE. Distinguish from ciclonium bromide, p.1716, an unrelated antispasmodic.

Pharmacopoeias. In *Jpn.*

Profile

Oxapium iodide is an antimuscarinic that has been used as an antispasmodic in the treatment of gastrointestinal disorders and renal calculi.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Esperan.

Oxyphencyclimine Hydrochloride *(BANM, rINNM)*

Hidrocloruro de oxifenciclimina; Oksifensiklimin Hidroklorür; Oxyphencyclimine, Chlorhydrate d'; Oxyphencyclimini Hydrochloridum. 1,4,5,6-Tetrahydro-1-methylpyrimidin-2-ylmethyl α-cyclohexylmandelate hydrochloride.

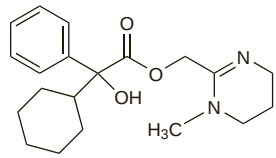
Оксифенциклимина Гидрохлорид

$C_{20}H_{28}N_2O_3$,HCl = 380.9.

CAS — 125-53-1 (oxyphencyclimine); 125-52-0 (oxyphencyclimine hydrochloride).

ATC — A03AA01.

ATC Vet — QA03AA01.



(oxyphencyclimine)

Profile

Oxyphencyclimine hydrochloride is a tertiary amine antimuscarinic with effects similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of peptic ulcer disease and for the relief of smooth muscle spasms in gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Daricon; ***Thai.:*** Daricon†; Med-Spastic†; Oxyno; Proclimine.

Multi-ingredient: ***Hong Kong:*** Rudd-U†; ***Turk.:*** Spazmo-Valibrin.

Oxyphenonium Bromide *(BAN, rINN)*

Bromuro de oxifenonio; Oksyfenoniowy bromek; Oxphenonii Bromidum; Oxyphenonii Bromidum; Oxyphenonium Bromatum; Oxyphénonium, Bromure d'. 2-(α-Cyclohexylmandeloyloxy)ethyldiethylmethylammonium bromide.

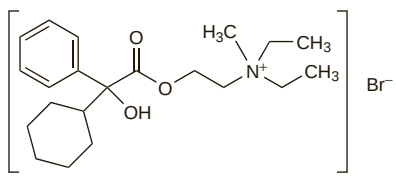
Оксифенония Бромид

$C_{21}H_{34}BrNO_3$ = 428.4.

CAS — 14214-84-7 (oxyphenonium); 50-10-2 (oxyphenonium bromide).

ATC — A03AB03.

ATC Vet — QA03AB03.



Pharmacopoeias. In *Pol.*

Profile

Oxyphenonium bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been given orally to relieve visceral spasms.

Preparations

Proprietary Preparations (details are given in Part 3)

India: Antrenyl; ***Pol.:*** Spasmophen; ***S.Afr.:*** Spastrex†.

Multi-ingredient: ***Cz.:*** Endiform†.

Palonosetron Hydrochloride

(USAN, rINNM)

Hidrocloruro de palonosetrón; Palonosétron, Chlorhydrate de; Palonosetroni Hydrochloridum; RS-25259-197. (3a*S*)-2,3,3a,4,5,6-Hexahydro-2-[(3*S*)-3-quinuclidinyl]-1*H*-benz[*de*]isoquinolin-1-one hydrochloride.

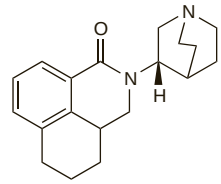
Палоносетрона Гидрохлорид

$C_{19}H_{24}N_2O$,HCl = 332.9.

CAS — 135729-56-5 (palonosetron); 135729-55-4 (palonosetron hydrochloride); 135729-62-3 (palonosetron hydrochloride).

ATC — A04AA05.

ATC Vet — QA04AA05.



(palonosetron)

Stability. The stability of palonosetron hydrochloride at concentrations of 5 and 30 micrograms/mL was assessed in polyvinyl chloride bags of the following 4 infusion solutions: glucose 5%, sodium chloride 0.9%, glucose 5% in sodium chloride 0.45%, and glucose 5% in lactated Ringer's solution. All solutions were considered to be physically and chemically stable for at least 48 hours at room temperature exposed to light, and for 14 days under refrigeration.[1]

Palonosetron 50 micrograms/mL was found to be physically and chemically stable during simulated Y-site administration with the following drugs: fentanyl citrate 50 micrograms/mL, hydromorphone hydrochloride 500 micrograms/mL, morphine sulfate 15 mg/mL, pethidine hydrochloride 10 mg/mL, and sufentanil citrate (12.5 micrograms/mL of sufentanil).[2]

1. Trissel LA, Xu QA. Physical and chemical stability of palonosetron HCl in 4 infusion solutions. *Ann Pharmacother* 2004; **38:** 1608–11.
2. Trissel LA, *et al.* Physical and chemical stability of palonosetron hydrochloride with five opiate agonists during simulated Y-site administration. *Am J Health-Syst Pharm* 2007; **64:** 1209–13.

Adverse Effects and Precautions

As for Ondansetron, p.1757, although no dosage reduction is considered necessary in hepatic impairment. Diarrhoea, fatigue, and abdominal pain may also occur. Patients with a history of constipation or signs of subacute intestinal obstruction should be monitored if given palonosetron.

Effects on the cardiovascular system. For a discussion of the effects of 5-HT_3 antagonists on the cardiovascular system, see under Ondansetron, p.1757.

Interactions

As for Ondansetron, p.1757.

Pharmacokinetics

Palonosetron has a volume of distribution of around 7 to 8 litres/kg; plasma protein binding is about 62%. About 50% of a dose is metabolised in the liver by cytochrome P450 isoenzymes (notably CYP2D6, but also CYP3A4 and CYP1A2). About 80% of a dose is recovered in the urine within 144 hours, as palonosetron and its metabolites. The mean elimination half-life is reported to be about 40 hours.

◊ References.

1. Hunt TL, *et al.* Evaluation of safety and pharmacokinetics of consecutive multiple-day dosing of palonosetron in healthy subjects. *J Clin Pharmacol* 2005; **45:** 589–96.
2. Shah A, *et al.* Pharmacokinetic evaluation and safety profile of a 15-minute versus 30-second infusion of palonosetron in healthy subjects. *J Clin Pharmacol* 2006; **46:** 1139–45.