SCHEDULING STATUS:
S3

PROPRIETARY NAME AND DOSAGE FORM:
BIO GLIBENCLAMIDE 5 (Tablets)

COMPOSITION:
Each tablet contains 5 mg glibenclamide.
Excipients: lactose (49 % per tablet), maize starch, pregelatinised starch, purified water, purified talc, colloidal silicon dioxide and magnesium stearate.
BIO GLIBENCLAMIDE 5 contains lactose 79,0 mg tablet.

PHARMACOLOGICAL CLASSIFICATION:
A 21.2 Oral hypoglycaemics

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties
Glibenclamide is an oral antidiabetic medicine with a hypoglycaemic effect. It forms part of the sulfonylurea group and causes hypoglycaemia by stimulating insulin release from pancreatic β cells.
Pharmacokinetic properties
Glibenclamide is readily absorbed from the gastrointestinal tract and is extensively bound to plasma proteins. Peak plasma concentrations occur within 2 to 4 hours. It is almost completely metabolised in the liver with about 50 % of the dose excreted in the urine and 50 % via the bile.

INDICATIONS:
BIO GLIBENCLAMIDE 5 is indicated as an adjunct to diet to lower the blood glucose in patients with non-insulin-dependent diabetes mellitus (type II) whose hyperglycaemia cannot be controlled by diet alone.

CONTRAINDICATIONS:
Hypersensitivity to glibenclamide, or any of the excipients.
Diabetes mellitus complicated by fever, trauma, or gangrene.
Patients with impaired renal or hepatic function or serious impairment of thyroid or adrenal function.
Diabetes mellitus in patients with a history of metabolic decompensation e.g. acidosis, diabetic pre-coma and coma.
Type 1 diabetes mellitus.
Pregnancy and lactation (see PREGNANCY AND LACTATION).

WARNINGS AND SPECIAL PRECAUTIONS:
The administration of oral hypoglycaemic medication has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin, although controversy exists concerning interpretation of these findings.
Adjustment of dosage of BIO GLIBENCLAMIDE 5 may be required in patients suffering from recurrent infections, traumas, shock or after anaesthesia. When major surgery is to be performed, insulin therapy should be substituted for BIO GLIBENCLAMIDE 5.
Intolerance to alcohol, characterised by facial flushing, may also occur (see INTERACTIONS).
Hypoglycaemic reactions may occur. The incidence of hypoglycaemia can be reduced if BIO GLIBENCLAMIDE 5 is taken with or immediately after a meal.
Since BIO GLIBENCLAMIDE 5 contains lactose, it is not recommended for patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or of glucose-galactose malabsorption.

INTERACTIONS:
The risk of hypoglycaemia may be increased or prolonged if moderate or large amounts of alcohol are consumed concomitantly with BIO GLIBENCLAMIDE 5 (see WARNINGS AND SPECIAL PRECAUTIONS).
Concomitant administration of BIO GLIBENCLAMIDE 5 and anticoagulants can increase their anticoagulant and hypoglycaemic effects.
Asparaginase, corticosteroids, diuretics (thiazide) and lithium have intrinsic hyperglycaemic activity in both diabetics and non-diabetics. The dosage of BIO GLIBENCLAMIDE 5 may need to be adjusted during and after treatment.
Beta-adrenergic blocking agents may decrease the hypoglycaemic effects of BIO GLIBENCLAMIDE 5 by inhibition of insulin secretion, modification of carbohydrate metabolism, and increased peripheral insulin resistance, leading to hyperglycaemia. A dose adjustment of BIO GLIBENCLAMIDE 5 may be required.
Monoamine oxidase inhibitors, quinidine, quinine or large dose salicylates have an intrinsic hypoglycaemic activity in both diabetic and non-diabetic patients. Dosage reduction may need to be considered if given concomitantly with BIO GLIBENCLAMIDE 5.
Chloramphenicol may decrease the metabolism of BIO GLIBENCLAMIDE 5 due to inhibition of hepatic microsomal enzymes. Dosage adjustments may be necessary during and after concurrent use.
A diminished hypoglycaemic effect, possibly requiring an increased dose of BIO GLIBENCLAMIDE 5, has been seen or might be expected with epinephrine (adrenaline), aminoglutethimide, chlorpromazine, diazoxide, oral contraceptives, rifamycins, and thyroid hormones.
An increased hypoglycaemic effect has occurred or might be expected with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, allopurinol, some analgesics, azole antifungals, cimetidine, clofibrate and related compounds, fluoroquinolones, heparin, octreotide, tetracycline and tricyclic antidepressants.
Propranolol may mask the symptoms of hypoglycaemia, and may inhibit normal physiological response to hypoglycaemia.
The hypoglycaemic effects may be enhanced by halofenate, cyclophosphamide, dicoumarol, phenylbutazone and sulphonamides.

