SCHEDULING STATUS:
S4

PROPRIETARY NAME (and dosage form):
AZITHROMYCIN 500 BIOTECH (tablets)

COMPOSITION:
Each AZITHROMYCIN 500 BIOTECH tablet contains azithromycin dihydrate equivalent to 500 mg azithromycin base.
Inactive excipients: AZITHROMYCIN 500 BIOTECH contains microcrystalline cellulose, maize starch, sodium starch glycollate, silica colloidal anhydrous, magnesium stearate, sodium laurisulfate and film-coated with white Opadry® which contains lactose monohydrate, hypromellose, marcogol 4000, purified water and titanium dioxide.
Contains sugar: Lactose monohydrate 14.4 mg / tablet

PHARMACOLOGICAL CLASSIFICATION:
A.20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION:
AZITHROMYCIN 500 BIOTECH is widely distributed throughout the body following oral administration; bioavailability is approximately 37 %. No significant decrease in bio-availability was observed when azithromycin tablets were administered with food. The time taken to peak plasma levels is 2-3 hours. Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2 to 4 days. Kinetic studies of variable times ranging from hours to days after oral intake have shown markedly higher azithromycin levels in tissue than in plasma (up to 50 times the maximum observed concentration in plasma thus showing that the drug is highly bound in tissue).
After a single dose of 500 mg, concentrations in target tissue such as the lung, tonsil and prostate exceed the MIC90 for likely pathogens.
In vitro sensitivity does not necessarily imply *in vivo* efficacy. Azithromycin demonstrates activity *in vitro* against a wide range of Gram-positive and Gram-negative bacteria including:
Staphylococcus aureus; Streptococcus pneumoniae, Streptococcus pyogenes (Group A) and other *Streptococcus* species; *Haemophilus influenzae; Moraxella catarrhalis; Bordetella pertussis; Borrelia burgdorferi; Haemophilus ducreyi;* and *Chlamydia trachomatis*. Azithromycin also demonstrates *in vitro* activity against *Mycoplasma pneumoniae* and *Treponema pallidum*.

INDICATIONS:
Adults: AZITHROMYCIN 500 BIOTECH is indicated for mild to moderate infections caused by susceptible organisms; in lower respiratory tract infections including bronchitis due to *Haemophilus influenza, Moraxella catarrhalis, Streptococcus pneumoniae* or *Staphylococcus aureus* and pneumonia due to *Streptococcus pneumoniae* or *Haemophilus influenzae*; uncomplicated skin and soft tissue infections; sinusitis due to *Haemophilus influenzae, Streptococcus pneumoniae* or *Staphylococcus aureus*; and as an alternative to first line therapy of pharyngitis/tonsillitis. AZITHROMYCIN 500 BIOTECH is indicated in the treatment of uncomplicated genital infections due to *Chlamydia trachomatis*, in sexually transmitted diseases in men and women.
Children: 1 year and over AZITHROMYCIN 500 BIOTECH tablets are indicated for pharyngitis/ tonsillitis and otitis media caused by susceptible organisms in children over 45 kg. (AZITHROMYCIN suspension is recommended in children under 45 kg).

CONTRA-INDICATIONS:
AZITHROMYCIN 500 BIOTECH tablets is contra-indicated in patients with a known hypersensitivity to azithromycin, erythromycin or any of the macrolide antibiotics.
Because of the theoretical possibility of ergotism, AZITHROMYCIN 500 BIOTECH and ergot derivatives should not be co-administered.
Use in hepatic impairment:
AZITHROMYCIN 500 BIOTECH should not be used in patients with hepatic disease because the liver is the principal route of excretion of AZITHROMYCIN 500 BIOTECH.
Use during pregnancy and lactation:
The safety and efficacy of AZITHROMYCIN 500 BIOTECH in pregnancy and lactation have not been established.

