Pharmacode position may change as per Supplier’s m/c requirement & additional small pharma code may appear on the front / back panel

APPROVED

ZATYP TABLETS
P1525981

ZATYP TABLETS
P1525981

SKEDULERINGSTATUS

S4

1. NAAM VAN DIE MEDISYNE

ZATYP TABLETS 500 mg filmbedekte tablette

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

ZATYP TABLETS 500 mg filmbedekte tablette
Elke filmbedekte tablet bevat asitromisiendihidraat Ph.Eur 500 mg
Bevat suiker (15,4 mg laktosemonohidraat).
Raadpleeg afdeling 6.1 vir die volledige lys hulpstowwe.

3. FARMASEUTIESE VORM

ZATYP TABLETS 500 mg filmbedekte tablette
Wit tot afwit, ovaalvormige filmbedekte bikonvekse tablette, met “6” & “7” weerskante van die breeklyn op die een kant en “D” op die ander kant gedruk.

4. KLINIESE BESONDERHEDE

4.1. Terapeutiese indikasies

Volwassenes
ZATYP TABLETS is aangedui vir ligte tot matige infeksies wat deur vatbare organismes veroorsaak word; vir infeksies van die onderste lugweë waaronder brongitis vanweë *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.
Vir seksueel oordraagbare siektes in mans en vroue is **ZATYP TABLETS** aangedui vir die behandeling van ongekompliseerde infeksies in die genitalieë vanweë *Chlamydia trachomatis* en sjankroïed as gevolg van *Haemophilus ducreyi.*
Kinders van 1 jaar en ouer: **ZATYP TABLETS** is aangedui vir faringitis/tonsillitis en otitis media veroorsaak deur vatbare organismes in kinders swaarder as 45 kg.

4.2. Dosis en metode van toediening

ZATYP TABLETS moet as ’n enkele daaglikse dosis met of sonder voedsel gegee word.
ZATYP TABLETS moet heel afgesluk word.

Volwassenes
Vir alle indikasies, behalwe seksueel oordraagbare siektes, is die totale dosis 1,5 g wat as 500 mg per dag vir drie dae gegee word.
Vir seksueel oordraagbare siektes veroorsaak word deur *Chlamydia trachomatis* of *Haemophilus ducreyi*, die dosis is 1 g gegee as ’n enkele dosis.

Spesiale populasies
Gebruik deur pasiënte met swak lewerfunksie
ZATYP TABLETS is teenaangedui vir pasiënte met erge swak lewerfunksie (kyk afdeling 4.3).

Gebruik deur bejaardes
Die gewone volwasse dosis word aanbeveel. Bejaarde pasiënte kan meer vatbaar wees vir die ontwikkeling van Torsade de Pointes-ritmeversteuring as jonger pasiënte (kyk afdeling 4.4).

Gebruik deur kinders
Kinders swaarder as 45 kg: dosis soos vir volwassenes.
Hierdie formulering is nie geskik vir kinders ligter as 45 kg nie.

Metode van toediening
Oraal

4.3. Kontra-indikasies

ZATYP TABLETS is teenaangedui vir pasiënte met ’n bekende hipersensitiwiteit vir asitromisien, eritromisien of enige van die makroliedantibiotika, of vir enige van die hulpstowwe genoem in afdeling 6.1.
Vanweë die teoretiese moontlikheid vir ergotisme, moet **ZATYP TABLETS** en ergotderivate nie saam toegedien word nie.

Gebruik met swak lewerfunksie:
Aangesien die lewer die belangrikste uitskeidingsweg van **ZATYP TABLETS** is, moet dit nie deur pasiënte met lewersiektes gebruik word nie.

4.4. Spesiale waarskuwings en voorsorgmaatreëls tydens gebruik

Hipersensitiwiteit
Ernstige allergiese reaksies, waaronder angio-edeem, anafilakse, en dermatologiese reaksies, waaronder die Stevens-Johnsonsindroom, Akute Algemene Eksantemiese Pustulose (AAEP), Geneesmiddelreaksie met Eosinofilie en Sistemiese Simptome (GRESS) en toksiese epidermale nekrolise is aangemeld. Sommige van hierdie reaksies met **ZATYP TABLETS** het tot herhaling van simptome gelei en ’n langer tydperk van waarneming en behandeling was nodig.
As ’n allergiese reaksie voorkom, moet **ZATYP TABLETS** gestaak en geskikte behandeling gegee word. Mediese praktisyns moet daarop let dat allergiese simptome weer kan voorkom wanneer die simptomatiese behandeling gestaak word.

