SCHEDULING STATUS:
S4

PROPRIETY NAME AND DOSAGE FORM:
BIO-DOMPERIDONE 10 (Film-coated tablet)

COMPOSITION:
Each film-coated tablet contains 10 mg domperidone.
Excipients:
Core tablet: crospovidone, hydrogen vegetable oil, lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose (PH 102), povidone (K 30), sodium lauryl sulphate.
Coating: hypromellose, polyethylene glycol.
Contains Sugar

PHARMACOLOGICAL CLASSIFICATION:
A.5.7.2 Anti-emetics and anti-vertigo preparations

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Domperidone is a dopamine antagonist. It produces an anti-emetic effect through its action on the dopamine-receptor in the chemo-emetic trigger zone. Domperidone does not cross the blood-brain barrier to any significant degree and therefore exerts a relatively minor effect on cerebral dopaminergic receptors. Domperidone has been shown to increase the duration of antral and duodenal contractions thus improving gastric emptying. Domperidone does not alter gastric secretions and has no effect on intracranial pressure or on the cardiovascular system.
Pharmacokinetic properties
Domperidone is absorbed after oral administration in the fasting state with peak plasma concentrations at approximately 1 hour after administration. Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation. Due to this extensive first-pass hepatic and intestinal metabolism, the absolute bioavailability of oral domperidone is low (approximately 15 %).
Domperidone is 90 – 95 % bound to plasma proteins. The plasma half-life after a single oral dose is approximately 7 – 9 hours and is prolonged in patients with severe renal impairment.
Urinary and faecal excretion amount to 31 % and 66 % of the oral dose, respectively. The proportion of domperidone excreted unchanged is small (approximately 1 % of urinary and 10 % of faecal excretion).

INDICATIONS:
BIO-DOMPERIDONE 10 is indicated for:
- Delayed gastric emptying of functional origin with gastro-oesophageal reflux and/or dyspepsia.
- Control of nausea and vomiting of central or local origin.
- As an anti-emetic in patients receiving cytostatic and radiation therapy.
- Facilitates radiological examination of the upper gastrointestinal tract.

CONTRAINDICATIONS:
BIO-DOMPERIDONE 10 is contraindicated:
- In patients with a known hypersensitivity to domperidone or any of the excipients
- In patients with a prolactin secreting or producing pituitary tumour (prolactinoma)
- Whenever stimulation of gastric motility is to be avoided or could be harmful (e.g. in the presence of gastrointestinal haemorrhage, obstruction or perforation)
- Bradycardia or heart-block
- Pre-existing cardiac disease
- Known congenital long QT interval or family history thereof.
- Co-administration with oral ketoconazole, itraconazole and other medicines inhibiting the hepatic cytochrome enzyme CYP3A4, such as macrolide antibiotics e.g. erythromycin, azithromycin, roxithromycin, clarithromycin, HIV protease inhibitors, azole antifungals.

The safe use during pregnancy and lactation has not been established (see PREGNANCY AND LACTATION).

WARNINGS AND SPECIAL PRECAUTIONS:
BIO-DOMPERIDONE 10 should not be administered to children under 12 years of age.
BIO-DOMPERIDONE 10 should be used with caution in patients with renal impairment or in those at risk of fluid retention. In patients with severely-impaired renal function (creatinine clearance < 30 ml/minute, serum creatinine approximately 530 mmol/L), the elimination half-life of BIO-DOMPERIDONE 10 was increased from 7,4 to 20,8 hours. The dosing frequency should be reduced to once or twice daily; depending on the severity of impairment, and the dose may need to be reduced. Patients who are on long-term therapy should be monitored on a regular basis. Do not exceed the maximum daily dose of 80 mg.
BIO-DOMPERIDONE 10 should be used with caution in patients with hepatic impairment and in the elderly since BIO-DOMPERIDONE 10 is mainly metabolised in the liver.
BIO-DOMPERIDONE 10 should not be given to patients being treated with monoamineoxidase inhibitors (see INTERACTIONS), as dopamine levels can be increased.

