190 mm

SCHEDULING STATUS: S3

PROPRIETARY NAME AND DOSAGE FORM
GLIBENCLAMIDE 5 OETHMAAN tablets

COMPOSITION
Each **GLIBENCLAMIDE 5 OETHMAAN** Tablet contains:
Glibenclamide ..... 5 mg
Contains sugar (lactose) ..... 79 mg
Excipients: Colloidal silicon dioxide, lactose, magnesium stearate, maize starch and purified talc.

CATEGORY AND CLASS
A 21.2 Oral hypoglycaemic

PHARMACOLOGICAL ACTION
Pharmacodynamic Properties
Glibenclamide is a sulphonylurea with hypoglycaemic effect.

INDICATIONS
Maturity onset diabetics (non-insulin dependent or Type II), who do not respond satisfactorily on dietary regime and exercise.

CONTRAINDICATIONS
Hypersensitivity to **GLIBENCLAMIDE 5 OETHMAAN** and other sulphonylureas.

Cross-sensitivity to other sulphonamide- or thiazide-type medications may also occur.

Chronic liver disease including that caused by uncompensated cardiac failure or alcoholism.

Metabolic decompensation with acidosis and ketosis.

Precomatose states and diabetic coma.

Renal or hepatic dysfunction. Insulin dependent diabetes mellitus.

Pregnancy and lactation (see "**HUMAN REPRODUCTION**").

GLIBENCLAMIDE 5 OETHMAAN is contra-indicated in diabetes mellitus complicated by fever, infection, febrile diseases, pancreatitis, burns, trauma or gangrene, serious impairment of thyroid function, adrenal function or other severe conditions where the sulphonylurea is unlikely to control the hyperglycaemia. Insulin should be administered in such patients.

Safety and efficacy for use in paediatrics has not been established due to the rarity of Type II diabetes mellitus in this age group.

WARNINGS AND SPECIAL PRECAUTIONS
The administration of **GLIBENCLAMIDE 5 OETHMAAN** may be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin.

Because of its long duration of action, elderly and debilitated patients are particularly susceptible to the hypoglycaemic effect of sulphonylureas. Care should be taken in such patients or **GLIBENCLAMIDE 5 OETHMAAN** avoided.

Special Precautions
In patients suffering from recurrent infections, trauma, shock or after anaesthesia, adjustment to the dosage of **GLIBENCLAMIDE 5 OETHMAAN** may be required. When major surgery is to be performed, **GLIBENCLAMIDE 5 OETHMAAN** should be substituted with insulin therapy.

Care is necessary during exercise as hypoglycaemia may be provoked.

The treatment of diabetes with **GLIBENCLAMIDE 5 OETHMAAN** requires regular follow-up checks. Strict adherence to diet and regularity in taking the tablets are essential to maintain physical efficiency and to prevent the blood glucose from becoming too high or too low.

Signs of excessive drop in blood glucose (hypoglycaemia) include intense hunger, sweating, tremor, restlessness, irritability, depression of mood, headache and disturbed sleep.

Signs of increased blood glucose (hyperglycaemia) include severe thirst, dryness of the mouth, frequent micturition and dry skin.

Effects on the ability to drive and use of machines
Until optimal control has been achieved, or when changing from one antidiabetic agent to another, or if the tablets have not been taken regularly, alertness and reaction time may be altered to such an extent that the patient cannot safely cope with road traffic or operate machinery.

Contains lactose
Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose- galactose malabsorption or fructose intolerance should not take **GLIBENCLAMIDE 5 OETHMAAN**. Lactose may have an effect on the glycaemic control of patients with diabetes mellitus.

INTERACTIONS
A disulfiram-like reaction may occur in patients taking alcohol during treatment with **GLIBENCLAMIDE 5 OETHMAAN**, and may increase the risk of hypoglycaemia.

The hypoglycaemic effects of **GLIBENCLAMIDE 5 OETHMAAN** may be enhanced by chloramphenicol, clofibrate or halofenate, cyclophosphamide, anticoagulants (coumarin or indandione derivative), dicoumarol, monoamine oxidase inhibitors, phenylbutazone, beta adrenergic blocking agents, some sulfonamides, salycilates in high doses, anabolic steroids, bezafibrate, biguanides, fenfluramine, fenyramidol, miconazole, high doses of parenteral pentoxifylline, phosphamides, ACE- inhibitors, fluoxetine, guanethidine, probenecid, reserpine, sulphinpyrazole, tritoqualine, theophylline, bromocriptine, pyridoxine, disopyramide, allopurinol, miconazole, fluconazole, cimetidine, ranitidine and tetracyclines.