WARNINGS:
Rare serious allergic reactions, including angioedema and anaphylaxis (rarely fatal), haven been reported. Some of these reactions with azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment.
Pseudomembranous colitis has been reported and may range in severity from mild to life threatening. Thus, it is important to consider this diagnosis in patients with diarrhoea before administration of AZITHROMYCIN 500 BIOTECH. Observation for signs of superinfection with non-susceptible organisms, including fungi, is recommended.
Use in renal impairment:
There are no data regarding AZITHROMYCIN 500 BIOTECH usage in patient with renal impairment, thus caution should be exercised when prescribing AZITHROMYCIN 500 BIOTECH in these patients.
Use in children under 1 year of age:
The safety and efficacy of AZITHROMYCIN 500 BIOTECH in children less than 1 year have not been established.

INTERACTIONS:
Ergot derivatives
AZITHROMYCIN 500 BIOTECH and ergot derivatives should not be co-administered because of the theoretical possibility of ergotism.
Special administration advised with the following:
Antacids
In patients receiving AZITHROMYCIN 500 BIOTECH and antacids, AZITHROMYCIN 500 BIOTECH should be taken at least 1 hour before or 2 hours after the antacid.
Cimetidine
A single dose of cimetidine administered 2 hours before AZITHROMYCIN 500 BIOTECH had no effect on the pharmacokinetics of azithromycin.
No interactions reported with the following:
Carbamazepine
No significant effect was observed on the plasma levels of carbamazepine or its active metabolite, in a pharmacokinetic interaction study in healthy volunteers.
Methylprednisolone
In a pharmacokinetic interaction study in healthy volunteers, AZITHROMYCIN 500 BIOTECH had no signification effect on the pharmacokinetics of methylprednisolone.
Theophylline
There is no evidence of any pharmacokinetic interaction when AZITHROMYCIN 500 BIOTECH and theophylline are co-administered to healthy volunteers.
Zidovudine
In a preliminary pharmacokinetic study of AZITHROMYCIN 500 BIOTECH in HIV-positive patients treated with zidovudine, no significant effect on the pharmacokinetic parameters of zidovudine and its glucuronide metabolite was found. The only significant difference in azithromycin kinetics was a shortening of the time to reach maximal concentration when the first and last day levels were compared.
Special precautionary monitoring is advised with the following:
Cyclosporin
Some of the related macrolide antibiotics interfere with the metabolism of cyclosporine. In the absence of pharmacokinetic studies or clinical data investigating potential interaction between AZITHROMYCIN 500 BIOTECH tablets and cyclosporine, caution should be exercised before co-administration of these two drugs. Cyclosporin levels should be monitored and the dose adjusted accordingly if co-administration is necessary.
Digoxin
Some of the macrolide antibiotics have been reported to impair the metabolism of digoxin (in the gut) in some patients. Therefore, in patients receiving concomitant AZITHROMYCIN 500 BIOTECH, a related azalide antibiotic, and digoxin the possibility of raised digoxin levels should be considered.
Warfarin
In a pharmacokinetic interaction study, azithromycin did not alter the anticoagulant effect of a single 15 mg dose of warfarin administered to healthy volunteers. AZITHROMYCIN 500 BIOTECH and warfarin may be co-administered but monitoring of the prothrombin time should be continued as routinely performed.
Terfenadine
There have been less frequent reports of an interaction in patients receiving azithromycin and terfenadine where the possibility of such an interaction could not entirely be excluded.

