SCHEDULING STATUS:
S3

PROPRIETY NAME AND DOSAGE FORM:
BIO CIMETIDINE 200 (film-coated tablets)
BIO CIMETIDINE 400 (film-coated tablets)

COMPOSITION:
Each BIO CIMETIDINE 200 film-coated tablet contains cimetidine 200 mg
Each BIO CIMETIDINE 400 film-coated tablet contains cimetidine 400 mg
Excipients: colloidal anhydrous silica, corn starch, magnesium stearate, powdered cellulose, povidone, sodium lauryl sulphate, sodium starch glycolate.
Coating: Opadry white, talc.
Sugar free

PHARMACOLOGICAL CLASSIFICATION:
A 11.4.3 Antacids, other.

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Cimetidine is a histamine H_2-receptor antagonist and accordingly it inhibits stimulated and basal gastric acid secretion and reduces pepsin output. It competitively inhibits the action of histamine and other H_2-agonist at the histamine H_2-receptor.
Pharmacokinetic properties
Cimetidine is readily absorbed from the gastrointestinal tract and peak plasma concentrations are obtained about an hour after administration on an empty stomach. Food delays the rate of absorption with the peak plasma concentration occurring after about 2 hours. The elimination half-life is around two hours and increases with renal impairment. Cimetidine is only partially metabolised in the liver and most is excreted unchanged in the urine.

INDICATIONS:
BIO CIMETIDINE is indicated in:
The treatment of duodenal and benign gastric ulceration and peptic oesophagitis, recurrent ulceration, stomal ulceration and other conditions where reduction of gastric acid secretion has been shown to be beneficial.
Maintenance therapy for periods of up to one year in those patients with recurrence of duodenal ulceration after short-term therapy.
BIO CIMETIDINE is indicated in the management of those patients who are at high risk from haemorrhage of the upper-intestinal tract due to hepatic failure and treatment with immunosuppressive agents, following kidney transplant.
Management of pathological hypersecretion such as Zollinger-Ellison Syndrome, systemic mastocytosis, multiple endocrine adenomas.
Erosive gastro-oesophageal reflux disease (G.O.R.D.).

CONTRAINDICATIONS:
BIO CIMETIDINE is contraindicated in patients with a known hypersensitivity to cimetidine.
Safety in pregnancy and lactation has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:
The dosage of cimetidine should be reduced in patients with impaired renal function. Suggested doses according to creatinine clearance are; creatinine clearance of 0-15 mℓ per minute, 200 mg twice daily; 15-30 mℓ per minute, 200 mg three times daily; 30-50 mℓ per minute, 200 mg four times daily; over 50 mℓ per minute, normal dosage. Before giving BIO CIMETIDINE to patients with gastric ulcer, the possibility of malignancy should be excluded since cimetidine may mask symptoms and delay diagnosis.
Safety and/or efficacy have not been established in the use of BIO CIMETIDINE in children.

INTERACTIONS:
Cimetidine inhibits the activity of cytochrome P450 in the liver, thereby slowing the hepatic metabolism of many medicines. This will prolong the half-life of some medicines such as cyclosporine, lignocaine (lidocaine), nifedipine, phenttoin, suxamethionium, theophylline and warfarin, when administered with cimetidine and a reduction in the dosage of these medicines may be needed. If concurrent administration of warfarin and cimetidine is necessary, the close monitoring of the prothrombin time is advisable.