The hypoglycaemic effects may be diminished by adrenaline, corticosteroids, diuretics, oestrogens, oestrogen-progestin- containing oral contraceptives, isoniazid, morphine, abuse of laxatives, high doses of nicotinates, phenothiazines, acetazolamide, clonidine, diazoxide, glucagon, phenytoin, saluretics, sympathomimetics, lithium, thyroid hormones, theophylline, calcium channel blockers and rifampicin.

Beta-adrenergic receptor blocking agents may mask symptoms of hypoglycaemia.

HUMAN REPRODUCTION
The use of **GLIBENCLAMIDE 5 OETHMAAN** tablets during pregnancy and lactation is contraindicated (see "**CONTRAINDICATIONS**").

First signs of pregnancy must be reported to the doctor without delay.

DOSAGE AND DIRECTIONS FOR USE
A reduction in dosage may be necessary in patients with renal dysfunction.

Initially half a tablet (2,5 mg) daily. The daily dose can be raised gradually in steps of half tablets up to a maximum of three tablets daily. The initial dose and the subsequent adjustments to the daily dosage should be determined by the results of medical and laboratory examinations. Doses greater than 10 mg may be given in two divided doses. Increasing the dose above 15 mg daily is unlikely to produce further benefit.

Important:
In combination therapy with either insulin or another diabetic agent, diabetic control should be checked by blood sugar readings, because of the possibility of hypoglycaemia. In combined therapy with a biguanide there may be a greater risk of cardiovascular mortality than with the use of **GLIBENCLAMIDE 5 OETHMAAN** alone.

SIDE EFFECTS
Metabolism and nutrition disorders:
More frequent:
Prolonged hypoglycaemia has been reported following the ingestion of **GLIBENCLAMIDE 5 OETHMAAN.**

The incidence of hypoglycaemia can be reduced if **GLIBENCLAMIDE 5 OETHMAAN** is taken with or immediately after a meal.

Weight gain may occur especially when **GLIBENCLAMIDE 5 OETHMAAN** is used in combination with insulin.

Renal and urinary disorders:
Less frequent:
GLIBENCLAMIDE 5 OETHMAAN is reported to exert a mild diuretic action although the syndrome of inappropriate ADH secretion (SIADH) has occurred in patients receiving **GLIBENCLAMIDE 5 OETHMAAN.**
Frequent:
Polyuria

Gastrointestinal disorders:
Frequent:
Mild effects include nausea, vomiting, heartburn and epigastric pain. Anorexia is usually dose dependent.

Skin and subcutaneous tissue disorders:
Frequent:
Photosensitivity has been reported.
Less frequent:
Skin rashes and pruritus may occur. Rashes are usually hypersensitivity reactions and may progress to more serious disorders. Other severe effects may be manifestations of hypersensitivity reactions. These include erythema multiforme exfoliative dermatitis, Stevens-Johnson syndrome and erythema nodosum.

Blood and lymphatic system disorders:
Less Frequent:
Other severe effects may be manifestations of hypersensitivity reactions. These include leucopenia, thrombocyto penia, aplastic anaemia, pancytopenia, eosinophilia, agranulocytosis and haemolytic anaemia.

Hepato-biliary disorders:
Less frequent:
Cholestatic jaundice and altered liver enzyme values may be a manifestation of hypersensitivity reaction. Other less frequent side effects include cholestatis, hepatic function impairment, hepatic porphyria, hepatitis or porphyria cutanea tarda.

Eye disorders:
Frequent:
Blurred vision

General disorders:
Dizziness, weakness, drowsiness, paraesthesia and a metallic taste, and are usually dose dependent. Intolerance to alcohol characterized by facial flushing may occur

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
Hypoglycaemic reactions such as excessive perspiration and light headedness.

To treat hypoglycaemia, dextrose or glucose should be taken at once with water and repeated in 10 to 15 minutes, if needed. If coma occurs, up to 50 ml of a 50 % solution of dextrose should be given intravenously, or dextrose or sucrose may be given by stomach tube.

Hypoglycaemia should be treated with urgency. Treatment is supportive and symptomatic.