Hepatotoksisiteit
Aangesien die lewer is die belangrikste roete van uitskeiding van asitromisien is, moet **ZATYP TABLETS** nie gebruik word deur pasiënte met ’n lewersiekte nie (kyk afdeling 4.3).
Abnormale lewerfunksie, hepatitis, cholestatiese geelsug, lewernekrose en lewerversaking, waarvan sommige sterftes veroorsaak het, is aangemeld. Staak **ZATYP TABLETS** onmiddellik indien tekens en/of simptome van hepatitis voorkom.

Ergotderivate
In pasiënte wat ergotderivate ontvang het, is ergotisme aangebring deur gelyktydige toediening van sekere makroliedantibiotika. Daar is geen data oor die moontlikheid van ’n interaksie tussen ergot en **ZATYP TABLETS** nie. Vanweë die teoretiese moontlikheid vir ergotisme, moet **ZATYP TABLETS** en ergotderivate nie saam toegedien word nie (kyk afdeling 4.3).

Superinfeksie
Dit word aanbeveel dat daar opgelet word vir tekens van superinfeksie deur nie-vatbare organismes, waaronder swamme.

Pseudomembraankolitis
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 diarree ontwikkel na toediening van **ZATYP TABLETS**.

Diarree vanweë *Clostridium difficile*
Diarree Vanweë *Clostridium difficile* (DVCD) as gevolg van oorgroei van *Clostridium difficile* in die ingewande, is met die gebruik van **ZATYP TABLETS** aangemeld, en dit kan in erns wissel van ligte diarree tot dodelike kolitis.
As DVCD vermoed word of bevestig is, moet gebruik van **ZATYP TABLETS** gestaak word. Toepaslike beheer van vloeistof- en elektrolietbalans, proteïenaanvulling, behandeling van *Clostridium difficile* met antibiotika en chirurgiese evaluering moet indien klinies aangedui gedoen word.

Swak nierfunksie
In pasiënte met kreatinienopruiming < 30 mL/min is ’n toename van 33 % in sistemiese blootstelling aan **ZATYP TABLETS** waargeneem (kyk afdeling 5.2). Akute nierversaking en interstisiële nefritis is aangemeld (kyk afdeling 4.8).

Verlenging van die QT-interval
Langer duur vir repolarisasie van die hart en QT-interval wat ’n risiko vir die ontwikkeling van hartdisritmie en Torsades de Pointes inhou, is tydens behandeling met ander makroliede, waaronder **ZATYP TABLETS**, waargeneem (sien afdeling 4.8).
Voorskrywers moet spesifiek die risiko vir QT-verlenging in gedagte hou, wat dodelik kan wees in risikogroepe, waaronder:

- Pasiënte met aangebore of gedokumenteerde QT-verlenging
- Pasiënte wat tans behandel word met ander aktiewe stowwe wat bekend is dat hulle die QT-interval verleng, soos antidisritmika van klasse IA en III, antipsigotiese middels, antidepressante en fluoorkinolone
- Pasiënte met elektrolietversteuring, veral in gevalle van hipokalemie en hipomagnesemie
- Pasiënte met klinies relevante bradikardie, hartritmestoornis of swak hartfunksie
- Bejaarde pasiënte: bejaarde pasiënte is meer vatbaar vir medisyne-verwante effekte op die QT-interval
- Myasthenia gravis

Verergering van simptome van myasthenia gravis en die aanvang van die miastenie-sindroom is aangemeld in pasiënte wat asitromisien ontvang het.

Gebruik deur kinders van jonger as 1 jaar
Die veiligheid en effektiwiteit van **ZATYP TABLETS** vir kinders jonger as 1 jaar is nie bepaal nie.

Laktose-onverdraagbaarheid
Pasiënte met die skaars oorerflike probleem van onverdraagbaarheid van galaktose, totale laktasetekort of wanabsorpsie van glukose/galaktose, moet nie hierdie medisyne gebruik nie.
Dit bevat laktose wat ’n effek op die glisemiese beheer in pasiënte met diabetes mellitus kan hê.

4.5. Interaksies met ander medisyne en ander vorms van interaksie

Ergotderivate
Vanweë die teoretiese moontlikheid vir ergotisme, moet **ZATYP TABLETS** en ergotderivate nie saam toegedien word nie (kyk afdeling 4.3 en afdeling 4.4).

Setirisien
In gesonde vrywilligers het toediening van ’n 5-dag-regimen van asitromisien saam met 20 mg setirisien by gelykvlakke tot geen farmakokinetiese interaksie en geen beduidende veranderinge in die QT-interval veroorsaak nie.
Asitromisien het nie ’n beduidende interaksie met die hepatiese sitochroom P450-stelsel nie. Daar word nie geglo dat dit verband hou met die farmakokinetiese medisyne-interaksies wat met eritromisien voorkom nie. Induksie of inaktivering van hepatiese sitochroom P450 via sitochroom-metabolietkompleks kom nie met asitromisien voor nie.