PREGNANCY AND LACTATION:
The safety and efficacy of AZITHROMYCIN 500 BIOTECH in pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE:
AZITHROMYCIN 500 BIOTECH should be administered as a single dose with or without food. AZITHROMYCIN 500 BIOTECH tablets should be taken whole.
Adults:
For all indications other than sexually transmitted diseases, the total dose is 1,5 g which should be given as 500 mg daily for 3 days.
For sexually transmitted diseases caused by chlamydia trachomatis the dose is 1g given as a single dose.
Use in the elderly:
Normal adult dosage is recommended.
Use in children:
Children over 45 kg – dose as per adults.
This formulation is not suitable for children under 45 kg.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
The majority of side-effects are gastrointestinal in origin with anorexia, nausea, abdominal discomfort (pain/cramps), flatulence, vomiting and diarrhoea less frequently resulting in dehydration, dyspepsia, constipation and loose stools.
There have been reports of hearing impairment including hearing loss, deafness and or tinnitus in some patients receiving AZITHROMYCIN 500 BIOTECH.
Interstitial nephritis and acute renal failure have been reported.
Cases of abnormal liver function including hepatitis and cholestatic jaundice have been reported.
Reductions in neutrophil counts have occasionally been observed.
The following side-effects have occurred: Chest pain, meleana, nephritis, vaginitis, headache, vertigo, dizziness, convulsions, somnolence and fatigue.
There have been rare reports of taste disturbances.
Palpitations and arrhythmias including ventricular tachycardia have been reported although a causal relationship to AZITHROMYCIN 500 BIOTECH has not been established.
Asthenia and parathesia have been reported although a causal relationship may not have been established.
Allergic reactions including arthralgia, oedema, urticarial, rash, photosensitivity, angioedema and anaphylaxis (less frequently fatal) have occurred – see WARNINGS. Less frequently, serious skin reactions including erythema multiforme, Stevens Johnson syndrome and toxic epidermal necrolysis, have occurred.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
There is no data on overdosage with AZITHROMYCIN 500 BIOTECH. Typical symptoms of overdosage with macrolide antibiotics include hearing loss, severe nausea, vomiting and diarrhoea. Gastric lavage and general supportive measures are indicated.

IDENTIFICATION:
White to off-white capsule shaped film coated tablet with a breakline notch on one side and other side is plain.

PRESENTATION:
AZITHROMYCIN 500 BIOTECH tablets are packed into white, opaque PVC/ Aluminium blisters of 2, 3 or 10 tablets each. All pack sizes may not necessarily be marketed at one time.

STORAGE INSTRUCTIONS:
Store at or below 25 °C.
Do not remove the blisters form the outer carton until required for use.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:
AZITHROMYCIN 500 BIOTECH: A39/20.1.1/0382

NAME AND BUSINESS ADDRESS OF THE HOLDER OF CERTIFICATE OF REGISTRATION:
Biotech Laboratories (Pty) Ltd.
Ground Floor, Block K West, Central Park
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DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION:
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SKEDULERINGSTATUS:
S4

HANDELSNAAM (en doseervorm):
AZITHROMYCIN 500 BIOTECH (tablette)

SAMESTELLING:
Elke AZITHROMYCIN 500 BIOTECH-tablet bevat asitromisiendihidraat gelykstaande aan 500 mg asitromisien-basis.
Onaktiewe hulpstowwe: AZITHROMYCIN 500 BIOTECH bevat mikrokristallyne sellulose, mieliestysel, natriumstyselglikollaat, watervrye kolloïdale silika, magnesiumstearaat, natriumlourielsulfaat en is filmbedek met wit Opadry® wat laktosemonohidraat, hypromellose, makrogol 4000, gesuiwerde water en titaandioksied bevat.
Bevat suiker: Laktosemonohidraat, 14.4 mg / tablet

