SCHEDULING STATUS:
S5

PROPRIETARY NAME (AND DOSAGE FORM):
BIOTECH TRAZODONE 50 (capsules)
BIOTECH TRAZODONE 100 (capsules)

COMPOSITION:
BIOTECH TRAZODONE 50: Each capsule contains 50 mg trazodone hydrochloride as active ingredient and the following inactive ingredients: colloidal silica anhydrous, lactose monohydrate, magnesium stearate and a gelatine capsule shell containing the following colourants: erythrosine, indigo carmine, patent blue V, titanium dioxide and yellow iron oxide.
BIOTECH TRAZODONE 100: Each capsule contains 100 mg trazodone hydrochloride as active ingredient and the following inactive ingredients: colloidal silica anhydrous, lactose monohydrate, magnesium stearate and a gelatine capsule shell containing the following colourants: erythrosine, patent blue V, titanium dioxide and yellow iron oxide.
Contains Sugar (Lactose Monohydrate)

PHARMACOLOGICAL CLASSIFICATION:
A 1.2 Psychoanaleptics (antidepressants)

PHARMACOLOGICAL ACTION:
Trazodone is a triazolpyridine antidepressant also known as an atypical antidepressant. It weakly inhibits the reuptake of serotonin at presynaptic neurones and has an antagonistic action at 5-HT2A/2C receptors. It does not appear to have significant antimuscarinic properties but has a marked sedative effect.
Pharmacokinetics
Trazodone is readily absorbed from the gastrointestinal tract. Absorption is affected by food. Protein binding is high at about 89 to 95%. Trazodone is extensively metabolised in the liver to its active metabolite m-chlorophenylpiperazine via the cytochrome P450 isoenzyme CYP3A4.
Trazodone is mainly excreted in the urine, almost entirely in the form of its metabolites, either in free or in conjugated form, some is excreted via biliary elimination in the faeces.
The terminal elimination half-life of trazodone is 5 to 9 hours.

INDICATIONS:
BIOTECH TRAZODONE is indicated in the treatment of:
• Depression
• Mixed anxiety and depression

CONTRAINDICATIONS:
The concurrent administration with other psychotropic medicine should only be done with due recognition of the possibility of potentiation of the effects (refer to INTERACTIONS).
• Hypersensitivity to trazodone.
• Myocardial infarction during the acute recovery phase.
• Pregnancy and lactation.

WARNINGS:
BIOTECH TRAZODONE is not recommended for use in children.
BIOTECH TRAZODONE should be used with caution in patients with cardiovascular disorders, such as ischaemic heart disease and arrhythmias.
BIOTECH TRAZODONE should be used with caution in epilepsy. In general, antidepressants may antagonise the activity of antiepileptics by lowering the convulsive threshold (refer to INTERACTIONS).
BIOTECH TRAZODONE should be used with caution in patients with renal or severe hepatic impairment.
Suicide is an inherent risk in a depressed patient and patients should be closely monitored during early antidepressant therapy with BIOTECH TRAZODONE until significant improvement is observed.
The safe use of BIOTECH TRAZODONE in patients with porphyria has not been established.
Safety during pregnancy and lactation has not been established (refer to PREGNANCY AND LACTATION).