Farmakokinetiese studies is gedoen met asitromisien en die volgende middels bekend daarvoor dat hulle beduidende P450 bemiddelde metabolisme ondergaan:
Atorvastatien
Gelyktydige toediening van atorvastatien (10 mg daagliks) en asitromisien (500 mg daagliks) het nie die plasmakonsentrasies van atorvastatien verander nie (gebaseer op ’n bepaling van HMG-KoA-reduktase-remming). Daar was egter na bemarking gevalle van rabdomiolise in pasiënte wat asitromisien saam met statiene ontvang het.

Efavirens
Toediening van ’n enkele dosis van 600 mg asitromisien saam 400 mg efavirens per dag vir 7 dae het geen klinies beduidende farmakokinetiese interaksies tot gevolg gehad nie.

Flukonasool
Gelyktydige toediening van ’n enkele dosis van 1 200 mg **ZATYP TABLETS** het nie die farmakokinetika van ’n enkele dosis van 800 mg flukonasool verander nie. Die totale blootstelling en halfleeftyd van **ZATYP TABLETS** was onveranderd na die toediening van flukonasool, maar ’n klinies onbeduidende afname in C_{maks} (18 %) van **ZATYP TABLETS** is waargeneem.

Indinavir
Gelyktydige toediening van ’n enkele dosis van 1 200 mg **ZATYP TABLETS** het geen statisties beduidende uitwerking gehad op die farmakokinetika van indinavir wat as 800 mg drie keer per dag vir 5 dae gegee is nie.

Midasolaam
In gesonde vrywilligers het die toediening van 500 mg **ZATYP TABLETS** per dag vir 3 dae geen klinies beduidende veranderinge in die farmakokinetiese en farmakodinamiese eienskappe van ’n enkele dosis van 15 mg midasolaam veroorsaak nie.

Nelfinavir
Gelyktydige toediening van **ZATYP TABLETS** (1 200 mg) en nelfinavir (750 mg drie keer per dag) het by gelykvlakke gelei tot hoër konsentrasies van asitromisien. Geen klinies beduidende newe-effekte is waargeneem nie, en hoewel ’n dosisaanpassing van **ZATYP TABLETS** nie aanbeveel word as dit saam met nelfinavir toegedien word nie, is dit nodig om noukeurig vir bekende newe-effekte van **ZATYP TABLETS** te monitor.

Sildenafiel
In normale gesonde manlike vrywilligers was daar geen bewyse van ’n effek van asitromisien (500 mg daagliks vir 3 dae) op die AOK en C_{maks} van sildenafiel of die belangrikste sirkulerende metaboliet daarvan nie.

Triasolaam
In 14 gesonde vrywilligers het die toediening van 500 mg asitromisien op dag 1 en 250 mg op dag 2 saam met 0,125 mg triasolaam op dag 2 geen beduidende effek op enige van die farmakokinetiese veranderlikes vir triasolaam gehad nie, vergeleke met triasolaam en placebo.

Trimetoprim/sulfametoksasool
Gelyktydige toediening van trimetoprim/sulfametoksasool (160 mg/800 mg) vir 7 dae saam met 200 mg asitromisien op dag 7 het geen beduidende effek gehad op piekkonsentrasies, totale blootstelling of urienuitskeiding van trimetoprim of sulfametoksasool nie. Konsentrasies van asitromisien in die serum was soortgelyk aan dié wat in ander studies gesien is.

Spesiale toediening word met die volgende aanbeveel:
Teensuurmiddels
In ’n farmakokinetiese studie wat die effekte van toediening van teensuurmiddels saam met asitromisien ondersoek het, is geen effek op die algehele biobeskikbaarheid gesien nie, hoewel die piek serumkonsentrasies ongeveer 24 % laer is. Pasiënte wat **ZATYP TABLETS** en teensuurmiddels saam gebruik, moet die medisyne nie op dieselfde tyd drink nie. **ZATYP TABLETS** moet ten minste 1 uur voor of 2 uur na ’n teensuurmiddel gedrink word.

Simetidien
’n Enkele dosis simetidien wat 2 uur voor **ZATYP TABLETS** toegedien is, het geen effek op die farmakokinetika van **ZATYP TABLETS** gehad nie.