INTERACTIONS:
The main metabolic pathway of BIO-DOMPERIDONE 10 is through CYP3A4. As an inhibitor of CYP3A4, macrolide antibiotics can block the metabolism of domperidone, resulting in increased plasma concentrations of domperidone.
Use caution when using BIO-DOMPERIDONE 10 with MAO inhibitors e.g. selegiline used for the treatment of Parkinson's disease or tranylcypromine and moclobemide used for the treatment of depression as dopamine levels can be increased (see WARNINGS AND SPECIAL PRECAUTIONS).
The effect of BIO-DOMPERIDONE 10 may be antagonised by anti-muscarinic agents and opioid analgesics.
Due to the gastro-kinetic effects of BIO-DOMPERIDONE 10, the absorption of concomitant oral medication (particularly sustained release or enteric coated formulations) can be influenced.
BIO-DOMPERIDONE 10 increases with serum prolactin levels, and therefore may interfere with other hypoprolactaemic agents and with some diagnostic tests.
BIO-DOMPERIDONE 10 should not be taken concomitantly with anti-acids, anti-secretory agents (histamine H_2-receptor antagonists such as cimetidine; proton pump inhibitors; selective antimuscarinics or prostaglandin analogues), or sodium bicarbonate as they lower the oral bioavailability of BIO-DOMPERIDONE 10.
Reduced gastric acidity impairs the absorption of BIO-DOMPERIDONE 10.
Co-administration of ketoconazole and itraconazole with BIO-DOMPERIDONE 10 is contraindicated. (see CONTRAINDICATIONS).
BIO-DOMPERIDONE 10 suppresses the peripheral effects (digestive disorders, nausea and vomiting) of dopaminergic agonists, by antagonism of dopamine receptors in the chemoreceptor trigger zone.

PREGNANCY AND LACTATION:
BIO-DOMPERIDONE 10 should not be administered to pregnant or lactating women (see CONTRAINDICATIONS).
Administration to pregnant mothers shortly before giving birth, or during labour, may result in the new-born infant being born hypotonic, collapsed and hypoglycaemic.

DOSAGE AND DIRECTIONS FOR USE:
Acute conditions (nausea and vomiting)
Adults: Two tablets (20 mg) three to four times per day, 15 to 30 minutes before meals and, if necessary, before retiring to bed.
Children over 12 years and weighing 35 kg or more: One tablet (10 mg) three to four times per day, 15 to 30 minutes before meals and, if necessary, before retiring to bed.
Tablets are not recommended for children weighing less than 35 kg.
Children < 12 years: The formulation is not suitable for this indication, in children.
Chronic conditions (mainly dyspepsia)
Adults: One tablet (10 mg) three times per day, 15 to 30 minutes before meals and, if necessary, before retiring to bed. The dosage may be doubled. In patients with severe renal insufficiency the elimination half-life of domperidone was increased from 7,4 – 20,8 hours. The dosing frequency should be reduced to once or twice daily, depending on the severity of impairment, and the dose may need to be reduced.
Patients on prolonged therapy should be reviewed regularly (see WARNINGS AND SPECIAL PRECAUTIONS).