INTERACTIONS:
BIOTECH TRAZODONE may enhance the CNS depressant effects such as drowsiness, dry mouth, tachycardia, blurred vision and constipation of:
• Muscle relaxants
• Antidyskinetics
• Volatile anaesthetics
• Phenothiazines
• Sedatives
• Antidepressants
• Alcohol
• Antihistamines
• Barbiturates
• Pimozide
(Refer to SPECIAL PRECAUTIONS)
BIOTECH TRAZODONE may increase plasma concentrations of:
• Digoxin and resultant digoxin toxicity
• Phenytoin and possibly other hydantoin anticonvulsants
• Carbamazepine
In general, antidepressants may antagonise the activity of antiepileptics by lowering the convulsive threshold (refer to WARNINGS).
Concurrent administration with monoamine oxidase inhibitors (MAOIs) or within two weeks of stopping treatment with BIOTECH TRAZODONE is not recommended. The concurrent administration of BIOTECH TRAZODONE with tricyclic or related antidepressants and lithium may enhance neurotoxic side effects (refer to CONTRAINDICATIONS).
The concurrent use of BIOTECH TRAZODONE with amiodarone may increase the risk of ventricular arrhythmias.
Antihypertensives with CNS depressant effects such as clonidine may potentiate CNS depression when concurrently used with BIOTECH TRAZODONE and the dose of other antihypertensives may need to be reduced because BIOTECH TRAZODONE may increase the likelihood of hypotension.
The dose of warfarin may need to be increased when used with BIOTECH TRAZODONE.
BIOTECH TRAZODONE is metabolised by the cytochrome P450 isoenzyme CYP3A4 and inhibitors of this isoenzyme may limit the elimination of BIOTECH TRAZODONE. Therefore the dosage of BIOTECH TRAZODONE may need to be reduced when given with medicine known to be potent inhibitors of CYP3A4 such as the azole antifungals itraconazole and ketoconazole, and the HIV-protease inhibitors such as ritonavir.
Inducers of CYP3A4 such as carbamazepine may reduce the plasma concentration of BIOTECH TRAZODONE.

PREGNANCY AND LACTATION:
Safety during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:
The dosage of BIOTECH TRAZODONE must be individualised for each patient by titration and will depend on the diagnosis and severity of the condition as well as the individual patient's response. The daily dosage is usually administered as three divided doses.
BIOTECH TRAZODONE should be taken with food.
Adults:
For the treatment of depression:
The optimal dosage range is between 300 – 400 mg/day in three divided doses. A starting dose of 150 mg/day is suggested for the first week, gradually increasing it to 300 mg/day or higher depending on the clinical response (dosages of 600 mg/day have been reported).
For the treatment of mixed anxiety and depression:
A starting dose of 100 – 150 mg/day is recommended. When depression is the predominant symptom, an increased dose of 300 – 400 mg/day may be required to achieve a satisfactory response.
Withdrawal of BIOTECH TRAZODONE should be gradual. Abrupt discontinuation of the treatment should be avoided (refer to WARNINGS).
Elderly patients are more likely to experience the sedative and hypotensive effects of BIOTECH TRAZODONE and a lower initial dose is recommended with adjustments made as needed and tolerated. (refer to SPECIAL PRECAUTIONS).

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
Side-Effects
Blood and lymphatic system disorders
Frequency not known: Agranulocytosis, thrombocytopenia and anaemia.
Immune system disorders
Frequency not known: Allergic reaction.
Endocrine disorders
Hyponatraemia possibly due to inappropriate secretion of antidiuretic hormone has been associated with the use of BIOTECH TRAZODONE, particularly in the elderly.
Nervous system disorders
Frequent: Headache, dizziness, drowsiness.
Less frequent: Tremors, confusional states, weakness, unusual excitement.
Frequency not known: Decreased alertness, restlessness, irritability, insomnia, serotonin syndrome and convulsions (especially during concurrent use with other psychotropic medicine) (refer to CONTRAINDICATIONS).
Gastrointestinal disorders
Frequent: Nausea, vomiting, dry mouth and an unpleasant taste.
Less frequent: Constipation, diarrhoea.
Hepatobiliary disorders
Frequency not known: Jaundice and hepatocellular damage.
Musculoskeletal, connective tissue and bone disorders
Frequency not known: Arthralgia, weakness, muscle tremors.
General disorders
Frequency not known: Weight loss.
Cardiac disorders
Less frequent: Tachycardia, hypotension.
Eye disorders
Less frequent: Blurred vision.
Skin and subcutaneous tissue disorders
Less frequent: Skin rash.
Reproductive system disorders
Less frequent: Priapism
Special Precautions:
BIOTECH TRAZODONE should be administered with care in patients receiving barbiturates, muscle relaxants and volatile anaesthetics since it can potentiate the CNS depressant effects of these substances (refer to INTERACTIONS).
The risk-benefit should be considered when the following medical problems exist:
• Active alcoholism
• Cardiac disease, especially arrhythmias
• Hepatic function impairment
• Renal function impairment
The elderly are more prone to develop sedative and hypotensive effects with the use of BIOTECH TRAZODONE (refer to DOSAGE AND DIRECTIONS).
BIOTECH TRAZODONE therapy should be withdrawn gradually (refer to DOSAGE AND DIRECTIONS).
Effects on ability to drive and use machinery:
BIOTECH TRAZODONE can cause drowsiness, dizziness, light-headedness and hypotension. Patients affected should not be driving a motor vehicle or operate machinery.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Signs and symptoms of an overdosage may include drowsiness, loss of muscle coordination, nausea and vomiting, priapism, respiratory arrest, seizures and ECG changes.
No specific antidote is known. Gastric lavage might be useful. Treatment is symptomatic and supportive.