DOSAGE AND DIRECTIONS FOR USE:
BIO CIMETIDINE may be given by mouth or the nasogastric route, and the total daily dose should not exceed 2,4 g. When BIO CIMETIDINE is given orally, the day time doses should be taken with meals.
Duodenal and Gastric ulcers
A single dose of 800 mg daily taken at bedtime, for 4 weeks in the case of duodenal ulcer, and 6 weeks for a gastric ulcer. Where appropriate, a maintenance dose of 400 mg at bedtime or 200 mg twice daily should be taken for a period up to a year.
Oesophageal reflux
A dose of 400 mg four times daily (with meals and at bedtime) for 4-8 weeks is recommended.
Zollinger-Ellison Syndrome
A dose of 400 mg four times daily (with meals and at bedtime) for 4-8 weeks is recommended. This dose can be increased to a maximum of 2,4 g per day, if necessary.
Maintenance treatment: Prophylaxis of recurrent ulcer
400 mg at bedtime or increase to 400 mg twice a day, if necessary for up to one year.
The dose of cimetidine should be reduced in patients with impaired renal function – see WARNINGS AND SPECIAL PRECAUTIONS.

SIDE EFFECTS:
The most common side effects reported include diarrhoea, dizziness, tiredness, headaches and rashes. Reversible confusional states, especially in the elderly or seriously ill patients with renal failure, have been reported. Cimetidine has a weak anti-androgenic effect and gyneacomastia and impotence have been reported in less frequent cases where men have been taking high doses for long periods, such as those with Zollinger-Ellison Syndrome. Other adverse effects that have been reported less frequently include hypersensitivity reactions, fever, arthralgia, myalgia blood disorders including agranulocytosis or neutropenia and thrombocytopenia, intestinal nephritis, hepatotoxicity and cardiovascular disorders.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Treatment of overdosage should consist of gastric lavage or emesis, if ingestion occurred not more than four hours before, followed by symptomatic and supportive measures only.

IDENTIFICATION:
BIO CIMETIDINE 200: White biconvex round film-coated tablet.
BIO CIMETIDINE 400: White bar-shaped biconvex film-coated tablet.

PRESENTATION:
Blister strips (14 tablets per strip) with clear, colourless polyvinylchloride (PVC) moulded to accept one tablet per pocket and sealed with soft, matte, silver, printed aluminium foil. Strips are packed into cartons with a package insert.
BIO CIMETIDINE 400 pack sizes included 14 and 56.
Securitainer (polypropylene) containing tablets and package insert. Sealed with a securitainer snap-on cap (polyethylene) and labelled with a glossy adhesive printed label.
BIO CIMETIDINE 200 pack sizes included 60 and 150 tablets.

STORAGE INSTRUCTIONS:
Store at or below 25 °C, protected from light.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
BIO CIMETIDINE 200: 31/11.4.3/0679
BIO CIMETIDINE 400: 31/11.4.3/0680

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: 14 July 1999
Date of latest revision of the text as approved by Council: 30 November 1999
Date of notification with regard to amended Reg. 9 and 10: 27 February 2015.

Botswana:	
Bio Cimetidine 200 Reg. No. BOT0600855	S2
Bio Cimetidine 400 Reg. No. BOT0600856	S2

Zimbabwe:	
Bio Cimetidine 200 Reg. No. 96/16.7/3089	PP10
Bio Cimetidine 400 Reg. No. 96/16.7/3090	PP10

Namibia:	
Bio Cimetidine 200 Reg. No 12/11.4.3/0011	NS2
Bio Cimetidine 400 Reg. No. 12/11.4.3/0012	NS2

PI310679/80-7

SKEDULERINGSTATUS:
S3

EIENDOMSNAAM EN DOSEERVORM:
BIO CIMETIDINE 200 (filmbedekte tablette)
BIO CIMETIDINE 400 (filmbedekte tablette)

SAMESTELLING:
Elke BIO CIMETIDINE 200 filmbedekte tablet bevat 200 mg simetidien
Elke BIO CIMETIDINE 400 filmbedekte tablet bevat 400 mg simetidien
Onaktiewe bestanddele: kolloïdale anhidriese silica, mieliestysel, magnesiumstearaat, verpoeierde sellulose, povidoon, natrium lauryl sulfaat, natriumstysel glikolaat.
Filmbedekking: Opadry wit, talk.
Suikervry

FARMAKOLOGIESE KLASSIFIKASIE:
A 11.4.3 Teensuurmiddels, ander.