SIDE EFFECTS:
Nervous system disorders
Less frequent: Dry mouth; headache; dizziness, irritability, nervousness; thirst and extrapyramidal effects (difficulty in speaking; loss of balance or muscle control).
Have been reported but frequency is unknown: Dystonic reactions (extrapyramidal phenomena) may occur.
Where the blood brain barrier is not fully developed (mainly in young babies) or is impaired, the possible occurrence of neurological side effects cannot be excluded.
Eye disorders
Less frequent: Conjunctivitis.
Endocrine disorders
Less frequent: Endocrinological effects (hot flushes, menstrual irregularities).
Reproductive system and breast disorders
Less frequent: Mastalgia. Reversible raised serum prolactin levels have been observed which may lead to galactorrhoea and gynaecomastia.
Skin and subcutaneous tissue disorders
Less frequent: Pruritus; rash; urticaria and oedema.
General disorders and administrative site conditions
Less frequent: Stomatitis; asthenia; lethargy.
Renal and urinary disorders
Less frequent: Change in urinary frequency; dysuria.
Gastrointestinal disorders
Less frequent: Abdominal cramps; change in appetite; constipation; diarrhoea and heartburn.
Muscoskeletal, connective tissue and bone disorders
Less frequent: Leg cramps.
Cardiac disorders
Less frequent: Palpitations.
Vascular disorders
Have been reported but frequency is unknown: Hypertensive crisis in patients with phaeochromocytoma may occur with administration of BIO-DOMPERIDONE 10.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
The following are the clinical effects of an overdose: dysrhythmia (dizziness, fainting, irregular heartbeat); drowsiness; disorientation; extrapyramidal reactions, especially in children and hypotension.
There is no specific antidote or specific agent for domperidone overdose. In the event of overdosage gastric lavage as well as the administration of activated charcoal may be useful. Symptomatic and supportive measures are recommended.
Anticholinergic agents, anti-parkinson medication or antihistamines with anticholinergic properties may be useful in controlling the extrapyramidal effects associated with domperidone toxicity.

IDENTIFICATION:
White, round, film-coated, biconvex tablets.

PRESENTATION:
BIO-DOMPERIDONE tablets are available in transparent PVC-Aluminium blister packs of 10 or 100 tablets.

STORAGE INSTRUCTIONS:
Store at or below 25 °C. Keep the blister in the outer carton until required for use.
Protect from light.
KEEP OUT OF REACH AND SIGHT OF CHILDREN.

REGISTRATION NUMBER:
42/5.7.2/0836

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
BIOTECH LABORATORIES (PTY) LTD
Ground Floor, Block K West, Central Park
400 16th Road, Randjespark, Midrand, 1685
South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT:
Date of registration: 26 November 2010
Date of latest revision of the text as approved by Council:
22 September 2010
Date of notification with regard to amended Reg. 9 and 10:
02 February 2015

P420836-2

SKEDULERINGSTATUS:
S4

EIENDOMSNAAM EN DOSSERING:
BIO-DOMPERIDONE 10 (Film-bedekte tablet)

SAMESTELLING:
Elke film-bedekte tablet bevat 10 mg domperidoon.
Onaktiewe bestandele:
Kern tablet: krospovidoon, waterstof groente olie, lactose monohidraat, magnesium stereaat, stysel, mikrokristalline sellulose (PH 102), povidoon (K 30), natrium lauriel sulfaat.
Filmbedekking: hirpomellose, polyetileen glukol.
Bevat Suiker

FARMAKOLOGIESE KLASSIFIKASIE:
A.5.7.2 Anti-emetikum en anti-vertigo voorbereidings.

FARMAKOLOGIESE WERKING:
Farmakodinamika
Domperidoon is 'n dopamien antagonis. Dit produseer 'n anti-emetiese effek deur die reaksie daarvan op die dopamien reseptor in die chemo-emetiese reaksie sone. Domperidoon gaan nie oor die bloed-brein grens in enige beduidende mate nie en daarom oefen dit 'n relatiewe klein invloed op serebrale dopaminerge reseptore. Domperidoon het getoon om gastriese lediging te versnel deur die antrale en duodenale kontraksies te verbeter. Domperidoon veroorsaak geen verandering in gastriese uitskeidings nie en het geen effek op intrakraniale druk of die kardiovaskulêre stelsel nie.
Farmakokinetika
Domperidoon word ongeveer 1 uur na orale toediening in die vastende toestand met piek plasma konsentrasies geabsorbeer. Domperidoon ondergaan vinnige en omvattende hepatise metabolisme deur hidroksilering en N-dealkilering. As gevolg van hierdie uitgebreide eerste-deurgang hepatiese en intestinale metabolisme, is die volkome biobeskikbaarheid van orale domperidoon laag, (ongeveer 15 %).
90 – 95 % van Domperidoon is aan plasmaproteïne gebind. Die plasma halfleeftyd na 'n enkele orale dosis is ongeveer 7 – 9 ure en is langer in pasiënte met ernstige swak nierfunksie.
Urinêre en fekale uitskeiding is onderskeidelik 31 % en 66 % van die orale dosis. Die verhouding van domperidoon wat onveranderd uitgeskei word is klein (ongeveer 1 % urinêr en 10 % fekale uitskeiding).

