PROFESSIONAL INFORMATION

SCHEDULING STATUS S4

1 NAME OF MEDICINE
OMECTRON ODT 4 (Orodispersible Tablets)

OMECTRON ODT 8 (Orodispersible Tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
OMECTRON ODT 4
Each orodispersible tablets contains 4 mg ondansetron.

Excipient with known effect:
Each 4 mg orodispersible tablet contains 55,906 mg lactose monohydrate as well as 0,994 mg aspartame (phenylalanine).

OMECTRON ODT 8
Each orodispersible tablets contains 8 mg ondansetron.

Excipient with known effect:
Each 8 mg orodispersible tablet contains 111,812 mg lactose monohydrate as well as 1,988 mg aspartame (phenylalanine).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Orodispersible Tablets.

White, round flat-faced bevel-edged tablets.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
OMECTRON ODT is indicated for:
- The management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy;
- The prevention and treatment of post-operative nausea and vomiting.

Routine prophylaxis is not recommended for patients in whom there is little expectation that nausea and vomiting will occur. The study population in all trials thus far consisted of mainly women undergoing laparoscopic procedures. While some men were included in some trials with similar results, clearance of the medicine is more rapid in men and insufficient numbers of men have been clinically studied to be certain that efficacy and safety have been established. Few patients undergoing major abdominal surgery have been studied.

4.2 Posology and method of administration
Posology

Chemotherapy and Radiotherapy Induced Nausea and Vomiting
The emetogenic potential of cancer treatment varies according to the doses and combinations of chemotherapy and radiotherapy regimens used.

Adults
Emetogenic Chemotherapy and Radiotherapy
For most patients receiving emetogenic chemotherapy or radiotherapy, ondansetron 8 mg should be administered as a slow IV or IM injection in not less than 30 seconds, immediately before treatment, or orally 1 - 2 hours before treatment, followed by 8 mg orally twelve hourly.

In circumstances where delayed or prolonged emesis is expected after the first 24 hours, OMECTRON ODT may be continued orally, 8 mg twice daily for up to five days after a course of treatment.

Highly Emetogenic Chemotherapy
A single dose of ondansetron 8 mg by slow IV or IM injection in not less than 30 seconds, immediately before chemotherapy has been shown to be effective in many patients. Higher doses may be required in some patients particularly those on high dose cisplatin and the doses should be adjusted according to the severity of the emetogenic challenge. In these patients the following dose schedules have been shown to be effective:
- A dose of 8 mg by slow IV or IM injection immediately before chemotherapy, followed by two further IV or IM doses of 8 mg two to four hours apart, or by a constant infusion of 1 mg/hour for up to 24 hours.

OR
- A single dose of 16 mg diluted in 50 - 100 ml of saline or other compatible infusion fluid and infused over not less than 15 minutes immediately before chemotherapy. A single dose greater than 16 mg should not be given. The efficacy of ondansetron in highly emetogenic chemotherapy may be enhanced by the addition of a single intravenous dose of dexamethasone phosphate 20 mg administered 30 - 45 minutes prior to first ondansetron dose prior to chemotherapy.

To protect against delayed or prolonged emesis after the first 24 hours, OMECTRON ODT may be continued orally, 8 mg twice daily for up to 5 days after a course of treatment.

Children
Experience is currently limited, but ondansetron was effective and well tolerated in children over the age of 4 years, when given intravenously at a dose of 5 mg/m^2 over 15 minutes, immediately before chemotherapy, followed by oral therapy at doses of OMECTRON ODT 4 mg every 12 hours for up to 5 days.

Elderly
Efficacy and tolerance in patients aged over 65 years was similar to that seen in younger adults indicating no need to alter dosage or route of administration in the elderly.

Prevention and Treatment of Post-Operative Nausea and Vomiting
Adults
Immediately before induction of anaesthesia, or post-operatively if the patient experiences nausea and/or vomiting occurring shortly after surgery, administer 4 mg undiluted intramuscularly or intravenously. If given intravenously it must be administered in not less than 30 seconds, preferably over 2 - 5 minutes. Alternatively, for the prevention of post-operative nausea and vomiting, 16 mg may be given orally one hour prior to induction of anaesthesia.

Repeat dosing for patients who continue to experience nausea and/or vomiting post-operatively has not been studied. While recommended as a fixed dose for all, few patients above 80 kg or below 40 kg have been studied.

Children
For prevention of post-operative nausea and vomiting in paediatric patients two years and older having surgery performed under general anaesthesia, ondansetron may be administered by slow intravenous injection at a dose of 0,1 mg/kg up to a maximum of 4 mg either prior to, at or after induction of anaesthesia.

For the treatment of established post-operative nausea and vomiting in paediatric patients two years and older, ondansetron may be administered by slow intravenous injection at a dose of 0,1 mg/kg up to a maximum of 4 mg.