IDENTIFICATION:
BIOTECH TRAZODONE 50: Hard gelatine green-violet coloured capsule.
BIOTECH TRAZODONE 100: Hard gelatine yellow-violet coloured capsule.

PRESENTATION:
Clear PVC and silver aluminium foil blister strips each containing 10 capsules per strip. The strips are packed in an outer carton with 100 capsules each per carton.

STORAGE INSTRUCTIONS:
Store in a cool dry place at or below 25 °C and protect from light. Keep the capsules in the blister in the outer carton until required for use.
KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:
BIOTECH TRAZODONE 50: 43/1.2/0698
BIOTECH TRAZODONE 100: 43/1.2/0699

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 THIS PACKAGE INSERT:
Date of Registration: 10 April 2014
Date of latest revision of the text as approved by Council: 10 April 2014
Date of notification with regard to amended Reg. 9 and 10: 20 February 2015

Namibia:	
BIOTECH Trazodone 50 mg, Reg. No.: 16/1.2/0120	NS3
BIOTECH Trazodone 100 mg, Reg. No.: 16/1.2/0121	NS3

Zimbabwe:	
BIOTECH TRAZODONE 50 mg	
Reg. Nr.: 2017/13.2.1/5466	P.P.10
BIOTECH TRAZODONE 100 mg	
Reg. Nr.: 2017/13.2.1/5467	P.P.10

SKEDULERINGSTATUS:
S5

EIENDOMSNAAM (en doseervorm):
BIOTECH TRAZODONE 50 (kapsules)
BIOTECH TRAZODONE 100 (kapsules)

SAMESTELLING:
BIOTECH TRAZODONE 50: Elke kapsule bevat 50 mg trasodoon hidrochloried as aktiewe bestanddeel en bevat ook die volgende onaktiewe bestanddele: anhidriese kolloïdale silika, laktose monohidraat, magnesiumstearaat en 'n gelatien kapsuulomhulsel wat die volgende kleurstowwe bevat: eritrosien, indigo karmyn, gepatenteerde blou V, titaniumdioksied en geel ysteroksied.
BIOTECH TRAZODONE 100: Elke kapsule bevat 100 mg trasodoon hidrochloried as aktiewe bestanddeel en bevat ook die volgende onaktiewe bestanddele: anhidriese kolloïdale silika, laktose monohidraat, magnesiumstearaat en 'n gelatien kapsuulomhulsel wat die volgende kleurstowwe bevat: eritrosien, indigo karmyn, gepatenteerde blou V, titaniumdioksied en geel ysteroksied. Bevat Suiker (Laktose Monohidraat)

FARMAKOLOGIESE KLASSIFIKASIE:
A 1.2 Psigo-analeptikums (antidepressante)