Geen farmakokinetiese interaksies is aangemeld in studies van ZATYP TABLETS wat saam met die volgende gegee is nie:

- *Karbaamasepien, metielprednisoloon, didanosien* (dideoksi-inosien), teofillien, rifabutien (maar die toediening van **ZATYP TABLETS** en rifabutien het met die ontwikkeling van neutropenie gepaardgegaan. **ZATYP TABLETS** is nie bepaal nie (sien afdeling 4.8)
- Sidovudien (enkele dosisse van 1 000 mg en veelvuldige dosisse van 1 200 mg of 600 mg asitromisien het min effek gehad op die plasmafarmakokinetika of urinêre uitskeiding van sidovudien of sy glukuroniedmetaboliet. Toediening van asitromisien verhoog egter die konsentrasies van gefosforileerde sidovudien, die klinies aktiewe metaboliet, in perifere mononukleêre selle in die bloed. Die kliniese belang van hierdie bevinding is onduidelik, maar dit kan voordelig vir pasiënte wees).

Spesiale voorkomende monitering word met die volgende aanbeveel:
Siklosporien
In ’n farmakokinetiese studie met gesonde vrywilligers wat ’n orale dosis van 500 mg/dag asitromisien vir 3 dae gekry het en daarna ’n enkele dosis van 10 mg/kg siklosporien, is gevind dat die resulterende C_{maks} en AOK_{0-5} aansienlik hoër is (C_{maks} is 24 % hoër en AOK_{0-5} was 5 107 en 4 210 µg.h/mL met en sonder asitromisien, onderskeidelik, p ≤ 0,05). Gevolglik moet hierdie twee middels versigtig saam gegee word. As gelyktydige toediening nodig is, moet siklosporienvlakke gemonitor en die dosis dienooreenkomstig aangepas word.

P-glikoproteïensubstrate
Dit is gemeld dat toediening van **ZATYP TABLETS** saam met P-glikoproteïensubstrate, soos digoksien of dabigatraan, hoër serumvlakke van die P-glikoproteïensubstraat tot gevolg het. Daarom, as **ZATYP TABLETS** en P-glikoproteïensubstrate, soos digoksien of dabigatraan, saam toegedien word, moet die moontlikheid van hoër serumkonsentrasies van die middels in gedagte gehou word. Kliniese monitering en monitering van digoksienvlakke in die serum is tydens behandeling met **ZATYP TABLETS** en na die staking daarvan nodig.
Dit is gemeld dat sommige antibiotika die metabolisme van digoksien in sommige pasiënte (in die ingewande) benadeel. Daarom moet die moontlikheid van hoër digoksienvlakke in ag geneem word in pasiënte wat **ZATYP TABLETS**, ’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. In die tydperk na bemarking is berigte egter ontvang van sterker antikoagulasie ná toediening van **ZATYP TABLETS** saam met warfarien. Hoewel ’n oorsaaklike verband nie bepaal is nie, moet oorweeg word om protrombientyd meer dikwels te monitor wanneer **ZATYP TABLETS** gebruik word in pasiënte wat kumarientipe orale antikoagulante kry.

4.6. Fertiliteit, swangerskap en borsvoeding

Die veiligheid en effektiwiteit van **ZATYP TABLETS** tydens swangerskap and borsvoeding is nie bepaal nie.

Swangerskap
Studies van voortplanting in diere is gedoen met dosisse wat tot matige toksiese konsentrasies vir die moeder het. In hierdie studies is geen bewyse van skade aan die fetus as gevolg van asitromisien gesien nie. Geen voldoende en behoorlik gekontroleerde studies met swanger vroue is gedoen nie. Aangesien studies van voortplanting in diere nie altyd die respons in mense kan voorspel nie, moet **ZATYP TABLETS** slegs tydens swangerskap gebruik word as dit werklik nodig is.

Borsvoeding
Asitromisien word na bewering in menslike borsmelk uitgeskei, maar daar is geen voldoende en goed gekontroleerde kliniese studies met voedende vroue wat die farmakokinetika van uitskeiding van asitromisien in menslike borsmelk bepaal het nie.

ZATYP TABLETS moet slegs deur voedende vroue gebruik word indien geen voldoende alternatiewe beskikbaar is nie.

4.7. Effek op vermoë om ’n voertuig te bestuur en masjiene te gebruik

Newe-effekte soos duiseligheid, stuiptrekkings, vertigo, lomerigheid en sinkopee is met die gebruik van **ZATYP TABLETS** aangemeld. Hierdie newe-effekte kan die vermoë van die pasiënt aantas om motor te bestuur of masjinerie te hanteer.