FARMAKOLOGIESE KLASSIFIKASIE:
A.20.1.1 Breë- en mediumspektrum antibiotika

FARMAKOLOGIESE WERKING:
AZITHROMYCIN 500 BIOTECH word na orale toediening wyd versprei; biobeskikbaarheid is ongeveer 37%. Geen betekenisvolle afname in biobeskikbaarheid is waargeneem toe asitromisientablette saam met voedsel toegedien is nie. Die tyd tot piek vlakke in die plasma is 2-3 uur. Die terminale eliminasiehalfleeftyd uit plasma weerspieël die halfleeftyd van uitputting uit die weefsel van 2 tot 4 dae noukeurig. Kinetiese studies van wisselende tye, wat wissel van ure tot dae na orale inname, het 'n aansienlike hoër asitromisienvlak in weefsel getoon as in plasma (tot 50 keer die maksimum waargenome konsentrasie in plasma) wat daarop dui dat die middel sterk in die weefsel gebind is.
Na 'n enkele dosis van 500 mg oorskry konsentrasies in die teikenweefsel soos die longe, mangels en prostaat die MIC90 vir waarskynlike patogene.
In vitro-gevoeligheid impliseer nie noodwendig *in vivo*-doeltreffendheid nie. Asitromisien het *in vitro* aktiwiteit teen 'n wye verskeidenheid Gram-positiewe en Gram-negatiewe bakterieë, waaronder:
Staphylococcus aureus; Streptococcus pneumoniae, Streptococcus pyogenes (Groep A) en ander *Streptococcus*-spesies; *Haemophilus influenzae; Moraxella catarrhalis; Bordetella pertussis; Borrelia burgdorferi; Haemophilus ducreyi* en *Chlamydia trachomatis*. Asitromisien toon ook *in vitro*-aktiwiteit teen *Mycoplasma pneumoniae* en *Treponema pallidum*.

INDIKASIES:
Volwassenes: AZITHROMYCIN 500 BIOTECH is aangedui vir ligte tot matige infeksies wat deur vatbare organismes veroorsaak word; vir infeksies van die onderste lugweë waaronder brongitis as gevolg van *Haemophilus influenza, Moraxella catarrhalis, Streptococcus pneumoniae* of *Staphylococcus aureus* en longontsteking vanweë *Streptococcus pneumoniae* of *Haemophilus influenzae*; ongekompliseerde vel- en sagteweefselinfeksies; sinusitis vanweë *Haemophilus influenzae, Streptococcus pneumoniae* of *Staphylococcus aureus* en as alternatief vir eerstelinieterapie van faringitis/tonsillitis. AZITHROMYCIN 500 BIOTECH is aangedui vir die behandeling van ongekompliseerde genitale infeksies as gevolg van *Chlamydia trachomatis* en vir seksueel oordraagbare siektes in mans en vroue.
Kinders van 1 jaar en ouer: AZITHROMYCIN 500 BIOTECH-tablette is aangedui vir faringitis/tonsillitis en otitis media veroorsaak deur vatbare organismes in kinders swaarder as 45 kg. (Azithromycin suspensie word aanbeveel vir kinders onder 45 kg).

KONTRA-INDIKASIES:
AZITHROMYCIN 500 BIOTECH-tablette is teenaangedui vir pasiënte met 'n bekende hipersensitiwiteit vir asitromisien, eritromisien of enige van die makroliedantibiotika.
Vanweë die teoretiese moontlikheid van ergotisme, moet AZITHROMYCIN 500 BIOTECH en ergotderivate nie saam toegedien word nie.
Gebruik met swak lewerfunksie:
AZITHROMYCIN 500 BIOTECH moet nie deur pasiënte met lewersiekte gebruik word nie, omdat die lewer die belangrikste uitskeidingsweg van AZITHROMYCIN 500 BIOTECH is.
Gebruik tydens swangerskap en borsvoeding:
Die veiligheid en effektiwiteit van AZITHROMYCIN 500 BIOTECH tydens swangerskap en borsvoeding is nie bepaal nie.

WAARSKUWINGS:
Skaars ernstige allergiese reaksies, waaronder angio-edeem en anafilakse (selde dodelik), is aangemeld. Sommige van hierdie reaksies met asitromisien het tot herhalende simptome gelei en 'n langer tydperk van waarneming en behandeling was nodig.
Pseudomembraankolitis is aangemeld en kan in graad wissel van lig tot lewensbedreigend. Dit is dus belangrik om hierdie diagnose in gedagte te hou vir pasiënte wat na toediening van AZITHROMYCIN 500 BIOTECH diarree ontwikkel. Dit word aanbeveel dat daar opgelet word vir tekens van superinfeksie deur nie-vatbare organismes, swamme onderandere.
Gebruik met swak nierfunksie:
Daar is geen gegewens rakende die gebruik van AZITHROMYCIN 500 BIOTECH deur pasiënte met swak nierfunksie nie, en daarom moet AZITHROMYCIN 500 BIOTECH versigtig aan hierdie pasiënte voorgeskryf word.
Gebruik deur kinders van jonger as 1 jaar:
Die veiligheid en effektiwiteit van AZITHROMYCIN 500 BIOTECH vir kinders van jonger as 1 jaar is nie bepaal nie.