PREGNANCY AND LACTATION:
BIO GLIBENCLAMIDE 5 is contraindicated during pregnancy and breastfeeding (see CONTRAINDICATIONS).
First signs of pregnancy must be reported to the doctor without delay, because a change to insulin and/or dietary treatment is necessary.

DOSAGE AND DIRECTIONS FOR USE:
Dosage should be adapted to each individual patient and is determined by results of medical examinations.
In general the initial dose is 2,5 mg daily (half a BIO GLIBENCLAMIDE 5 tablet). The daily dose can then be raised gradually in steps of half tablets, but only after repeating medical examination. Raising the dose beyond three tablets daily does not produce any increased response.
When changing over from another oral antidiabetic preparation, with a similar mode of action, the dosage of BIO GLIBENCLAMIDE 5 is determined by the amount of the previously administered dose and the medical examination. It may be considered that the effect of 1 g tolbutamide or glycodiazine, 0,5 g carbutamide or 250 mg chlorpropamide corresponds roughly to that of 5 mg BIO GLIBENCLAMIDE (1 tablet).
In combination therapy with a biguanide, there may be a greater risk of cardiovascular mortality than with the use of gliclazide alone.

SIDE EFFECTS:
Blood and lymphatic system disorders
Frequent: Hypoglycaemia (mild, including nocturnal hypoglycaemia).
Less frequent: Anaemia (aplastic or haemolytic), blood dyscrasias (agranulocytosis, leukopenia, pancytopenia), eosinophilia, thrombocytopenia. Severe hypoglycaemia that leads to convulsions and coma.
Metabolism and nutritional disorders
Frequent: Weight gain.
Skin and subcutaneous tissue disorders
Less frequent: Erythema multiforme or exfoliative dermatitis; photosensitivity.
Hepato-biliary disorders
Less frequent: Cholestasis, cholestatic jaundice, hepatic function impairment, hepatic porphyria, hepatitis or porphyria cutanea tarda.
General disorders and administrative site conditions
Frequent: Changes in sensation of taste, dizziness, drowsiness, headache, weakness, and paraesthesia.
Gastrointestinal disorders
Frequent: Gastrointestinal disturbances (constipation, diarrhoea, flatulence, heartburn, loss of or increase in appetite, nausea, stomach fullness, vomiting, epigastric pain).
Renal and urinary disorders
Frequent: Polyuria

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Hypoglycaemic symptoms, e.g. excessive perspiration, light-headedness, etc. can be treated by giving the patient a glucose load.

IDENTIFICATION:
White, caplet shaped tablets and a breakline on both sides.

PRESENTATION:
BIO GLIBENCLAMIDE 5 is packed into:
- Polypropylene securitainers covered with non-absorbent cotton and sealed with a polypropylene closure, or
- HDPE containers covered with non-absorbent cotton and sealed with a polypropylene screw cap with an induction sealing wad.
- Patient ready pack (PRP): White opaque PE zip lock pouch, printed on the front and back side, with perforation on top side.