FARMAKOLOGIESE WERKING:
Trasodoon is 'n triasoolpiridien antidepressant wat ook bekend staan as 'n atipiese antidepressant. Dit inhibeer die heropname van serotonien by presinaptiese neurone en het 'n antagonistiese werking op 5-HT2A/2C reseptore. Dit blyk nie om merkwaardige antimuskariniese eienskappe te toon nie, maar het wel 'n merkbare kalmerende effek.
Farmakokinetika
Trasodoon word maklik in die spysverteringskanaal geabsorbeer. Absorpsie word geaffekteer deur voedsel. Proteïen binding is hoog teen ongeveer 89 tot 95 %.
Trasodoon word aansienlik in die lewer gemetaboliseer tot die aktiewe metaboliet m-chlorofenielpiperasien, via die sitochroom P450 isoënsiem CYP3A4.
Trasodoon word hoofsaaklik deur die urine uitgeskei, byna geheel en al in die vorm van sy metaboliete, óf in 'n vrye- of in gekonjugeerde vorm. Sommige word fekaal uitgeskei deur bilière eliminasie.
Die terminale eliminasie halfleeftyd van trasodoon is 5 tot 9 ure.

INDIKASIES:
BIOTECH TRAZODONE word geïndikeer vir die behandeling van:
• Depressie
• Gemengde angstigheid en depressie

KONTRAÏNDIKASIES:
Die gelyktydige administrasie met ander psigotropiese medisyne moet slegs gedoen word met behoorlike in agneming van die moontlikheid van potensiëring van die effekte (verwys na die INTERAKSIES).
• Hipersensitiwiteit vir trasodoon.
• Miokardiale infarksie gedurende die akute herstellingsfase.
• Swangerskap en borsvoeding.

WAARSKUWINGS:
BIOTECH TRAZODONE word nie voorgestel vir die gebruik in kinders nie.
BIOTECH TRAZODONE moet versigtig gebruik word in pasiënte met kardiovaskulêre afwykings soos iskemiese hartsiektes en aritmie.
BIOTECH TRAZODONE moet versigtig gebruik word in pasiënte met epilepsie. Antidepressante kan in die algemeen die werking van antiepileptikums teëwerk deur die stuipdrumpel te verlaag (verwys na die INTERAKSIES).
BIOTECH TRAZODONE moet versigtig gebruik word in pasiënte met nierversaking of ernstige lewerinkorting.
Selfmoord is 'n inherente risiko in 'n depressiewe pasiënt en pasiënte moet noukeurig gemonitor word gedurende vroeë antidepressant terapie met BIOTECH TRAZODONE totdat noemenswaardige verbetering opgemerk word.
Die veilige gebruik van BIOTECH TRAZODONE in pasiënte met porfirie is nog nie vasgestel nie.
Die veilige gebruik gedurende swangerskap en borsvoeding is nog nie vasgestel nie (verwys na SWANGERSKAP EN BORSVOEDING).

INTERAKSIES:
BIOTECH TRAZODONE mag die SSS onderdrukkende effekte soos lomerigheid, droë mond, tagikardie, versteurde visie en konstipasie verhoog van die volgende medikasie:
• Spierverslappers
• Antidiskinetiese middels
• Onbestendige narkosemiddels
• Fenotiasines
• Verdowingsmiddels
• Antidepressante
• Alkohol
• Antihistamiene
• Barbituraat
• Pimozide
(Verwys na SPESIALE VOORSORGMAATREËLS)
BIOTECH TRAZODONE mag die plasma konsentrasies van die volgende verhoog:
• Digoksien en gevolglike digoksien toksisiteit
• Fenitoïen en moontlik ook ander hidantoïen epileptikums
• Karbamasepien
Antidepressante mag in die algemeen die aktiwiteit van antiepileptikums verswak deur die stuipdrumpel te verlaag (verwys na WAARSKUWINGS).
Die gesamentlike gebruik met monoamienoksidase inhibeerders (MAOIs) of gebruik daarvan binne twee weke nadat behandeling met BIOTECH TRAZODONE gestaak is, word nie aanbeveel nie. Die gebruik van BIOTECH TRAZODONE tesame met trisikliese of verwante anti-depressante en litium kan neurotoksiese newe-effekte verhoog (verwys na KONTRAÏNDIKASIES).
Die gebruik van BIOTECH TRAZODONE saam met amiodaroon mag die risiko van ventrikulêre aritmie verhoog.
Antihipertensiewe middels met SSS onderdrukkende effekte, soos klonidien, kan die werking van SSS onderdrukking versterk as dit saam met BIOTECH TRAZODONE gebruik word.
Die dosis van ander antihipertensiewe middels mag dalk verlaag word omdat BIOTECH TRAZODONE die potensiaal het om hipotensie te veroorsaak.
Dit mag nodig wees om die dosis van warfarien te verhoog wanneer dit saam met BIOTECH TRAZODONE gebruik word.
BIOTECH TRAZODONE word gemetaboliseer deur die sitochroom P450 isoënsiem CYP3A4 en inhibeerders van hierdie isoënsiem mag die verwydering van BIOTECH TRAZODONE beperk. Die dosis van BIOTECH TRAZODONE kan daarom verminder word as dit saam met medisyne geneem word wat bekende sterk inhibeerders van CYP3A4 te wees, soos die asool teenfungusmiddels itrakonasool, en ketokonasool, en ook die MIV-protease inhibeerders, soos ritonavir.
Induseerders van CYP3A4 soos karbamasepien mag die plasma konsentrasie van BIOTECH TRAZODONE verminder.