INTERAKSIES:
Ergotderivate
AZITHROMYCIN 500 BIOTECH en ergotderivate moet nie saam toegedien word nie vanweë die teoretiese moontlikheid van ergotisme.
Spesiale toediening word met die volgende aanbeveel:
Teensuurmiddels
Pasiënte wat AZITHROMYCIN 500 BIOTECH en teensuurmiddels saam ontvang, moet AZITHROMYCIN 500 BIOTECH minstens 1 uur voor of 2 uur na die teensuurmiddel drink.
Simetidien
'n Enkele dosis simetidien wat 2 uur voor AZITHROMYCIN 500 BIOTECH toegedien is, het geen effek op die farmakokinetika van asitromisien gehad nie.
Geen interaksies is met die volgende aangemeld nie:
Karbamasepien
Geen noemenswaardige effek op die plasmavlakke van karbamasepien of die aktiewe metaboliet daarvan is in 'n farmakokinetiese interaksiestudie met gesonde vrywilligers waargeneem nie.
Metielprednisoloon
In 'n farmakokinetiese interaksiestudie met gesonde vrywilligers, het AZITHROMYCIN 500 BIOTECH geen betekenisvolle effek op die farmakokinetika van metielprednisoloon gehad nie.
Teofillien
Daar is geen bewyse van enige farmakokinetiese interaksie as AZITHROMYCIN 500 BIOTECH en teofillien saam aan gesonde vrywilligers gegee word nie.
Sidovudien
In 'n voorlopige farmakokinetiese studie van AZITHROMYCIN 500 BIOTECH aan MIV-positiewe pasiënte wat met sidovudien behandel is, is geen betekenisvolle effek op die farmakokinetiese parameters van sidovudien en die glukuroniedmetaboliet daarvan gevind nie. Die enigste beduidende verskil in die kinetika van asitromisien was die verkorting van die tyd om maksimum konsentrasie te bereik as die vlakke op die eerste en die laaste dae vergelyk word.
Spesiale voorkomende monitering word met die volgende aanbeveel:
Siklosporien
Sommige van die verwante makroliedantibiotika beïnvloed die metabolisme van siklosporien. In die afwesigheid van farmakokinetiese studies of kliniese gegewens wat die moontlike interaksie tussen AZITHROMYCIN 500 BIOTECH-tablette en siklosporien ondersoek het, moet daar versigtig opgetree word voordat hierdie twee middels saam toegedien word. Siklosporienvlakke moet gemonitor word en die dosis dienooreenkomstig aangepas word indien gesamentlike toediening nodig is.
Digoksien
Dit is gemeld dat sommige antibiotika die metabolisme van digoksien in sommige pasiënte (in die ingewande) benadeel. Daarom moet die moontlikheid van verhoogde digoksienvlakke in ag geneem word in pasiënte wat AZITHROMYCIN 500 BIOTECH, 'n verwante asaliedantibiotikum, en digoksien saam ontvang.
Warfarien
In 'n studie van farmakokinetiese interaksie het asitromisien nie die antikoagulerende effek van 'n enkele dosis warfarien aan gesonde vrywilligers verander nie. AZITHROMYCIN 500 BIOTECH en warfarien kan gelyktydig toegedien word, maar kontrole van die protrombientyd moet steeds roetinegewys voortgesit word.
Terfenadien
Daar was soms verslae van 'n interaksie in pasiënte wat asitromisien en terfenadien saam ontvang het, waar die moontlikheid van so 'n interaksie nie heeltemal uitgesluit kon word nie.