Pack sizes:
PP securitainers of HDPE containers are available in pack sizes of 100 and 500 tablets.
PE zip lock patient ready packs (PRP's) are availabe in pack sizes of 28, 56 or 84 tablets.
All pack sizes may not necessarily be marketed at one time.

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

REGISTRATION NUMBER:
V/21.2/0345

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: 12 January 1990
Date of latest revision of the text as approved by Council: 02 March 2012
Date of notification with regard to amended Reg. 9 and 10: 06 February 2015

Namibia: Reg. No.: 13/21.2/0135	NS2

SKEDULERINGSTATUS:
S3

EIENDOMSNAAM EN DOSEERVORM:
BIO GLIBENCLAMIDE 5 (Tablette)

SAMESTELLING:
Elke tablet bevat 5 mg glibenklamied.
Onaktiewe bestanddele: laktose monohidraat (49 % per tablet), mieliestysel, pregegelatiniseerde stysel, gesuiwerde water, gesuiwerde talk, kolloïdale silikondioksied en magnesiumstearaat.
BIO GLIBENCLAMIDE 5 bevat laktose 79,0 mg per tablet.

FARMAKOLOGIESE KLASSIFIKASIE:
A 21.2 Orale hipoglukemiemiddels

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
Glibenklamied is 'n orale anti-diabetiese medisyne met hipoglisemiese werking. Dit vorm deel van die sulfonielureum groep en bewerkstellig hipoglisemie deur insulienvrystelling van die pankreas se β selle te stimuleer.
Farmakokinetiese eienskappe
Glibenklamied word geredelik vanuit die spysverteringskanaal geabsorbeer, and is breedvoerig aan plasmaproteiene gebonde. Piek plasma konsentrasies word binne 2 tot 4 ure bereik. Dit word bykans in die geheel gemetaboliseer deur die lewer, met ongeveer 50 % van die dosis wat uitgeskei word in uriene en 50 % deur die gal.

INDIKASIES:
BIO GLIBENCLAMIDE 5 word aanvullend tot dieet aangedui, om die bloedglukosevlakke te verlaag by pasiënte met nie-insulien afhanklike (tipe II) diabetes mellitus, wie se hiperglisemie nie met dieet alleen beheer kan word nie.

KONTRAINDIKASIES:
Hipersensitiwiteit teenoor glibenklamied, of enige van die onaktiewe bestandele.
Diabetes mellitus gekompliseer deur koors, trauma of gangreen.
Pasiënte met ingekorte nier- of lewerfunksie, of ernstig ingekorte tiroïed of adrenale funksie.
Diabetes mellitus in pasiënte met 'n geskiedenis van metaboliese dekompensasie bv asidose, diabetiese pre-koma en koma.
Tipe 1 diabetes mellitus.
Swangerskap en Borsvoeding (sien SWANGERSKAP EN BORSVOEDING).

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Daar is aangemeld dat die mondelingse toediening van hipoglukemiese medikasie, geassosieer word met verhoogde kardiovaskulêre mortaliteit in vergelyking met behandeling wat slegs dieet of dieet plus insulien behels. Daar bestaan wel kontroversie rakende die interpretasie van hierdie bevindings.
Dosisaanpassings van BIO GLIBENCLAMIDE 5 mag nodig wees vir pasiënte wat ly aan herhalende infeksies, trauma, skok asook na narkose. Wanneer ernstige chirurgie onderneem gaan word, moet die gebruik van insulien behandeling vervang word met BIO GLIBENCLAMIDE 5.
'n Onverdraagsamheid teenoor alkoholgebruik, gekenmerk deur blosing, kan ook voorkom (sien INTERAKSIES).
Hipoglisemiese reaksies mag voorkom. Die gebeurlikheid van hipoglisemie kan verlaag word indien BIO GLIBENCLAMIDE 5 tydens, of direk na 'n maaltyd geneem word.
In die lig daarvan dat BIO GLIBENCLAMIDE 5 laktose bevat, word dit nie aanbeveel vir pasiënte met seldsame oorerflike probleme van galaktose onverdraagsaamheid, erge laktase tekort or glukose-galaktose wanabsorpsie nie.