INDIKASIES:
BIO-DOMPERIDONE 10 is aangedui vir:
- Vertraagde gastriese lediging van funksionele oorsprong met gastroësofageale refluks en/of dispepsie.
- Beheersing van naarheid en braking van sentrale of lokale oorsprong.
- 'n Anti-emetikum in pasiënte wat sitostatiese- en bestralingsterapie ontvang.
- Fasilitering in radiologiese ondersoeke van die boonste gastroïntestinale kanaal.

KONTRA-INDIKASIES:
BIO-DOMPERIDONE 10 word gekontra-indikeer:
- In pasiënte met 'n bekende hipersensitiwiteit vir domperidoon of enige van die bindmiddels.
- In pasiënte met 'n prolaktien uitskeidende of -vervaardigende pituïtêre tumor of (prolaktinoma).
- Wanneer stimulasie van gastriese motiliteit vermy moet word of skadelik kan wees (bv. In die teenwoordigheid van gastroïntestinale bloeding, obstruksie of perforasie).
- In bradikardie of hartblok.
- In voorafbestaande hartsiekte.
- In bekende aangebore lang QT tydperk of 'n familiegeskiedenis daarvan.
- In gesamentlike dosering met ketokonasool, itrakonasool en ander medisyne wat die hepatise sitochroom CYP3A4 inhibeer, soos makroliede antibiotika bv. eritromisien, azitromisien, roxitromisien, klaritromisien, MIV protease inhibeerder, asook antifungusmiddels.

Die veilige gebruik tydens swangerskap en laktasie is nog nie vasgestel nie (sien SWANGERSKAP EN LAKTASIE).

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
BIO-DOMPERIDONE 10 moet nie toegedien word aan kinders onder die ouderdom van 12 jaar nie.
BIO-DOMPERIDONE 10 moet met sorg gebruik word in pasiënte met nierinkorting of in dié met die risiko van vloeistofretensie. In pasiënte met ernstige ingekorte nierfunksie (kreatinien opruiming < 30 ml/minuut, serum kreatinien ongeveer 530 mmol/L), die eliminasie halfleeftyd van BIO-DOMPERIDONE 10 is vermeerder van 7,4 tot 20,8 ure. Die doserings-frekwensie moet verminder word na een of twee maal per dag; die dosis mag dalk verminder word afhangende van die erns van die inkorting. Pasiënte wat op langtermyn terapie is, moet op 'n gereelde basis gemonitor word. (sien SPESIALE VOORSORGMAATREËLS).
Moet nie die maksimum daaglikse dosis van 80 mg oorskry nie.
BIO-DOMPERIDONE 10 moet met omsigtigheid gebruik word in pasiënte met ingekorte lewerfunksie en in die bejaarde pasiënt omdat BIO-DOMPERIDONE 10 hoofsaaklik in die lewer gemetaboliseer word. Omsigtigheid moet uitgeoefen word by pasiënte met nierinkorting of in die aan die risiko van vloeistofretensie. In pasiënte met ernstige nierontoereikendheid (kreatinienopruiming <30 ml/min), waar die serum kreatinien meer as 6 mg/100 ml is, d.w.s. meer as 0,6 mmol/L, is die eliminasie halfleeftyd van BIO-DOMPERIDONE 10 verhoog van 7,4 tot 20,8 uur. Die doseringsfrekwensie moet verminder word tot een of twee maal per dag, afhangend van die erns van die waardedaling, en die dosis moet verminder word. Pasiënte op langdurige behandeling moet gereeld gemonitor word. (sien WAARSKUWINGS).
BIO-DOMPERIDONE 10 moet nie aan pasiënte gegee word wat behandel is met monoamienoksidase inhibeerders nie (sien INTERAKSIES), omdat dopamien vlakke verhoog kan word.