4.8. Ongewensde effekte

a. Getabuleerde opsomming van nadelige reaksies

Orgaanstelsel	Newe-effekte
Versteurings van bloed en limfstelsel	
Minder dikwels	Neutropenie
Versteurings van die immuunstelsel	
Minder dikwels	Angioedeem
Oogversteurings	
Minder dikwels	Abnormale visie
Versteurings van die ore en labirint	
Minder dikwels	Gehoorgestremdheid, waaronder gehoorverlies, doofheid en/of tinnitus
Hartversteurings	
Minder dikwels	Borspyn, ritmestoornisse, waaronder ventrikulêre tagikardie, hartkloppings, verlenging in QT, Torsade de Pointes
Gastro-intestinale versteurings	
Dikwels	Ongemak in die buik (pyn/krampe), diarree, naarheid
Minder dikwels	Winderigheid, los stoelgang, braking
Minder dikwels	Malaena
Hepatobiliêre versteurings	
Minder dikwels	Abnormale lewerfunksie
Versteurings van die vel en subkutane weefsel	
Minder dikwels	Veluitslag
Minder dikwels	Allergiese reaksies
Versteurings van die niere en urienweg	
Minder dikwels	Nefritis

Na bemarking is die volgende nadelige effekte met onbekende frekwensie ook aangemeld:

Orgaanstelsel	Newe-effekte
Infeksies en infestasies	Moniliase, vaginitis
Versteurings van bloed en limfstelsel	Trombositopenie
Versteurings van die immuunstelsel	Anafilakse
Versteurings in metabolisme en voeding	Anoreksie
Psigiatriese versteurings	Senuweeagtigheid, aggressiewe reaksie, agitasie, angs
Versteurings van die senustelsel	Duiseligheid, stuiptrekkings, hoofpyn, hiperaktiwiteit, hipo-estesie, parestesie, slaperigheid, sinkopee, perversie en/of verlies van smaak/reuk
Versteurings van die ore en labirint	Doofheid, tinnitus, swak gehoor, vertigo
Hartversteurings	Palpitasies, aritmie waaronder ventrikulêre tagikardie, verlening van QT-interval, Torsade de Pointes
Vaskulêre versteurings	Hipotensie

Aanmeld van vermeende nadelige reaksies
Dit is belangrik om vermeende nadelige reaksies wat na magtiging van die medisinale produk voorkom, aan te meld. Dit maak voortgesette monitering van die balans tussen voordeel en risiko van die medisinale produk moontlik. Gesondheidspraktisyns word versoek om alle vermeende nadelige reaksies by SAHPRA aan te meld met die vorm “6.04 Adverse Drug Reaction Reporting Form” wat aanlyn by SAHPRA se publikasies gekry kan word: https://www.sahpra.org.za/Publications/Index/8.

4.9. Oordosis

Die newe-effekte wat ervaar is met hoër dosisse as die aanbevole was soortgelyk aan dié wat teen normale dosisse gesien is.
Tipiese simptome van oordosering met makroliedantibiotika is onder meer gehoorverlies, erge naarheid, braking en diarree. Algemene ondersteunende maatreëls is aangedui.

5. FARMAKOLOGIESE EIENSKAPPE

5.1. Farmakodinamiese eienskappe

Asitromisien is ’n asalied, ’n subklas van die makroliedantibiotika. Chemies is dit ’n derivaat van eritromisien A deur die invoeging van ’n stikstofatoom in die laktoonring. Die chemiese naam van asitromisien is 9-deoksi-9a-asa-9a-metiel-9a-homo-eritromisien A. Die molekulêre massa is 749,0. Asitromisien bind aan die 23S rRNA van die 50S ribosomale subeenheid. Dit blokkeer proteïensintese deur die transpeptidase-/translokasiestap van proteïensintese en die bou van die 50S ribosomale subeenheid te rem.

Hartelektrofisiologie
Verlenging van die QTc-interval is bestudeer in ’n ewekansige, plasebo-gekontroleerde parallelle proef met 116 gesonde proefpersone wat óf chlorokien (1 000 mg) alleen óf in kombinasie met asitromisien (500 mg, 1 000 mg en 1 500 mg een keer per dag) ontvang het. Gelyktydige toediening van asitromisien het die QTc-interval op dosis- en konsentrasie-afhanklike wyse aansienlik verhoog. In vergelyking met chlorokien alleen, was die maksimum gemiddelde toename in QTcF (en die bogrens van die 95 % betroubaarheidsinterval), 5 (10) ms, 7 (12) ms en 9 (14) ms met die mede-toediening van 500 mg, 1 000 mg en 1 500 mg asitromisien, onderskeidelik.

Uitvloeipompe kom voor in ’n aantal bakterieë, insluitend Gram-negatiewes, soos *Haemophilus influenzae* (waar hulle intrinsiek hoër MIKs kan hê) en stafilokokke. In streptokokke en enterokokke word ’n uitvloeipomp wat 14- en 15-lidmakroliede herken (wat onderskeidelik eritromisien en asitromisien insluit) deur *mef*(A)-gene gekodeer.