The patient should be observed over 3 to 5 days in case hypoglycaemia recurs.

IDENTIFICATION
White to off-white, flat, oblong, bevel-edged tablet with breakline.

PRESENTATION
Blisters, securitainers, sealed aluminium bags or amber glass bottles of 28, 30, 56, 84 or 100 tablets.

Blisters, securitainers or amber glass bottles of 500 tablets.

STORAGE INSTRUCTIONS
Store well closed in a dry place at or below 25 °C and protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
T/21.2/150

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Oethmaan Biosims (PTY) Ltd.
207A Sherwood House
Greenacres Office Park
c/o Victory and Rustenburg Roads
Victory Park, Johannesburg, 2195

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION
Date of registration: 3 October 1988
Date of last approval by Council: 30 November 2007

I723002

280 mm

190 mm

SKEDULERINGSTATUS: S3

HANDELSNAAM EN DOSEERVORM:
GLIBENCLAMIDE 5 OETHMAAN (tablette)

SAMESTELLING:
Elke **GLIBENCLAMIDE 5 OETHMAAN** Tablet bevat:
Glibenklamied ..... 5 mg
Bevat suiker (laktose) ..... 79 mg
Onaktiewe bestanddele: Koloidale silicon dioksied, laktose, magnesium stearaaat, mieliestysel en gesuiwerde talk

FARMAKOLOGIESE KLASSIFIKASIE:
A 21.2 Hipoglukemieslukmiddels

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe
Glibenklamied is 'n sulfonielureum met 'n hipoglusemiese uitwerking.

INDIKASIES:
Volwasse aanvang diabete (nie-insulienafhanklike of Tipe II) wat nie voldoende gekontroleer kan word op dieët en oefening alleen nie.

KONTRA-INDIKASIES:
Hipersensitiwiteit teenoor **GLIBENCLAMIDE 5 OETHMAAN** en ander sulfonielureums. Kruissensitiwiteit teenoor ander sulfoonamied - of tiasiedtipe medisyne kan ook voorkom.

Chroniese lewersiektetoestande insluitende dié veroorsaak deur nie-gekompenseerde hartversaking of alkoholisme.
Metaboliese dekompensasie met asidose en ketose.
Prekomatose toestande en diabetiese koma.
Nier- of lewerwanfunksie.
Insulienafhanklike diabetes mellitus.
Swangerskap en laktasie (sien "**MENSLIKE VOORTPLANTING**").

GLIBENCLAMIDE 5 OETHMAAN is teenaangedui by diabetes mellitus wat gekompliseer word deur koors, infeksie, koorssiektes, pankreatitis, brandwonde, besering of gangreen, ernstige verswakking van die tiroïedwerking, bynierwerking of ander ernstige toestande waarin dit onwaarskynlik is dat die sulfonielureum die hipoglisemie sal beheer nie. Insulien moet aan sulke pasiënte gegee word.

Die veiligheid en effektiwiteit vir gebruik by pediatriese pasiënte is nie vasgestel nie vanweë die skaarsheid van Tipe II diabetes mellitus in hierdie ouderdomsgroep.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Die toediening van **GLIBENCLAMIDE 5 OETHMAAN** kan gepaard gaan met 'n toename in kardiovaskulêre mortaliteit in vergeleke met behandeling met slegs dieët of dieët plus insulien.

Vanweë die lang werkingsduur is bejaarde en verswakte pasiënte veral vatbaar vir die hipoglisemiese effek van sulfonielureums. Sorg moet gedra word by hierdie pasiënte of **GLIBENCLAMIDE 5 OETHMAAN** moet vermy word.

Spesiale Voorsorgmaatreëls
'n Aanpassing in die dosering van **GLIBENCLAMIDE 5 OETHMAAN** mag nodig wees by pasiënte wat aan terugkerende infeksies, trauma en skok ly of na narkose. Wanneer groot operasies uitgevoer moet word, moet **GLIBENCLAMIDE 5 OETHMAAN** met insulien behandeling vervang word.

Wees versigtig tydens oefening omdat hipoglisemie uitgelok kan word.

Die behandeling van diabetes met **GLIBENCLAMIDE 5 OETHMAAN** vereis gereelde opvolgondersoeke. Streng navolging van die dieët en gereelde inname van die tablette is noodsaaklik om fisiese effektiwiteit te behou en om te voorkom dat bloedglukosevlakke te hoog of te laag word.