SWANGERSKAP EN BORSVOEDING:
Die veilige gebruik gedurende swangerskap en borsvoeding is nog nie vasgestel nie.

DOSERING EN GEBRUIKSAANWYSINGS:
Die dosis van BIOTECH TRAZODONE moet individueel aangepas word vir elke pasiënt deur middel van titrasie en sal afhang van die diagnose en die erns van die toestand sowel as die individuele pasiënt se reaksie daarop. Die daaglikse dosis word gewoonlik toegedien as drie verdeelde dosisse.
BIOTECH TRAZODONE moet saam met voedsel geneem word.
Volwassenes:
Vir die behandeling van depressie:
Die optimale dosis wissel tussen 300 – 400 mg/dag in drie verdeelde dosisse. 'n Begin-dosis van 150 mg/dag word voorgestel vir die eerste week, wat dan stelselmatig vermeerder word na 300 mg/dag of hoër afhangende van die kliniese reaksie (dosisse van 600 mg/dag is al aangemeld).
Vir die behandeling van gemengde angstigheid en depressie:
'n Begindosis van 100 – 150 mg/dag word aanbeveel. Indien depressie die dominante simptoom is, kan 'n verhoging in dosis van 300 – 400 mg/dag benodig word om die bevredigende reaksie te bereik.
Onttrekking van die gebruik van BIOTECH TRAZODONE moet geleidelik plaasvind.
Onmiddellike staking van die behandeling moet vermy word (verwys na WAARSKUWINGS).
'n Laer inisiële dosis word voorgestel in bejaarde pasiënte, met aanpassings wat gemaak word na aanleiding van toleransie en soos benodig, omdat bejaarde pasiënte meer geneig is om die kalmerende en bloeddruk verlagende effekte van BIOTECH TRAZODONE te ervaar (verwys na SPESIALE VOORSORGMAATREËLS).