Repeat dosing for paediatric patients who continue to experience nausea and/or vomiting has not been studied and should thus not be given.

Elderly
There is limited experience in the use of ondansetron in the prevention and treatment of post-operative nausea and vomiting in the elderly.

Patients with renal/hepatic impairment
Renal insufficiency
No alteration of daily dosage or frequency of dosing, or route of administration are required. There is limited information available on severe renal impairment.

Hepatic impairment
Clearance of OMECTRON ODT is significantly reduced and serum half-life significantly prolonged in subjects with moderate or severe impairment of hepatic function. In such patients a total daily dose of 8 mg should not be exceeded.

Method of administration
For oral use.
Do not attempt to push the orodispersible through the lidding foil.
Peel back the lidding foil of one blister and gently remove the orodispersible tablet.
Place the orodispersible tablet on top of the tongue, where it will disperse within seconds, then swallow.

4.3 Contraindications
OMECTRON ODT is contraindicated in:
- Hypersensitivity to ondansetron or any of the excipients listed in section 6.1;
- Concomitant use with apomorphine (see section 4.5);
- Pregnancy (see section 4.6);
- Congenital long QT syndrome.

4.4 Special warnings and precautions for use
QT interval prolongation
OMECTRON ODT prolongs the QT interval in a dose-dependent manner (see section 5.1). In addition, *Torsade de Pointes* may occur in patients using OMECTRON ODT. Avoid OMECTRON ODT in patients with congenital long QT syndrome (see section 4.3). OMECTRON ODT should be administered with caution to patients who have or may develop prolongation of QTc, including patients with electrolyte abnormalities, congestive heart failure, bradydysrhythmias or patients taking other medicines that lead to QT prolongation or electrolyte abnormalities. Hypokalaemia and hypomagnesaemia should be corrected prior to OMECTRON ODT administration.

Hypersensitivity reactions
Hypersensitivity reactions may occur in patients who have exhibited hypersensitivity to other selective 5HT3 receptor antagonists.

Serotonin syndrome
There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the concomitant use of ondansetron and other serotonergic medicines (including selective serotonin reuptake inhibitors (SSRI) and serotonin noradrenaline reuptake inhibitors (SNRIs)). If concomitant treatment with OMECTRON ODT and other serotonergic medicines is clinically warranted, appropriate observation of the patient is advised.

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

Adenotonsillar surgery
In patients with adenotonsillar surgery prevention of nausea and vomiting with OMECTRON ODT may mask occult bleeding. Therefore, such patients should be followed carefully after OMECTRON ODT.

Hepatic impairment
Clearance of OMECTRON ODT is significantly reduced and serum half-life significantly prolonged in patients with moderate or severe impairment of hepatic function. In such patients, a total daily dose of 8 mg should not be exceeded.

Excipients
Lactose monohydrate
OMECTRON ODT contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp-lactase deficiency or glucose-galactose malabsorption should not take OMECTRON ODT.

Aspartame
OMECTRON ODT contains aspartame (artificial sweetener). Caution is advised in patients with phenylketonuria.

4.5 Interaction with other medicines and other forms of interaction
Ondansetron is metabolised by multiple hepatic cytochrome P450 enzymes CYP3A4, CYP2D6 and CYP1A2. Due to the multiplicity of metabolic enzymes capable of metabolising ondansetron, enzyme inhibition or reduced activity of one enzyme (e.g., CYP2D6 genetic deficiency) should be compensated for by other enzymes.

Caution should be exercised when OMECTRON ODT is co-administered with medicines that prolong the QT interval and/or cause electrolyte abnormalities (see section 4.4). The use of OMECTRON ODT with QT prolonging medicines may result in additional QT prolongation. Concomitant use of OMECTRON ODT with cardiotoxic medicines (e.g., anthracyclines (such as doxorubicin, daunorubicin) or trastuzumab), antibiotics (such as erythromycin), antifungals (such as ketoconazole), antidysrhythmics (such as amiodarone) and beta blockers (such as atenolol or timolol) may increase the risk of dysrhythmias (see section 4.4).

There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the concomitant use of ondansetron and other serotonergic drugs (including SSRIs and SNRIs) (see section 4.4).

Cases of profound hypotension and loss of consciousness may occur when OMECTRON ODT is administered concomitantly with apomorphine hydrochloride. Concomitant use of OMECTRON ODT and apomorphine may intensify QT prolongation (see section 4.3).

In patients treated with potent inducers of CYP3A4 (i.e., phenytoin, carbamazepine and rifampicin), the clearance of oral OMECTRON ODT may increase and ondansetron blood concentrations may decrease.

OMECTRON ODT may reduce the analgesic effect of tramadol.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential
Women of childbearing potential should consider the use of contraception.