INTERAKSIES:
Die risiko van hipoglisemie kan vererger, of verleng word, indien matig tot groot hoeveelhede alkohol tesame met BIO GLIBENCLAMIDE 5 ingeneem word (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).
Gelyktydige toediening van BIO GLIBENCLAMIDE 5 en antistolmiddels kan die antistollingsuitwerking en hipoglisemiese effekte van hierdie middels verhoog.
Asparaginase, kortikosteroïede, diuretikums (tiasied) en litium beskik intrinsiek oor 'n hiperglisemiese werking, beide in diabete sowel as nie-diabete. Dit mag dus nodig wees om die dosis van BIO GLIBENCLAMIDE 5 aan te pas gedurende, asook na behandeling.
Beta-adrenerge blokkeermiddels mag die hipoglisemiese werking van BIO GLIBENCLAMIDE 5 verlaag deur die inhibisie van insulien afskeiding, wysiging van koolhidraatmetabolisme, en 'n verhoging van perifere insulienweerstandigheid, wat dan lei tot hiperglisemie. Dit mag nodig wees om die dosis van BIO GLIBENCLAMIDE 5 aan te pas.
Mono-amienoksidase inhibitore, kinidien, kinien of groot dosisse salisilate beskik intrinsiek oor 'n hipoglisemiese werking, beide in diabetiese sowel as nie-diabetiese pasiënte. Dit mag nodig wees om 'n dosis vermindering te oorweeg indien dit gelyktydig met BIO GLIBENCLAMIDE 5 toegedien word.
Chlooramfenikol kan die metabolisme van BIO GLIBENCLAMIDE 5 verlaag, as gevolg van die inhibisie van hepatiese mikrosomale ensieme. Dosis aanpassings mag nodig wees, gedurende en na, gelyktydige gebruik.
'n Verlaagde hipoglisemiese effek, wat moontlik 'n verhoogde dosis BIO GLIBENCLAMIDE 5 noodsaak, is waargeneem of kan verwag word met die gebruik van epinifrien (adrenalien), aminoglutetimied, chloorpromasien, diasoksied, orale voorbehoedmiddels, rifamsien en skildklierhormone.
'n Verhoogde hipoglisemiese effek kan voorkom, of kan verwag word, met angiotensien-omsettingsensiem inhibitore, angiotensien reseptor blokkeerders, allopurinol, sommige analgetikum, azool-swamdoders, simetidien, klofibraat en verwante samestellings, fluorokinolone, heparien, oktreotiede, tetrasiklien en trisikliese antidepressante.
Propranolol kan die simptome van hipoglisemie versteek, en kan die liggaam se normale fisiologiese reaksie tot hipoglisemie inhibeer.
Die hipoglisemiese effek kan versterk word deur halofenaat, siklofosfamied, dicoumarol, fenielbutasoon en sulfoonamiede.

SWANGERSKAP EN BORSVOEDING:
Die gebruik van BIO GLIBENCLAMIDE 5 is teenaangedui gedurende swangerskap en borsvoeding (sien KONTRAINDIKASIES).
Die eerste tekens van swangerskap moet sonder oponthoud aan die dokter rapporteer word, aangesien 'n aanpassing van die insulien en/of dieetkundige behandeling nodig is.