SWANGERSKAP EN BORSVOEDING:
Die veiligheid en effektiwiteit van AZITHROMYCIN 500 BIOTECH tydens swangerskap en borsvoeding is nie bepaal nie.

DOSIS EN GEBRUIKSAANWYSINGS:
AZITHROMYCIN 500 BIOTECH moet as 'n enkele daaglikse dosis met of sonder voedsel gegee word.
AZITHROMYCIN 500 BIOTECH-tablette moet heel gedrink word.
Volwassenes:
Vir alle indikasies, behalwe seksueel oordraagbare siektes, is die totale dosis 1,5 g wat as 500 mg per dag vir 3 dae gegee word.
Vir seksueel oordraagbare siektes wat deur chlamydia trachomatis veroorsaak word, word die 1 g dosis as 'n enkele dosis gegee.
Gebruik deur bejaardes:
Die gewone volwasse dosis word aanbeveel.
Gebruik vir kinders:
Kinders meer as 45 kg - dosis soos vir volwassenes.
Hierdie formulering is nie geskik vir kinders ligter as 45 kg nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:
Die meeste newe-effekte is gastro-intestinaal van aard met anoreksie, naarheid, ongemak in die buik (pyn/krampe), winderigheid, braking en diarree, wat soms dehidrasie, slegte spysvertering, hardlywigheid en los stoelgang veroorsaak.
Daar was verslae of gehoorgestremdheid, waaronder gehoorverlies, doofheid en of tinnitus in sommige pasiënte wat AZITHROMYCIN 500 BIOTECH ontvang het.
Interstisiële nefritis en akute nierversaking is aangemeld.
Gevalle van abnormale lewerfunksie, waaronder hepatitis en cholestatiese geelsug, is aangemeld.
Daling in neutrofieltelling is af en toe waargeneem.
Die volgende newe-effekte het voorgekom: Borspyn, melena, nefritis, vaginitis, hoofpyn, vertigo,
duiseligheid, stuiptrekkings, lomerigheid en moegheid.
Daar was enkele verslae van smaakversteurings.
Hartkloppings en aritmie, waaronder ventrikulêre tagikardie, is aangemeld, hoewel daar nie 'n oorsaaklike verband met AZITHROMYCIN 500 BIOTECH is nie.
Astenie en parestesie is aangemeld, hoewel daar waarskynlik nie 'n oorsaaklike verband bestaan nie.
Allergiese reaksies, waaronder artralgie, edeem, urtikarie, veluitslag, fotosensitiwiteit, angio-edeem en anafilakse (selde dodelik), het voorgekom - kyk WAARSKUWINGS. Ernstige velreaksies, waaronder meervoudige eriteem, Stevens-Johnsonsindroom en toksiese epidermale nekrolise, het soms voorgekom.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Daar is geen data van oordosering met AZITHROMYCIN 500 BIOTECH nie. Tipiese simptome van oordosering met makroliedantibiotika is onder meer gehoorverlies, erge naarheid, braking en diarree. Maagspoeling en algemene ondersteunende maatreëls is aangedui.

IDENTIFIKASIE:
Wit tot naas-wit, kapsuulvormige filmbedekte tablet, met breeklyn aan een kant en ander kant glad.

AANBIEDING:
AZITHROMYCIN 500 BIOTECH is verpak in wit ondeursigtige stulpblaaie van PVC/aluminium wat in 2, 3 en 10 tablette bevat. Alle verpakkings groottes mag nie noodwendig op een slag bemark word nie.

BEWARINGSINSTRUKSIES:
Bewaar teen of benede 25 °C. Moenie die stulpblaaie uit die karton verwyder voordat dit benodig word nie.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
AZITHROMYCIN 500 BIOTECH: A39/20.1.1/0382

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
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Suid Afrika

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