Asitromisien toon kruisweerstand met eritromisien-weerstandige gram-positiewe organismes.
Ribosomale modifikasies bepaal kruisweerstand met ander klasse antibiotika waarvan die ribosomale bindingsentrums met die van die makroliede oorvleuel: die linkosamiede (waaronder klindamisien) en die streptogramiene B (wat byvoorbeeld die kinupristien-komponent van kinupristien/dalfopristin insluit). ’n Afname in die vatbaarheid vir makroliede oor tyd is veral opgemerk in *Streptococcus pneumoniae* en *Staphylococcus aureus*, en is ook waargeneem in viridans streptokokke en in *Streptococcus agalactiae.*
Asitromisien het *in vitro* aktiwiteit teen:

- Aërobiese en fakultatiewe gram-positiewe bakterieë (eritromisien-vatbare organismes)
- Aërobiese en fakultatiewe gram-negatiewe bakterieë

In vitro-weerstand teen asitromisien
Asitromisien-weerstandige organismes kom relatief gereeld voor in aërobiese en fakultatiewe gram-positiewe bakterieë, veral onder metisillien-weerstandige *Staphylococcus aureus* (MWSA) en penisillien-weerstandige *Streptococcus pneumoniae* (PWSP).

Pseudomonas spp. en die meeste *Enterobacteriaceae* is inherent bestand teen asitromisien, alhoewel asitromisien gebruik word vir die behandeling van infeksies deur *Salmonella enterica*, *Pneumocystis jirovecii* en *Toxoplasma gondii*.

In vitro-sensitiwiteit impliseer nie noodwendig *in vivo*-effektiwiteit nie.

5.2. Farmakokinetiese eienskappe

Absorpsie
Na orale toediening aan mense word asitromisien wyd deur die liggaam versprei; biobeskikbaarheid is ongeveer 37 %. Daar is geen beduidende afname in biobeskikbaarheid as asitromisien saam met etes gedrink word nie. Die tyd tot piek vlakke in die plasma is 2 - 3 uur.
In pasiënte wat met gemeenskapsverworwe longontsteking gehospitaliseer is, wat daagliks vir 2 tot 5 dae binneaarse infusies van 500 mg asitromisien teen ’n konsentrasie van 2 mg/mL oor een uur ontvang het, was die gemiddelde C_{maks} ± SA 3,63 ± 1,60 µg/mL, terwyl die trogvlak op 24 uur 0,20 ± 0,15 µg/mL was, en die AOK_{24} was 9,60 ± 4,80 µg·h/mL. Die gemiddelde C_{maks}, trogwaarde op 24 uur en AOK_{24} was 1,14 ± 0,14 µg/L, 0,18 ± 0,02 µg/mL en 8,03 ± 0,86 µg·h/mL, onderskeidelik, in normale vrywilligers wat ’n intraveneuse infusie van 500 mg asitromisien teen ’n konsentrasie van 1 mg/mL oor 3 uur ontvang het.

Verspreiding
Kinetiese studies oor tye wat wissel van ure tot dae na orale inname, het ’n aansienlike hoër vlak asitromisien in weefsel as in plasma getoon (tot 50 keer die maksimum waargenome konsentrasie in plasma) wat daarop dui dat die middel sterk in die weefsel gebind is. Konsentrasies in teikenweefsels soos die longe, mangels en prostaat oorskry die MIK_{90} vir waarskynlike patogene na ’n enkele dosis van 500 mg.

Uitskeiding
Die terminale eliminasiehalfleeftyd uit plasma weerspieël die halfleeftyd van uitputting uit die weefsel van 2 tot 4 dae noukeurig.
Ongeveer 12 % van ’n intraveneuse dosis word oor 3 dae as asitromisien in die urien uitgeskei, met die meerderheid in die eerste 24 uur. Uitskeiding van asitromisien in die gal na orale toediening is ’n belangrike eliminasieweg vir die onveranderde middel. Baie hoë konsentrasies onveranderde middel is in menslike gal gekry, saam met 10 metaboliete, gevorm deur N- en O-demetilering, deur hidroksilering van desosamien- en aglikoonringe, en deur splyting van die kladinose-konjugaat. Vergelyking van HDVC en mikrobiologiese bepalings in weefsels dui daarop dat metaboliete geen rol speel in die mikrobiologiese aktiwiteit van asitromisien nie.
In ’n studie met meervoudige dosisse in 12 normale vrywilligers wat vir vyf dae ’n intraveneuse dosis van 500 mg (1 mg/mL) oor een uur gekry het, was ongeveer 11 % van die hoeveelheid toegediende asitromisien binne 24 uur na die eerste dosis in die urien uitgeskei en 14 % na die 5de dosis. Hierdie waardes is groter as die gerapporteerde 6 % wat na orale toediening van asitromisien onveranderd in die urien uitgeskei word.
Die farmakokinetika van asitromisien in volwasse pasiënte met ligte tot matige swak nierfunksie (GFT 10 - 80 mL/min) is nie deur ’n enkele dosis van 1 g onmiddellik vrygestelde asitromisien beïnvloed nie. Statisties beduidende verskille in AOK_{0-120} (8,8 mg x hr/mL vs. 11,7 mg x hr/mL), Cmax (1,0 mg/mL vs. 1,6 mg/mL) en CLr (2,3 mL/min/kg vs 0,2 mL/min/kg) is waargeneem tussen die groep met eindstadium nierversaking (GFT < 10 mL/min/kg) en die groep met normale nierfunksie.