Pregnancy
The use of ondansetron during the first 12 weeks of pregnancy is associated with an increased risk of developing oral cleft palate and/or lip to the foetus. The use of OMECTRON ODT is contraindicated during the first 12 weeks of pregnancy irrespective of indication.

Lactation
Tests have shown that OMECTRON ODT passes into the milk of lactating animals. Mothers taking OMECTRON ODT should not breastfeed their babies.

Fertility
There is no information on the effects of ondansetron on human fertility.

4.7 Effects on ability to drive and use machines
OMECTRON ODT may affect the ability of patients to drive or operate machines and caution is advised until the effects of OMECTRON ODT in patients on treatment are known (see section 4.8).

4.8 Undesirable effects

a. Tabulated summary of adverse reactions

System Organ Class	Frequency	Undesirable effect
Immune system disorders	*Less frequent*	Immediate hypersensitivity reactions sometimes severe, including anaphylaxis, bronchospasm, shortness of breath, hypotension, shock, angioedema, urticaria
Nervous system disorders	*Frequent*	Headache
	Less frequent	Movement disorders (including extrapyramidal reactions such as oculogyric crisis, dystonic reactions and dyskinesia have been observed without definitive evidence of persistent clinical sequelae), seizures
Eye disorders	*Less frequent*	Transient blindness predominantly during intravenous administration
Cardiac disorders	*Less frequent*	Dysrhythmias, chest pain with or without ST segment depression, bradycardia, QTc prolongation (including *Torsade de Pointes*)
Vascular disorders	*Frequent*	Sensation of warmth or flushing
	Less frequent	Hypotension
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Hiccups
Gastrointestinal disorders	*Frequent*	Constipation
Hepatobiliary disorders	*Less frequent*	Asymptomatic increases in liver function tests

b. Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
There is limited experience of ondansetron overdose. In most cases, symptoms were similar to those already reported in patients receiving recommended doses (see section 4.8). Manifestations that may occur include visual disturbances, severe constipation, hypotension and a vasovagal episode with transient second-degree AV block. There is no specific antidote for ondansetron, therefore in cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate. Ondansetron prolongs QT interval in a dose-dependent fashion. ECG monitoring is recommended in cases of overdose.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
A 5.10 Medicines affecting autonomic functions. Serotonin antagonists.

Ondansetron is a potent, highly selective 5HT3 receptor-antagonist. Its precise mode of action in the control of nausea and vomiting is not known. Chemotherapeutic medicines and radiotherapy may cause release of 5HT in the small intestine initiating a vomiting reflex by activating vagal afferents via 5HT3 receptors. Ondansetron blocks the initiation of this reflex. Activation of vagal afferents may also cause a release of 5HT in the area postrema, located on the floor of the fourth ventricle, and this may also promote emesis through a central mechanism.

Thus, the effect of ondansetron in the management of the nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy is due to antagonism of 5HT3 receptors on neurons located both in the peripheral and central nervous system. In psychomotor testing ondansetron does not impair performance nor cause sedation. Ondansetron does not alter plasma prolactin concentrations.

5.2 Pharmacokinetic properties
Following oral administration of ondansetron, absorption is rapid with maximum plasma concentrations of about 30 ng/ml being attained approximately 1,6 hours after an 8 mg dose. The absolute oral bioavailability of the medicine is approximately 60 %. The disposition of ondansetron following both oral and intravenous dosing is similar with a terminal elimination half-life of about 3 hours and a steady-state volume of distribution of about 140 ℓ. Plasma protein binding is 70 - 76 %. Ondansetron is cleared from the systemic circulation predominantly by metabolism with less than 5 % of a dose excreted unchanged in the urine.

Studies in healthy elderly volunteers have shown a slightly increased oral bioavailability (65 %) and prolonged elimination half-life (5 hours) for ondansetron. In patients with severe hepatic impairment, systemic clearance is markedly reduced with prolonged elimination half-lives (15 - 32 hours) and an oral bioavailability approaching 100 % because of reduced pre-systemic metabolism.

In a study of 21 paediatric patients aged between 3- and 12-years undergoing elective surgery with general anaesthesia, the absolute values for both the clearance and volume of distribution of ondansetron following a single intravenous dose of 2 mg (3-7 years old) or 4 mg (8-12 years old) were reduced. The magnitude of the change was age-related, with clearance falling from about 300 ml/min at 12 years of age to 100 ml/min at 3 years. Volume of distribution fell from about 75 ℓ at 12 years to 17 ℓ at 3 years. Use of weight-based dosing (0,1 mg/kg up to 4 mg maximum) compensates for these changes and is effective in normalising systemic exposure in paediatric patients.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Lactose monohydrate
Low-substituted hydroxypropyl cellulose
Crospovidone
Calcium silicate
Aspartame
Peppermint flavour
Colloidal anhydrous silica
Magnesium stearate

6.2 Incompatibilities
Unknown

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store at or below 25 ºC.
Keep out of reach of children.