Tekens van 'n oormatige afname in bloedglukose (hipoglusemie) sluit intense honger, sweet, bewerasie, rusteloosheid, irriteerbaarheid, depressie van stemming, hoofpyn en slaapversteurings in.

Tekens van verhoogde bloedglukose (hiperglisemie) sluit erge dors, droë mond, veelvuldige urinering en droë vel in.

Effek op die vermoë om motors te bestuur of masjinerie te gebruik
Totdat optimale beheer bereik is, of wanneer van een antidiabetikum na 'n ander oorgeskakel word, of as die tablette nie gereeld gebruik is nie, kan oplettendheid en reaksietyd tot so 'n mate aangetas wees dat die pasiënt padverkeer en masjinerie nie veilig kan hanteer nie.

Bevat laktose.
Pasiënte met die skaars oorerflike toestand van onverdraagbaarheid van galaktose, die Laplandse laktasetekort of wanabsorpsie van glukose/galaktose of met onverdraagbaarheid van fruktose, moet nie **GLIBENCLAMIDE 5 OETHMAAN** drink nie. Laktose mag 'n het effek op die glukemiese beheer in pasiënte wat aan diabetes mellitus lui.

INTERAKSIES:
'n Disulfiram-tipe reaksie kan voorkom by pasiënte wat gelyktydig alkohol inneem tydens behandeling met **GLIBENCLAMIDE 5 OETHMAAN** en kan die risiko vir hipoglukemie verhoog.

Die hipoglusemiese effekte van **GLIBENCLAMIDE 5 OETHMAAN** kan vergroot word deur chlooramfenikol, klofibraat of halofenaat, siklofosfamied, teenstolmiddels (kumarien of indandioon-derivate), dikoumarol, monoamienoksidaseremmers, fenielbutasoon, beta-adrenergiese blokkeermiddels, sommige sulfoonamiede, salisilate in hoë dosisse, anaboliese steroïede, besafibraat, biguaniede, fenfluramien, feniramidool, mikonasool, hoë parenterale dosisse van pentoksifillien, fosfamiede, AOE-remmers, fluoksetien, guanetidien, probenesied, reserpien, sulfienpirasool, tritokualien, teofillien, broomkriptien, piridoksien, disopiramied, allopurinol, mikonasool, flukonasool, simetidien, ranitidien en tetrasikliene.

Die hipoglusemiese effekte kan verminder word deur adrenalien, kortikosteroïede, diuretika, estrogene, estrogeen-progestienbevattende orale voorbehoedmiddels, isoniasied, morfien, misbruik van lakseermiddels, hoë dosissise nikotinate, fenotiasiene, asetasoolamied, klonidien, diasoksied, glukagoon, fenitoïen, saluretika, simpatomimetika, litium, tiroïedhormone, teofillien, kalsiumkanaalblokkeerders en rifampisien.

Beta-adrenerge reseptorblokkeermiddels kan simptome van hipoglukemie maskeer.

MENSLIKE VOORTPLANTING:
Die gebruik van **GLIBENCLAMIDE 5 OETHMAAN** tablette tydens swangerskap en laktasie word teenaangedui (sien "**KONTRA-INDIKASIES**").
Die eerste tekens van swangerskap moet sonder versuim aan die dokter gerapporteer word.

DOSIS EN GEBRUIKSAANWYSINGS:
'n Vermindering in dosis mag benodig wees in pasiente met nier disfunksie'
Aanvanklik 'n halwe tablet (2,5 mg) daagliks. Die daaglikse dosis kan geleidelik verhoog word teen 'n tempo van 'n halwe tablet totdat 'n maksimum van drie tablette daagliks bereik is. Die aanvangsdosis en die daaropvolgende dosisaanpassings behoort bepaal te word deur die uitslae van mediese- en laboratoriumtoetse. Dosisse groter as 10 mg kan as twee verdeelde dosisse gegee word. Dit is onwaarskynlik dat verhoging van die dosis bo 15 mg enige verdere voordele sal meebring.

Let wel:
By kombinasieterapie met insulien of 'n ander diabetiese middel, behoort diabetiese beheer gekontroleer te word deur bloedsuikerlesings omdat daar 'n moontlikheid van hipoglusemie is. By kombinasieterapie met 'n biguanied kan daar 'n groter risiko van kardiovaskulêre mortaliteit wees as met die gebruik van **GLIBENCLAMIDE 5 OETHMAAN** alleen.