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
Simetidien is 'n histamine H_2-reseptor antagonis en dit rem dus gestimuleerde en basale maagsuurafskeiding en verminder ook pepsienafskeiding. Dit rem die werking van histamine en ander H_2-agoniste op die histamine H_2-reseptor kompetitief.
Farmakokinetiese eienskappe
Simetidien word geredelik uit die gastroïntestinale weg geabsorbeer en piek plasmakonsentrasies word ongeveer 1 uur na toediening op 'n leë maag verkry. Voedsel vertraag die tempo van absorpsie met piek plasmakonsentrasies dan na ongeveer 2 uur. Die eliminasiehalfleeftyd is ongeveer 2 uur en neem toe met verswakte nierfunksie. Simetidien word slegs gedeeltelik deur die lewer gemetaboliseer en die meeste word onveranderd in die uriene uitgeskei.

INDIKASIES:
BIO CIMETIDINE word aangedui vir:
Die behandeling van duodenale en benigne gastriese ulkusse en peptiese esofagitis, maagsere, herhalende ulserasie, stoma ulserasie en ander toestande waarin aangetoon is dat 'n afname in maagsuurafskeiding voordelig is.
Instandhoudingsterapie vir tydperke tot een jaar in pasiënte met herhalende duodenale ulkusse na korttermynbehandeling.
BIO CIMETIDINE is aangedui vir pasiënte wat 'n hoë risiko het vir bloeding van die boonste gastroïntestinale weg vanweë lewerversaking en behandeling met immuunonderdrukkende middels na 'n nieroorplanting.
Beheer van patologiese hipersekresie soos tydens Zollinger-Ellisonsindroom, sistemiese mastositose, endokrienadenomas.
Eroderende gastro-esofageale refluksiekte (G.E.R.S.).

KONTRAINDIKASIES:
BIO CIMETIDINE is teenaangedui in pasiënte met 'n bekende hipersensitiwiteit teenoor simetidien.
Veiligheid van gebruik tydens swangerskap en borsvoeding is nog nie vasgestel nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Die dosis van simetidien moet verlaag word vir pasiënte met verswakte nierfunksie. Die voorgestelde dosisse volgens kreatinienopruiming is: kreatinienopruiming van 0-15 mℓ per minuut, 200 mg twee maal per dag; 15 – 30 mℓ per minuut, 200 mg drie maal per dag; 30 – 50 mℓ per minuut, 200 mg vier maal per dag; meer as 50 mℓ per minuut, normale dosis.
Voordat BIO CIMETIDINE aan pasiënte met gastriese ulkusse gegee word, moet die moontlikheid van kwaadaardigheid uitgesluit word omdat simetidien die simtome kan verberg en die vroeë diagnose kan vertraag.
Die veiligheid en/of effektiwiteit van die gebruik van BIO CIMETIDINE in kinders is nog nie vasgestel nie.

INTERAKSIES:
Simetidien inhibeer die aktiwiteit van die sitochroom P450 in die lewer en vertraag ook hierdeur die hepatiese metabolisme van baie medisyne. Dit sal die halfleeftyd van sommige medisynes soos siklosporien, lignokaïen (lidokaïen), nifedipien, fenitoïen, suksamentonium, teofillien en warfarien verleng as dit saam met simetidien toegedien word en 'n afname in die dosis van hierdie medisyne mag nodig wees. As gelyktydige gebruik van warfarien en simetidien nodig is, is 'n noukeurige monitering van die protrombientyd wenslik.