6.5 Nature and contents of container
Two types of packaging material are proposed for OMECTRON ODT:
- Peel-off aluminium / aluminium blisters
- Aluminium / aluminium strips

Each blister or strip contains 10 tablets. Pack sizes of 10 or 30 tablets are packed in a carboard box.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 HOLDERS OF CERTIFICATE OF REGISTRATION
Trinity Pharma (Pty) Ltd.
106 16th Road
Midrand
South Africa
1686

8 REGISTRATION NUMBER(S)
OMECTRON 4 ODT: 48/5.10/0778
OMECTRON 8 ODT: 48/5.10/0779

9 DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
7 June 2022

10 DATE OF REVISION OF THE TEXT
N.A

TRINITY PHARMA

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PROFESSIONELE INLIGTING

SKEDULERINGSTATUS S4

1 HANDELSNAAM VAN DIE MEDISYNE
OMECTRON ODT 4 (Orale Oplosbare Tablette)

OMECTRON ODT 8 (Orale Oplosbare Tablette)

2 KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
OMECTRON ODT 4
Elke orale oplosbare tablet bevat 4 mg ondansetron.

Hulpstowwe met bekende effekte:
Elke 4 mg orale oplosbare tablet bevat 55,906 mg laktose monohidraat sowel as 0,994 mg aspartaam (fenielalanien).

OMECTRON ODT 8
Elke orale oplosbare tablet bevat 8 mg ondansetron.

Hulpstowwe met bekende effekte:
Elke 8 mg orale oplosbare tablet bevat 111,812 mg laktose monohidraat sowel as 1,988 mg aspartaam (fenielalanien).

Vir 'n volledige lys van hulpstowwe, sien afdeling 6.1.

3 FARMASEUTIESE DOSSEERVORM
Orale oplosbare Tablet.

Wit, ronde, plat tablette met skuins rande.

4 KLINIESE BESONDERHEDE
4.1 Terapeutiese aanduidings
OMECTRON ODT word aangedui vir:
- Die behandeling van naarheid en braking wat veroorsaak word deur sitotoksiese chemoterapie en radioterapie;;
- Die voorkoming en behandeling van post-operatiewe naarheid en braking.

Roetine-profilakse word nie aanbeveel vir pasiënte by wie daar `n lae verwagting is dat naarheid en braking sal voorkom nie. Die studiepopulasie in alle proewe tot dusver het hoofsaaklik bestaan uit vroue wat laparoskopiese prosedures ondergaan het. Terwyl sommige mans by sommige proewe met soortgelyke resultate ingesluit is, is die opruiming van die medisyne vinniger by mans en `n onvoldoende aantal mans is klinies bestudeer om seker te maak dat doeltreffendheid en veiligheid vasgestel is. `n Lae hoeveelheid pasiënte wat groot abdominale chirurgie ondergaan is bestudeer.

4.2 Dosering en metode van toediening
Dosering

Naarheid en braking veroorsaak deur chemoterapie en radioterapie
Die emetogeniese potensiaal van kankerbehandeling verskil volgens die dosis en kombinasies van chemoterapie en radioterapie-regimes wat gebruik word.

Volwassenes
Emetogeniese chemoterapie en radioterapie
Vir die meeste pasiënte wat emetogeniese chemoterapie of radioterapie ontvang, moet ondansetron 8 mg toegedien word as 'n stadige IV of IM inspuiting binne `n tydperk van nie minder nie as 30 sekondes nie, onmiddellik voor behandeling, of mondelings 1 - 2 uur voor behandeling, gevolg deur 8 mg mondelings elke twaalf uur daarna.

Tydens gevalle waar vertraagde of langdurige braking na die eerste 24 uur verwag word, kan behandeling met OMECTRON ODT mondelings voortgesit word, deur 8 mg twee keer daagliks vir tot vyf dae na 'n kursus van behandeling te neem.

Hoogs emetogeniese chemoterapie
`n Enkele dosis ondansetron 8 mg toegedien deur stadige IV of IM inspuiting in `n tydperk van nie minder nie as 30 sekondes onmiddellik voor chemoterapie, het getoon om effektief te wees in baie pasiënte. Hoër dosisse mag in sommige pasiënte benodig word, veral dié op hoë dossise van sisplatien. Die dosisse moet dus aangepas word volgens die erns van die emetogeniese uitdaging. In hierdie pasiënte het dit getoon dat die volgende doseringskedules effektief is:
- 'n Dosis van 8 mg deur stadige IV of IM inspuiting onmiddellik voor chemoterapie, gevolg deur twee verdere IV of IM dosisse van 8 mg twee tot vier uur uitmekaar, of deur 'n konstante infusie van 1 mg/uur vir tot 24 uur.