DOSIS EN GEBRUIKSAANWYSINGS:
Die dosis moet aangepas word vir elke individuele pasient, en word bepaal deur die uitslae van mediese ondersoeke.
Oor die algemeen is die aanvangsdosis 2,5 mg daagliks ('n halwe BIO GLIBENCLAMIDE 5 tablet). Die daaglikse dosis kan daarna geleidelik verhoog word met halftablette, maar slegs nadat die mediese ondersoeke herhaal is. 'n Dosisverhoging van meer as drie tablette daagliks, sal nie 'n verhoogde reaksie oplewer nie.
Wanneer daar oorgeskakel word vanaf 'n ander mondelingse anti-diabetiese voorbereiding, met 'n soortgelyke werkingsmeganisme, word die dosis van BIO GLIBENCLAMIDE 5 bepaal deur die voorheen toegediende dosis asook mediese ondersoeke.
Dit kan aanvaar word dat die uitwerking van 1 g tolbutamied of glikodiasien, 0,5 g karbutamied of 250 mg chloorpropamied rofweg ooreenstem met dié van 5 mg BIO GLIBENCLAMIDE (1 tablet).
Tydens kombinasiebehandeling met 'n biguanied, mag daar 'n verhoogde risiko van kardiovaskulêre mortaliteit bestaan, as wanneer slegs 'n gliklasied alleenlik gebruik word.

NEWE EFFEKTE:
Hematologiese- en limfstelsel afwykings
*Dikwels:*Hipoglisemie (ligte, insluitend nagtelike hipoglisemie).
Minder dikwels: Bloedarmoede (aplastiese of hemolitiese), bloedsiektes (agranulositose, leukopenie, pansitopenie), eosinofilie, trombositopenie. Ernstige hipoglisemie wat lei tot konvulsies en koma.
Metaboliese en voedingsafwykings
Dikwels: Gewigstoename.
Vel en subkutaneweefsel afwykings
Minder dikwels: Veelvuldige eriteem of eksfoliatiewe dermatitits; fotosensitiwiteit.
Hepato-billiêre afwykings
Minder dikwels: Cholestase, cholestatiese geelsug, ingekorte lewerfunksie, hepatiese porfirie, hepatitis of porfirie cutanea tarda.
Algemene afwykings en toedieningsplek kondisies
Dikwels: Veranderinge in smaaksensasie, duiseligheid, lomerigheid, hoofpyn, swakheid, en parestesie.
Spysverteringskanaal afwykings
Dikwels: Spysverteringskanaal versteurings (hardlywigheid, diarree, winderigheid, sooibrand, verlaagde of verhoogde eetlus, naarheid, maag volheid, braking, epigastriese pyn).
Renale en urinêre afwykings
Dikwels: Poliurie.

BEKENDE SIMPTOME VAN OORDOSERING EN DIE BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Hipoglisemiese simptome, bv. oormatige sweet, lighoofdigheid, ens. Kan behandel word deur 'n glukoselading aan die pasient toe te dien.

IDENTIFIKASIE:
Wit, kapsuul-vormige tablette met 'n breeklyn aan beide kante.

AANBIEDING:
BIO GLIBENCLAMIDE 5 word verpak in:
- Polipropileen veiligheidshouers, bedek met nie-absorberende watte en verseël met 'n polipropileen deksel, of
- HDPE houers, bedek met nie-absorberende watte en verseël met 'n polipropileen skroefprop asook 'n induksieverseëling.
- Pasiënt gereed pak (PGP): Wit, onderuitgetige PE ritsluit sak, gedruk aan die voor en agterkant, met gate in die boonste kant.

Verpakkingsgroottes:
PP-sekuriteitshouers van HDPE is beskikbaar in verpakkinggroottes van 100 en 500 tablette.
PE-ritssluitings sakke (PGP's) is beskikbaar in verpakkinggroottes van 28, 56 of 84 tablette.
Al die verpakkingsgroottes word nie noodwendig op een slag bemark nie.

BERGINGSINSTRUKSIES:
Bewaar by of benede 25 °C.
Beskerm teen lig.
HOU BUITE DIE BEREIK VAN KINDERS

REGISTRASIENOMMER:
V/21.2/0345

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFKAAT:
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Grond Vloer, Blok K Wes, Central Park
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Suid Afrika

DATUM VAN PUBLIKASIE VAN DIE VOUBILJET:
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