INTERAKSIES:
Die hoof metaboliese weg van BIO-DOMPERIDONE 10 is deur CYP3A4. Makroliede antibiotika, 'n inhibeerder van CYP3A4, kan die metabolisme van domperidoon blokkeer, wat dan lei tot verhoogde plasma-konsentrasies daarvan. BIO-DOMPERIDONE 10 moet met sorg gebruik word met MAO inhibeerders bv. selegilien wat gebruik word vir die behandeling van Parkinson se siekte of tranielsipromien en moklobemied wat gebruik word vir die behandeling van depressie, dopamien vlakke kan verhoog word as gevolg daarvan (sien SPESIALE VOORSORGMAATREËLS).
Die effek van BIO-DOMPERIDONE 10 mag teëgewerk word deur anti-muskariniese middelle en opioïede pynstillers. As gevolg van die gastro-kinetiese uitwerking van BIO-DOMPERIDONE 10, kan die absorpsie van meegaande orale medikasie (in die besonder volhoubare vrystelling of enteries-omhulde formulering) beïnvloed word.
BIO-DOMPERIDONE 10 vermeerder met serum prolaktien vlakke, en mag daarom met ander hipoprolaktemiese agente en sommige diagnostiese toetse inmeng. BIO-DOMPERIDONE 10 moet nie geneem word saam met anti-suur middels, anti-sekretoriese middels (histamien H_2-reseptor antagoniste soos simetidien; proton pomp inhibeerders; selektiewe anti-muskariniese middele of prostaglandien analoë), of sodium bikarbonaat nie, omdat hulle die orale biobeskikbaarheid van BIO-DOMPERIDONE 10 verlaag. Verminderde maagsuur benadeel die absorpsie van BIO-DOMPERIDONE 10. Gesamentlike toediening van ketokonasool en itrakonasool met BIO-DOMPERIDONE 10 is gekontraïndikeerd (sien KONTRAINDIKASIES).
BIO-DOMPERIDONE 10 onderdruk die perifere effekte (verteringsteurnisse, naarheid en braking) van dopaminerge agoniste deur die antagonisme van die dopamien reseptore in die snellerêreas van die chemoreseptore.

SWANGERSKAP EN LAKTASIE:
BIO-DOMPERIDONE 10 moet nie toegedien word aan swanger of lakterende vroue nie (sien KONTRAINDIKASIES).
Toediening aan swanger vroue kort voor die geboorte van die baba, of gedurende die geboorte mag lei daartoe dat die baba hipotonies of hipoglisemies gebore word en mag ook lei tot die ineenstorting van die baba.

DOSIS EN GEBRUIKSAANWYSINGS:
Akute toestande (Naarheid en braking)
Volwassenes: Twee tablette (20 mg) drie tot vier maal per dag, 15 tot 30 minute voor etes en indien nodig, voor slapenstyd.
Kinders bo 12 jaar en wat meer as 35 kg weeg: Een tablet (10 mg) drie tot vier maal per dag, 15 tot 30 minute voor etes en indien nodig, voor slapenstyd.
Tablette word nie aanbeveel vir kinders met 'n gewig minder as 35 kg nie.
Kinders > 12 jaar: Die formulering in hierdie indikasie is nie geskik vir kinders nie.
Chroniese toestande (hoofsaaklik dispepsie)
Volwassenes: Een tablet (10 mg) drie maal per dag, 15 tot 30 minute voor etes en indien nodig, voor slapenstyd. Die dosis kan verdubbel word.
Die uitskeidingshalfleeftyd van domperidoon is vermeerder van 7,4 – 20,8 ure in pasiënte met ernstige nierontoereikendheid. Die doserings-frekwensie moet verminder word na een of twee maal per dag afhangend van die erns van die beskadiging, en dit mag nodig wees om die dosis te verminder. Pasiënte op langtermyn terapie moet gereeld geherevalueer word (sien WAARSKUWINGS).