OF
- 'n Enkeldosis van 16 mg verdun in 50 - 100 ml soutoplossing of ander versoenbare infusievloeistof en toegedien oor nie minder nie as 15 minute onmiddellik voor chemoterapie. 'n Enkeldosis groter as 16 mg moet nie gegee word nie. Die doeltreffendheid van ondansetron in hoogs emetogeniese chemoterapie kan verhoog word deur die byvoeging van 'n enkele intraveneuse dosis deksametasoonfosfaat 20 mg toegedien 30 - 45 minute voor die eerste dosis ondansetron voor chemoterapie.

Om vertraagde of langdurige braking te verhoed na die eerste 24 uur, kan OMECTRON ODT mondelings voortgesit word, 8 mg twee keer daagliks vir tot 5 dae na 'n kursus van behandeling.

Kinders
Ervaring is tans beperk, maar ondansetron was effektief en goed verdra by kinders ouer as 4 jaar, wanneer dit binneaars toegedien is teen 'n dosis van 5 mg/m^2 oor 15 minute onmiddellik voor chemoterapie, gevolg deur orale terapie teen dosisse van [PRODUKNAAM] 4 mg elke 12 uur vir tot 5 dae.

Bejaardes
Doeltreffendheid en verdraagsaamheid by pasiënte ouer as 65 jaar was soortgelyk aan dié wat by jonger volwassenes gesien word, wat aandui dat dit nie nodig is om dosisse of toedieningsroetes by bejaardes te verander nie.

Voorkoming en behandeling van post-operatiewe naarheid en braking
Volwassenes
Onmiddellik voor induksie van narkose of post-operatief indien die pasiënt naarheid en/of braking ervaar kort na die operasie, dien 4 mg onverdund binnespiers of binneaars toe. Indien dit binneaars toegedien word, moet dit binne nie minder nie as 30 sekondes toegedien word, verkieslik oor `n tydperk van 2 - 5 minute. Alternatiewelik, vir die voorkoming van post-operatiewe naarheid en braking, kan 16 mg een uur voor die induksie van narkose oraal toegedien word.

Herhaalde doserings vir pasiënte wat steeds post-operatief naarheid en/of braking ervaar, is nie bestudeer nie. Alhoewel dit aanbeveel word as 'n vaste dosis vir almal, is min pasiënte bo 80 kg of onder 40 kg bestudeer.

Kinders
Vir die voorkoming van post-operatiewe naarheid en braking by pediatriese pasiënte van twee jaar en ouer wat chirurgie onder algemene narkose ondergaan, kan ondansetron toegedien word deur stadige binneaarse inspuiting teen 'n dosis van 0,1 mg/kg tot 'n maksimum van 4 mg óf voor, tydens of na induksie van die narkose.

Vir die behandeling van definitiewe post-operatiewe naarheid en braking by pediatriese pasiënte van twee jaar en ouer, kan ondansetron toegedien word deur stadige binneaarse inspuiting teen 'n dosis van 0,1 mg/kg tot 'n maksimum van 4 mg.

Herhaalde doserings vir pediatriese pasiënte wat steeds naarheid en/of braking ervaar, is nie bestudeer nie en moet dus nie gegee word nie.

Bejaardes
Daar is beperkte ondervinding in die gebruik van ondansetron tydens die voorkoming en behandeling van post-operatiewe naarheid en braking by bejaardes.

Pasiënte met nier- of lewerinkorting
Nierversaking
Geen verandering van die daaglikse dosis, frekwensie van dosering of toedieningsroete is nodig nie. Daar is beperkte inligting beskikbaar in gevalle van ernstige nierversaking.

Lewerversaking
Opruiming van OMECTRON ODT is aansienlik verminder en serumhalfleeftyd is aansienlik verleng in proefpersone met matige of ernstige inkorting van lewerfunksie. By sulke pasiënte moet 'n totale daaglikse dosis van 8 mg nie oorskry word nie.

Metode van toediening
Vir mondelinge gebruik.
Moenie probeer om die orale oplosbare tablet deur die foelieseël te druk nie.
Trek die foelieseël van een verseelde tablet af en verwyder die orale oplosbare tablet liggies.
Plaas die orale oplosbare tablet bo-op die tong, waar dit binne sekondes sal oplos en dan afgesluk kan word.