Swak lewerfunksie
In pasiënte met ligte (Klas A) tot matige (Klas B) swak lewerfunksie is daar geen bewyse van ’n duidelike verandering in die farmakokinetika van asitromisien in die serum in vergelyking met diegene met normale lewerfunksie nie. Dit lyk asof die opruiming van asitromisien in die urien meer is in hierdie pasiënte, miskien om te vergoed vir verminderde leweropruiming. Asitromisien is nie in pasiënte met erge swak lewerfunksie bestudeer nie en hulle moet die nie gebruik nie.

Bejaardes
Bejaarde vrywilligers (> 65 jaar) het na ’n regime van 5 dae effens hoër AOK-waardes gehad as jong vrywilligers (< 40 jaar), maar dit word nie as klinies beduidend beskou nie, en daarom word geen dosisaanpassing aanbeveel nie.

5.3 Prekliniese veiligheidsdata

Nie toepaslik nie

Omgewingsimpakstudies
ZATYP TABLETS is ’n goed gevestigde aktiewe bestanddeel wat in farmaseutiese preparate deur mense gebruik word. Gegewe die verwagte patroon van gebruik en wegdoening van die produk, sal die blootstelling van die omgewing aan die aktiewe bestanddeel en metaboliete na verwagting baie beperk wees. Dit word nie geag dat die gebruik van **ZATYP TABLETS** enige kommer oor omgewingskwessies voortbring of enige spesiale produketikettering vereis nie.

6. FARMASEUTIESE BESONDERHEDE

6.1. Lys van hulpstowwe

Asitromisiendihidraat
Anhidriese kalsiumwaterstoffosfaatdihidraat
Voorafgeswelde stysel
Natriumkruiskarmellose
Natriumlourielsulfaat
Magnesiumstearaat
Wit Opadry II 31K58902
Gesuiwerde water

6.2. Onverenigbaarhede

Nie toepaslik nie

6.3. Rakleeftyd

3 jaar

6.4. Spesiale voorsorgmaatreëls vir bewaring

Bêre by of onder 25 °C.
Bêre in die oorspronklike houer totdat dit vir gebruik benodig word.
HOU BUITE BEREIK VAN KINDERS.

6.5. Aard en inhoud van die houer

Stulpstroke van helder PVC film-aluminiumfolie:
ZATYP TABLETS word in bogenoemde stulpstroke verpak, en is verder verpak in voorafgedrukte kartonne met die voubiljet volgens die goedgekeurde verpakkingsgrootte.

Vir 500 mg:
3’s: Bedrukte karton met 1 stulpstrook met 3 tablette.

6.6. Spesiale voorsorgmaatreëls vir die wegdoen van gebruikte medisyne of afvalstowwe wat uit sodanige medisyne verkry word, en ander hantering van die produk

Geen spesiale vereistes nie.

7. NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

AUROGEN SOUTH AFRICA (Edms) Bpk
Woodhillkantoorpark, Gebou 1, Eerste Vloer
Phillip Engelbrechtlaan 53
Meyersdal Uitbr. 12, 1448
Johannesburg
Suid-Afrika

8. REGISTRASIENOMMER

50/20.1.1/0755

9. DATUM VAN EERSTE MAGTIGING

10 NOVEMBER 2020

SKEDULERINGSTATUS

S4

PASIëNTINLIGTINGSBLAD

ZATYP TABLETS (500 mg)
Asitromisiendihidraat
Bevat suiker (15,4 mg laktosemonohidraat)

Lees hierdie hele blad noukeurig deur voordat u begin om ZATYP TABLETS te drink.

- Hou hierdie blad. Dit mag nodig wees dat u dit weer moet lees.
- As u nog vrae het, moet u asseblief vir u dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer vra.
- **ZATYP TABLETS** is vir u persoonlik voorgeskryf en u moet nie u medisyne vir ander mense gee nie. Dit kan hulle skaad, selfs al is hulle simptome dieselfde as u s’n.