NEWE-EFFEKTE:
Senusisteemversteurings
Minder dikwels: Droë mond, hoofpyn, duiseligheid, prikkelbaarheid, senuweeagtigheid, dors, ekstrapiramidale effekte (probleme met spraak, balansverlies of spierbeheer).
Aangemeld, maar frekwensie onbekend: Distoniese reaksies (ekstra-piramidale verskynsels) kan voorkom.
Die moontlike voorkoms van neurologiese newe-effekte kan nie uitgesluit word waar die bloed-brein grens nie volledig ontwikkel is (hoofsaaklik in jong babas) of 'n waardedaling ondergaan nie.
Oogversteurings
Minder dikwels: Konjuntivitis
Endokriene versteurings
Minder dikwels: Endokrinologiese effekte (warm gloede, menstruele onreëlmatighede).
Reproduktiewe stelsel en bors versteurings
Minder dikwels: Mastalgie. Omkeerbare verhoogde serum prolaktien is waargeneem wat kan lei tot galaktoree en ginekomastie.
Velversteuring en subkutane verteurings
Minder dikwels: Pruritus, veluitslag, urtikaria en edeem.
Algemene versteurings en toedienings area versteurings
Minder dikwels: Stomatitis, astenie, luisteloosheid.
Renale en Urinêre versteurings
Minder dikwels: Verandering in urinêre frekwensie, disurie.
Gastroïntestinale versteurings
Minder dikwels: Abdominale krampe, verandering in eetlus, hardlywigheid, diaree en sooibrand.
Muskuloskeletale versteurings
Minder dikwels: Been krampe.
Kardiale versteurings
Minder dikwels: Palpitasies (hartkloppings).
Vaskulêre siektes
Aangemeld, maar frekwensie onbekend: Hipertensiewe krisis in pasiënte met feochromositoom mag voorkom met die toediening van BIO-DOMPERIDONE 10.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Die volgende is die kliniese gevolge van 'n oordosis: disritmie, (duiseligheid, floutes, onreëlmatige hartklop), lomerigheid, disoriëntasie, ekstra-piramidale reaksies (veral in kinders) en hipotensie.
Daar is geen spesifieke teenmiddel of spesifieke middels vir domperidoon oordosis nie. Maagspoeling sowel as die toediening van geaktiveerde houtskool kan nuttig wees in die geval van oordosering. Simptomatiese en ondersteunende maatreëls word aanbeveel. Anticholinergiese middels, anti-Parkinson medikasie of antihistamiene met anticholinergiese eienskappe kan nuttig wees in die beheer van ekstrapiramidale effekte wat geassosieer word met domperidoon toksisiteit.

IDENTIFIKASIE:
Wit, ronde, film-bedekte, bikonvekse tablet.

AANBIEDING:
BIO-DOMPERIDONE tablette is beskikbaar in deursigtige PVC-Aluminium stulpverpakkings van 10 of 100 tablette.

BERGINGSINSTRUKSIES:
Bewaar teen of benede 25 °C. Hou die stulpstrook in die buitenste karton totdat dit benodig word vir gebruik.
Beskerm teen lig.
HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIE NOMMER:
42/5.7.2/0836

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
BIOTECH LABORATORIUMS (EDMS.) BPK.
Grond Vloer, Blok K Wes, Central Park,
400 16de Weg, Randjespark, Midrand, 1685
Suid Afrika

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
Datum van registrasie: 26 November 2010
Datum van kennisgewing met betrekking tot Reg. 9 en 10:
02 Februarie 2015.

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