4.3 Kontra-indikasies
OMECTRON ODT is teenaangedui in:
- Hipersensitiwiteit vir ondansetron of enige van die hulpstowwe gelys in afdeling 6.1;
- Gelyktydige gebruik met apomorfien (sien afdeling 4.5);
- Swangerskap (sien afdeling 4.6);
- Ooreflike verlengde QT-sindroom.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
QT-interval verlenging
OMECTRON ODT verleng die QT-interval op 'n dosisafhanklike wyse (sien afdeling 5.1). Daarbenewens kan Torsade de Pointes voorkom by pasiënte wat OMECTRON ODT gebruik. Vermy OMECTRON ODT by pasiënte met aangebore verlengde QT-sindroom (sien afdeling 4.3). OMECTRON ODT moet met omsigtigheid toegedien word aan pasiënte wat verlenging van QTc het of dit kan ontwikkel, insluitend pasiënte met elektrolietafwykings, kongestiewe hartversaking, bradikardie of pasiënte wat ander medisyne neem wat tot QT-verlenging of elektrolietafwykings kan lei. Hipokalemie en hipomagnesie moet reggestel word voor OMECTRON ODT toegedien word.

Hipersensitiwiteitsreaksies
Hipersensitiwiteitsreaksies kan voorkom by pasiënte wat hipersensitief is vir ander selektiewe 5HT3-reseptorantagoniste is.

Serotoniensindroom
Volgens post-bemarkingsverslae van pasiënte met serotoniensindroom (insluitend veranderde geestelike status, outonome onstabiliteit en neuromuskulêre abnormaliteite) kom dit meestal voor na die gelyktydige gebruik van ondansetron met ander serotonergiese medisyne (insluitend selektiewe serotonien heropname inhibeerders (SSRIs) en serotonien heropname inhibeerders van noradrenalien (SNRIs)). Indien gelyktydige behandeling met OMECTRON ODT en ander serotonergiese medisyne klinies nodig is, word toepaslike monitering van die pasiënt aanbeveel.

Obstruksies van die ingewande
Aangesien dit bekend is dat OMECTRON ODT dikdermdeurgangstyd verhoog, moet pasiënte met tekens van subakute dermobstruksies gemonitor word na toediening.

Adenotonsillêre chirurgie
In pasiënte wat adenotonsillêre chirurgie ondergaan kan die voorkoming van naarheid en braking met OMECTRON ODT onderliggende inwendige bloeding vermom. Sulke pasiënte moet noukeurig na OMECTRON ODT toegendiening gemonitor word.

Lewerversaking
Opruiming van OMECTRON ODT is aansienlik verminder en serumhalfleeftyd aansienlik verleng in pasiënte met matige of ernstige inkorting van lewerfunksie. By sulke pasiënte moet 'n totale daaglikse dosis van 8 mg nie oorskry word nie.

Hulpstowwe
Laktosemonohidraat
OMECTRON ODT bevat laktosemonohidraat. Pasiënte met seldsame oorerflike probleme soos galaktose-intoleransie, Lapp-laktase-tekort of glukose-galaktose-wanabsorpsie moet nie OMECTRON ODT neem nie.

Aspartaam
OMECTRON ODT bevat aspartaam (kunsmatige versoeter). Pasiënte met fenielketonurie word aangeraai om versigtig te wees.

4.5 Interaksie met ander medisyne en ander vorme van interaksies
Ondansetron word gemetaboliseer deur verskeie hepatiese sitochroom P450-ensieme soos CYP3A4, CYP2D6 en CYP1A2. As gevolg van die groot hoeveelheid van metaboliese ensieme wat in staat is om ondansetron te metaboliseer, moet ensieminhibisie of verlaagde aktiwiteit van een ensiem (bv. CYP2D6 genetiese tekort) deur ander ensieme gekompenseer word.

Omsigtigheid moet aan die dag gelê word wanneer OMECTRON ODT saam met medisyne toegedien word wat die QT-interval verleng en/of elektrolietafwykings veroorsaak (sien afdeling 4.4). Die gebruik van OMECTRON ODT met QT-verlengende medisyne kan addisionele QT-verlenging tot gevolg hê. Gelyktydige gebruik van OMECTRON ODT met kardiotoksiese medisyne (bv. antrasikliene (soos doksorubisien, daunorubisien) of trastuzumab), antibiotika (soos eritromisien), antifungale middels (soos ketokonasool), antidisritmies (soos amiodaroon) en betablokkers (soos atenolol of timolol) kan die risiko van disritmieë verhoog (sien afdeling 4.4).

Volgens post-bemarking verslae wat pasiënte met serotoniensindroom beskryf (insluitend veranderde geestelike status, outonome onstabiliteit en neuromuskulêre abnormaliteite) kom dit meestal voor na die gelyktydige gebruik van ondansetron met ander serotonergiese medisyne (insluitend SSRI's en SNRI's) (sien afdeling 4.4).

Gevalle van ernstige hipotensie en verlies van bewussyn kan voorkom wanneer OMECTRON ODT gelyktydig met apomorfienhidrochloried toegedien word. Gelyktydige gebruik van OMECTRON ODT en apomorfien kan die QT-verlenging versterk (sien afdeling 4.3).