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
Newe-effekte
Bloed en limfsisteem afwykings
Frekwensie onbekend: Agranulositose, trombositopenie en anemie.
Immuunsisteem afwykings
Frekwensie onbekend: Allergiese reaksie.
Endokriene stelsel afwykings
Hiponatremie, moontlik 'n gevolg van 'n onvanpaste afskeiding van antidiuretiese hormoon is al geassosieer met die gebruik van BIOTECH TRAZODONE, veral in bejaarde mense.
Sentrale senuweestelsel afwykings
Algemeen: Hoofpyn, duiseligheid, lomerigheid.
Minder algemeen: Bewerasies, verwarringstoestande, swakheid, ongewone opgewondenheid.
Frekwensie onbekend: Verminderde waaksaamheid, rusteloosheid, prikkelbaarheid, slapeloosheid, serotonien sindroom en konvulsies (veral gedurende die gelyktydige gebruik met ander psigotropiese medisyne) (Verwys na KONTRAÏNDIKASIES).
Gastrointestinale afwykings
Algemeen: Naarheid, braking, droë mond, en 'n onaangename smaak.
Minder algemeen: Hardlywigheid, diarree.
Lewer en gal afwykings
Frekwensie onbekend: Geelsug en lewersel skade.
Muskuloskeletale, bindweefsel en been afwykings
Frekwensie onbekend: Artralgie, swakheid, spierbewing.
Algemene afwykings
Frekwensie onbekend: Gewigsverlies.
Kardiale afwykings
Minder algemeen: Tagikardie, hipotensie.
Oog afwykings
Minder algemeen: Versteurde visie.
Vel en subkutaneweefsel afwykings
Minder algemeen: Veluitslag.
Voortplantingstelsel afwykings
Minder algemeen: Priapisme
Spesiale Voorsorgmaatreëls
BIOTECH TRAZODONE moet met sorg gegee word aan pasiënte wat barbituraat, spierverslappers en onbestendige narkosemiddels gebruik, aangesien dit die werking van die SSS onderdrukkende middels se effekte kan versterk (verwys na INTERAKSIES).
Die risiko-voordeel moet oorweeg word wanneer die volgende mediese probleme bestaan:
• Aktiewe alkoholisme
• Hartsiekte, veral aritmie
• Lewerfunksie inkorting
• Swak nierfunksie
Bejaardes is meer geneig om kalmerende en hipotensiewe effekte te ontwikkel met die gebruik van BIOTECH TRAZODONE (verwys na DOSERING EN GEBRUIKSAANWYSINGS).
Die behandeling met BIOTECH TRAZODONE moet stelselmatig onttrek word (verwys na DOSERING EN GEBRUIKSAANWYSINGS).
Uitwerking op die vermoë om te bestuur en masjinerie te gebruik:
BIOTECH TRAZODONE kan lomerigheid, duiseligheid, lighoofdigheid en hipotensie veroorsaak. Pasiënte wat deur die effekte geraak is moet nie 'n motorvoertuig bestuur of masjinerie hanteer nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Tekens en simptome van oordosering sluit in lomerigheid, verlies van spierkoördinasie, naarheid en braking, priapisme, respiratoriese probleme, konvulsies en EKG veranderinge.
Geen spesifieke teenmiddel is bekend nie.
Maagspoeling kan nuttig wees. Behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:
BIOTECH TRAZODONE 50: Harde, groen-pers gekleurde gelatien kapsule.
BIOTECH TRAZODONE 100: Harde, geel-pers gekleurde gelatien kapsule.

AANBIEDING:
Helder PVC en silwer aluminium foelie stulpstroke, elk met 10 kapsules per strook. Die stulpstroke word verpak in 'n buitenste karton houer met 100 kapsules per karton houer.

BERGINGAANWYSINGS:
Bewaar in 'n koel, droë plek teen of benede 25 °C en beskerm teen lig.
Hou die kapsules in die stulpstroke in die buitenste kartonhouer totdat benodig word vir gebruik.
HOU BUITE DIE BEREIK VAN KINDERS

REGISTRASIENOMMER:
BIOTECH TRAZODONE 50: 43/1.2/0698
BIOTECH TRAZODONE 100: 43/1.2/0699

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

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Datum van die jongste hersiening van die teks; soos deur die Raad goedgekeur:
10 April 2014
Datum van kennisgewing met betrekking tot gewysigde Regulasie 9 & 10:
20 February 2015

Namibië:	
BIOTECH Trazodone 50 mg, Reg. Nr.: 16/1.2/0120	NS3
BIOTECH Trazodone 100 mg, Reg. Nr.: 16/1.2/0121	NS3

Zimbabwe:	
BIOTECH TRAZODONE 50 mg	
Reg. Nr.: 2017/13.2.1/5466	P.P.10
BIOTECH TRAZODONE 100 mg	
Reg. Nr.: 2017/13.2.1/5467	P.P.10

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