DOSIS EN GEBRUIKSAANWYSINGS:
BIO CIMETIDINE kan per mond of die naso-gastriese roete gegee word en die totale daaglikse dosis moet nie 2,4 g oorskry nie. Wanneer BIO CIMETIDINE mondelings gegee word, moet die dosis bedags tydens etes geneem word.
Duodenale en gastriese ulkusse
'n Enkelle dosis van 800 mg daagliks met slapenstyd vir 4 weke in die geval van 'n duodenale ulkus en 6 weke vir 'n gastriese ulkus. Waar van toepassing moet 'n onderhoudsdosis van 400 mg met slapenstyd of 200 mg twee maal per dag vir 'n tydperk van tot 'n jaar gebruik word.
Esofageale refluks
'n Dosis van 400 mg vier maal per dag (met etes en met slapenstyd) vir 4 – 8 weke word aanbeveel.
Zollinger-Ellisonsindroom
'n Dosis van 400 mg vier keer per dag (met etes en met slapenstyd) vir 4 – 8 weke word aanbeveel. Hierdie dosis kan tot 'n maksimum van 2,4 g per dag verhoog word indien nodig.
Onderhoudsbehandeling: Profilakse van terugkerende ulkusse
400 mg met slapenstyd of tot 400 mg twee maal per dag indien nodig, vir tot een jaar.
Die dosis van simetidien moet verminder word vir pasiënte met verswakte nierfunksie – sien NEWE EFFEKTE EN SPESIALE VOORSORGMAATREËLS.

NEWE EFFEKTE:
Die mees algemene newe effekte wat aangemeld is, sluit diarree, duiseligheid, moegheid, hoofpyn en veluitslag in. Omkeerbare verwardheid, veral in bejaarde of ernstig siek pasiënte met nierversaking is aangemeld. Simetidien het 'n swak anti-androgene effek en ginekomastie en impotensie is in enkele gevalle aangemeld waar mans hoë dosisse vir lang periodes gebruik het, soos met die wat aan Zollinger-Ellisonsindroom ly. Ander nadelige effekte wat minder gereeld aangemeld is, sluit hipersensitiwiteitsreaksies, koors, artralgie, mialgie bloedversteurings insluitende agranulositose of neutropenia en trombositopenie, intestinale nefritis, hepatotoksisiteite en kardiovaskulêre versteurings in.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Behandeling van oordosering moet bestaan uit maagspoeling of emese as inname nie meer as 4 uur van tevore plaasgevind het nie, gevolg deur simptomatiese en ondersteunende maatreëls.

IDENTIFIKASIE:
BIO CIMETIDINE 200: Wit, ronde, bikonvekse, filmbedekte tablet.
BIO CIMETIDINE 400: Wit, staafvormige bikonvekse, filmbedekte tablet.

AANBIEDING:
Stulpstroke (14 tablette per strook) met deursigtige, kleurlose polivinielchloried (PVC) wat gevorm is om een tablet per uitdrukholte te vat, dit word geseël met 'n sagte, silwer, mat gedruk aluminium foelie. Die stroke word verpak in 'n kartonhouer met 'n voubiljet.
BIO CIMETIDINE 400 verpakking groottes van 14 en 56 tablette.
Veiligheidshouer (polipropileen) wat tablette en 'n voubiljet bevat. Verseël met 'n veiligheidsprop (poliëtileen) en 'n glansetiket op die houer geplak.
BIO CIMETIDINE 200 verpakkingsgroottes sluit in 60 en 150 tablette.

BERGINGSINSTRUKSIES:
Bewaar teen of benede 25 °C, beskerm teen lig.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:
BIO CIMETIDINE 200: 31/11.4.3/0679
BIO CIMETIDINE 400: 31/11.4.3/0680

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT :
Biotech Laboratories (Edms) Bpk
Grond Vloer, Blok K Wes, Central Park
400 16de Weg, Randjespark, Midrand, 1685
Suid Afika

DATUM VAN PUBLIKASIE VAN DIE VOUBILJET:
Datum van Registrasie: 14 Julie 1999
Datum van die laaste hersiening van die voubiljet soos goedgekeur deur die Raad: 27 February 2015
Datum van kennisgewing met betrekking to gewysigde Reg. 9 en 10: 27 Februarie 2015

Botswana:	
Bio Cimetidine 200 Reg. Nr. BOT0600855	S2
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