Pasiënte wat behandel word met kragtige induseerders van CYP3A4 (d.w.s. fenitoïen, karbamasepien en rifampisien), kan die opruiming van orale OMECTRON ODT toeneem en die bloedkonsentrasies van ondansetron kan afneem.

OMECTRON ODT kan die pynstillende effek van tramadol verminder.

4.6 Vrugbaarheid, swangerskap en laktasie
Vroue van vrugbare potensiaal
Vroue van vrugbare potensiaal moet die gebruik van voorbehoedmiddels oorweeg.

Swangerskap
Die gebruik van ondansetron gedurende die eerste 12 weke van swangerskap word geassosieer met 'n verhoogde risiko om mondelinge gesplete verhemelte en/of lip in die fetus te ontwikkel. Die gebruik van OMECTRON ODT is teenaangedui gedurende die eerste 12 weke van swangerskap, ongeag die aanduiding.

Laktasie
Toetse het getoon dat OMECTRON ODT in die melk van lakterende diere voorkom. Moeders wat OMECTRON ODT neem, moet nie hul babas borsvoed nie.

Vrugbaarheid
Daar is geen inligting oor die uitwerking van ondansetron op menslike vrugbaarheid nie.

4.7 Effekte op die vermoë om te bestuur en masjiene te gebruik
OMECTRON ODT kan die vermoë van pasiënte om te bestuur of masjiene te gebruik beïnvloed. Versigtigheid word aangeraai totdat die effekte van OMECTRON ODT in pasiënte op behandeling vasgestel is (sien afdeling 4.8).

4.8 Ongewenste effekte

a. Getabelleerde opsomming van nadelige reaksies

Orgaanklas Stelsel	Frekwensie	Ongewenste Effek
Immuunstelselafwykings	*Minder gereeld*	Onmiddellike hipersensitiwiteitsreaksies, soms ernstig, insluitend anafilakse, brongospasma, kortasem, hipotensie, skok, angioedeem, urtikaria
Senuweestelselafwykings	*Gereeld*	Hoofpyn
	Minder gereeld	Bewegingsafwykings (insluitend ekstrapiramidale reaksies soos okulogiriese krisis, distoniese reaksies en diskinesie is waargeneem sonder definitiewe bewyse van aanhoudende kliniese gevolge), aanvalle
Oogafwykings	*Minder gereeld*	Voorbygaande blindheid hoofsaaklik tydens binneaarse toediening
Hartafwykings	*Minder gereeld*	Disritmieë, borspyn met of sonder ST-segment onderdrukking, bradikardie, QTc-verlenging (insluitend Torsade de Pointes)
Vaskulêre afwykings	*Gereeld*	Gevoel van warmte of gloede
	Minder gereeld	Hypotension
Respiratoriese, torakale en mediastinale afwykings	*Minder gereeld*	Hik
Gastrointestinale afwykings	*Gereeld*	Hardlywigheid
Hepatobiliêre afwykings	*Minder gereeld*	Asimptomatiese toenames in lewerfunksietoetse

b. Aanmelding van vermoedelike nadelige reaksies
Dit is belangrik om vermoedelike nadelige reaksies aan te meld na goedkeuring van die medisyne. Dit laat voortgesette monitering van die voordeel/risiko-balans van die medisyne toe. Gesondheidsorgverskaffers word gevra om enige vermeende nadelige reaksies by SAHPRA aan te meld via die "6.04 Adverse Drug Reactions Reporting Form", wat aanlyn gevind kan word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

4.9 Oordosering
Daar is beperkte ervaring van ondansetron oordosis. In die meeste gevalle was simptome soortgelyk aan dié wat reeds aangemeld is by pasiënte wat aanbevole dosisse ontvang het (sien afdeling 4.8). Manifestasies wat mag voorkom sluit in visuele versteurings, erge hardlywigheid, hipotensie en 'n vasovagale episode met verbygaande tweedegraadse AV-blok. Daar is geen spesifieke teenmiddel vir ondansetron nie, daarom moet dit in gevalle van vermoedelike oordosis simptomaties en ondersteunend behandel word soos toepaslik. Ondansetron verleng die QT-interval op 'n dosisafhanklike wyse. EKG-monitering word aanbeveel in gevalle van oordosis.

5 FARMAKOLOGIESE EIENSKAPPE
5.1 Farmakodinamiese eienskappe
A 5.10 Medisyne wat outonome funksies beïnvloed. Serotonien-antagoniste.