NEWE-EFFEKTE:
Metabolisme en voedingsiektes:
Meer dikwels:
Langdurige hipoglukemie is al aangemeld na inname van **GLIBENCLAMIDE 5 OETHMAAN.**

Die insidensie van hipoglisemie kan verlaag word as **GLIBENCLAMIDE 5 OETHMAAN** saam of onmiddellik na 'n maaltyd geneem word. Gewigstoename kan voorkom, veral wanneer **GLIBENCLAMIDE 5 OETHMAAN** in kombinasie met insulien gebruik word.

Nier- en urienwegsiektes:
Minder dikwels:
Dit is gerapporteer dat **GLIBENCLAMIDE 5 OETHMAAN**'n geringe diuretiese effek uitoefen hoewel die sindroom van onvoldoende ADH-sekresie (SOADH) voorgekom het by pasiënte wat **GLIBENCLAMIDE 5 OETHMAAN** ontvang.
Dikwels:
Poliurie

Gastroïntestinale siektes:
Dikwels:
Ligte newe-effekte sluit naarheid, braking, sooibrand en epigastriese pyn. Anoreksie is gewoonlik dosisafhanklik.

Vel- en subkutane weefselsiektes:
Dikwels:
Fotosensitiwiteit is al gerapporteer.

Minder dikwels:
Veluitslae en pruritus kan voorkom. Uitslae is gewoonlik hipersensitiwiteits reaksies en kan in meer ernstige toestande ontwikkel. Ander ernstige effekte kan wees as gevolg van die manifestasies van 'n hipersensitiwiteits reaksie. Die toestande sluit veelvuldige eriteem, eksfoliatiewe dermatitis, Stevens-Johnson se sindroom en knobbelhuidrooiheid in.

Bloed- en limfstelselsiektes:
Minder dikwels:
Ander ernstige effekte kan wees as gevolg van die manifestasies van 'n hipersensitiwiteits reaksie. Die toestande sluit leukopenie, trombositopenie, aplastiese anemie, pansitopenie, eosinofilie, agranulositose en hemolitiese anemie.

Hepatobiliêre siektes:
Minder dikwels:
Cholestatiese geelsug en veranderde lewerensiemwaardes kan 'n manifestering wees van 'n hipersensitiwiteitsreaksie. Ander newe-effekte wat minder dikwels voorkom, sluit in cholestase, ingekorte lewerfunksie, hepatiese porfirie, hepatitis of cutanea-tarda-porfirie.

Oogsiektes:
Dikwels:
Dowwe visie.

Algemene siektes:
Duiseligheid, swakheid, lomerigheid, parestesie en 'n metaalsmaak, en is gewoonlik dosisafhanklik.

Onverdraagbaarheid vir alkohol, met kenmerkende gesigsgloede, kan voorkom.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Hipoglusemiese reaksies soos oormatige sweet en lighoofdigheid.

Om die hipoglusemie te behandel behoort dekstrose of glukose onmiddellik met water geneem te word en weer na 10 tot 15 minute, indien nodig, herhaal te word. Indien koma voorkom, moet tot 50 ml van 'n 50 % oplossing van dekstrose binneaars toegedien word, of dekstrose óf sukrose kan met 'n maagvoedingsbuis toegedien word.

Hipoglisemie moet dringend behandel word. Behandeling is simptomaties en ondersteunend.

Die pasiënt moet vir 3 tot 5 dae onder observasie gehou word in geval hipoglusemie weer voorkom.

IDENTIFIKASIE:
Wit tot naaswit, plat, langwerpige, afgeskuinste tablet met breeklyn.

AANBIEDINGE:
Stulpverpakkings, veiligheidshouers, verseëlde aluminiumsakkies of amber glashouers met 28, 30, 56, 84 of 100 tablette.
Stulpverpakkings, veiligheidshouers of amber glashouers met 500 tablette.

BERGINGSINSTRUKSIES:
Bewaar diggesluit in 'n droë plek teen of benede 25 °C en beskerm teen lig.
HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
T/21.2/150

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
Oethmaan Biosims (EDMS) Bpk.
207A Sherwood House
Greenacres Besigheidspark
h/v Victoryweg en Rustenburgweg
Victory Park, Johannesburg, 2195

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
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280 mm