Ondansetron is 'n kragtige, hoogs selektiewe 5HT3-reseptor-antagonis. Die presiese werking daarvan in die beheer van naarheid en braking is nie bekend nie. Chemoterapeutiese medisyne en radioterapie kan vrystelling van 5HT in die dunderm veroorsaak wat 'n brakingrefleks begin deur vagale afferente terminale via 5HT3-reseptore te aktiveer. Ondansetron blokkeer die aanvang van hierdie refleks. Aktivering van vagale afferente terminale kan ook 'n vrystelling van 5HT in die area van die postrema veroorsaak, geleë op die basis van die vierde ventrikel, en dit kan ook braking bevorder deur middel van 'n sentrale meganisme.

Daarom dus die effek van ondansetron in die hantering van naarheid en braking wat deur sitotoksiese chemoterapie en radioterapie veroorsaak word, toegeskryf aan die antagonisme van 5HT3-reseptore op neurone wat beide in die perifere en sentrale senuweestelsel geleë is. In psigomotoriese toetse benadeel ondansetron nie motoriese prestasie nie en veroorsaak ook nie sedasie nie. Ondansetron verander nie plasmaprolaktienkonsentrasies nie.

5.2 Farmakokinetiese eienskappe
Na orale toediening van ondansetron vind absorpsie vinnig plaas met maksimum plasmakonsentrasies van ongeveer 30 ng/ml wat ongeveer 1,6 uur na 'n 8 mg dosis bereik word. Die absolute orale biobeskikbaarheid van die medisyne is ongeveer 60 %. Die verspreiding van ondansetron na beide orale en binneaarse dosering is soortgelyk met 'n terminale eliminasie-halfleeftyd van ongeveer 3 uur en 'n bestendige verspreidingsvolume van ongeveer 140 ℓ. Plasmaproteïenbinding is 70 - 76 %. Ondansetron word hoofsaaklik deur metabolisme uit die sistemiese sirkulasie verwyder, met minder as 5 % van 'n dosis wat onveranderd in die urine uitgeskei word.

Studies in gesonde bejaarde vrywilligers het 'n effens verhoogde orale biobeskikbaarheid (65 %) en verlengde eliminasie-halfleeftyd (5 uur) vir ondansetron getoon. By pasiënte met ernstige lewerversaking word sistemiese opruiming merkbaar verminder met verlengde eliminasie-halfleeftyd (15 - 32 uur) en 'n orale biobeskikbaarheid wat 100% nader as gevolg van verminderde pre-sistemiese metabolisme.

In 'n studie van 21 pediatriese pasiënte tussen die ouderdomme van 3 en 12 jaar wat elektiewe chirurgie met algemene narkose ondergaan het, is die absolute waardes vir beide die opruiming en volume van verspreiding van ondansetron na 'n enkele intraveneuse dosis van 2 mg (3-7 jaar oud) of 4 mg (8-12 jaar oud) verminder. Die omvang van die verandering was ouderdomsverwant, met opruiming wat gedaal het van ongeveer 300 ml/min op 12-jarige ouderdom tot 100 ml/min op 3 jaar. Volume van verspreiding het van ongeveer 75 ℓ op 12 jaar tot 17 ℓ op 3 jaar gedaal. Gebruik van gewigsgebaseerde doserings (0,1 mg/kg tot 4 mg maksimum) kompenseer vir hierdie veranderinge en is effektief om sistemiese blootstelling by pediatriese pasiënte te normaliseer.

6 FARMASEUTIESE BESONDERHEDE
6.1 Lys van hulpstowwe
Laktosemonohidraat
Lae-gesubstitueerde hidroksipropiel sellulose
Krospovidoon
Kalsiumsilikaat
Aspartaam
Pepermentgeur
Kolloïdale watervrye silika
Magnesiumstearaat

6.2 Onversoenbaarheid
Onbekend

6.3 Rakleeftyd
3 jaar

6.4 Spesiale voorsorgmaatreëls vir berging
Berg by of onder 25 ºC.
Hou buite bereik van kinders.

6.5 Aard en inhoud van verpakking
Twee tipes verpakkingsmateriaal word vir OMECTRON ODT voorgestel:
- Aftrekbare aluminium / aluminium stulpverpakking
- Aluminium / aluminium stroke

Elke stulpverpakking of strook bevat 10 tablette. Verpakkingsgroottes van 10 of 30 tablette word in 'n kartonhouer verpak.
Nie alle verpakkingsgroottes word moontlik bemark nie.

6.6 Spesiale voorsorgmaatreëls vir wegdoening en ander hantering
Geen spesiale vereistes vir wegdoening nie. Enige ongebruikte medisyne of afvalmateriaal moet in ooreenstemming met plaaslike vereistes weggedoen word.

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8 REGISTRASIENOMMER(S)
OMECTRON 4 ODT: 48/5.10/0778
OMECTRON 8 ODT: 48/5.10/0779

9 DATUM VAN EERSTE MAGTIGING / HERNUWING VAN DIE MAGTIGING
Moet nog bevestig word

10 DATUM VAN HERSIENING VAN DIE TEKS
7 Junie 2022