Wat in hierdie blad is:

1. Wat **ZATYP TABLETS** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **ZATYP TABLETS** gebruik
3. Hoe om **ZATYP TABLETS** te gebruik
4. Moontlike newe-effekte
5. Hoe om **ZATYP TABLETS** te stoor
6. Inhoud van die pak en ander inligting

Wat ZATYP TABLETS is en waarvoor dit gebruik word
ZATYP TABLETS is ’n antibiotikum wat behoort aan ’n groep antibiotika wat makroliede genoem word. Dit word gebruik om infeksies wat deur bakterieë en ander mikro-organismes veroorsaak word, te behandel.
ZATYP TABLETS word gewoonlik voorgeskryf vir die behandeling van lugweginfeksies soos inflammasie van die brongi, longinfeksie, mangelontsteking, keelontsteking, sinusitis en oorinfeksies, vel- en sagteweefselinfeksies (soos abses), of seksueel oordraagbare siektes soos sjankroïed (pynlike sere op die geslagsdele) of die wat deur ’n organisme genaamd Chlamydia veroorsaak word.

1. Wat u moet weet voordat u ZATYP TABLETS gebruik

Moenie ZATYP TABLETS drink nie:

- as u hipersensitief (allergies) is vir asitromisien, eritromisien of enige makroliedantibiotikum of vir enige van die ander bestanddele van **ZATYP TABLETS**.
- as u ergotderivate gebruik vir die behandeling van migraine en troshoofpyn. Hierdie medisyne kan, as dit saam met **ZATYP TABLETS** gedrink word, ’n toestand genaamd ergotisme in die liggaam veroorsaak.
- As ly vorm of het gely aan lewersiekte.

Waarskuwings en spesiale voorsorgmaatreëls
Wees besonder versigtig met ZATYP TABLETS
Voordat u **ZATYP TABLETS** drink, moet u dokter weet as u een van die volgende gehad het:

- Lewerprobleme: u dokter moet dalk u lewerfunksie monitor of die behandeling staak
- As u ergotderivate soos ergotamien (vir die behandeling van migraine) gebruik, aangesien hierdie medisyne nie saam met **ZATYP TABLETS** gedrink moet word nie
- Nierprobleme
- Hartsiektes
- As u aan ’n neuromuskulêre outo-immuunsiekte genaamd myasthenia gravis ly, kan u simptome erger word as u **ZATYP TABLETS** drink.

Sê dadelik vir u dokter as u onreëlmatige hartklop in u bors het of as u ’n abnormale hartklop het wanneer u **ZATYP TABLETS** drink.
As u diarree of los stoelgang tydens of na die behandeling ervaar, moet u dit dadelik vir u dokter sê. Moenie enige medisyne gebruik om die diarree te behandel sonder om dit eers met u dokter uit te klaar nie. As u diarree voortduur, moet u dit so gou as moontlik vir u dokter sê.
Sê vir u dokter as u ernstige reaksies op die vel of nuwe infeksies kry.

Gebruik van ander medisyne saam met ZATYP TABLETS

Sê altyd vir u gesondheidspraktisyn as u enige ander medisyne gebruik (waaronder aanvullende of tradisionele medisyne). Kyk **Moenie ZATYP TABLETS drink nie**.

Sê voordat u **ZATYP TABLETS** drink vir u dokter indien u een van die onderstaande medisyne gebruik:

- Ergot of ergotamien (om migraine te behandel) (kyk Wees veral versigtig met **ZATYP TABLETS**)
- Teensuurmiddels (vir slegte spysvertering)
- Siklosporien (om die immuunstelsel te onderdruk om verwerping van ’n oorgeplante orgaan of beenmurg te voorkom en te behandel).
- Digoksien (om hartversaking te behandel)
- Warfarien of enige soortgelyke medisyne om bloedklonte te voorkom

Swangerskap, borsvoeding en vrugbaarheid

As u swanger is of u baba borsvoed, moet u asseblief vir u dokter, apteker of ander gesondheidskundige om advies vra voordat u **ZATYP TABLETS** begin neem.

Die veiligheid en effektiwiteit van **ZATYP TABLETS** tydens swangerskap en borsvoeding is nie bepaal nie.

Motorbestuur en gebruik van masjinerie
ZATYP TABLETS kan duiseligheid, stuiptrekkings, vertigo, meer lomerigheid en tydelike verlies van bewussyn veroorsaak, wat u vermoë om ’n voertuig te bestuur en masjinerie te hanteer, kan beïnvloed.

Belangrike inligting oor sommige van die bestanddele van ZATYP TABLETS
As u dokter vir u gesê het dat u ’n onverdraagbaarheid teenoor sekere suikers het, moet u u dokter skakel voordat u hierdie medisyne gebruik.
Laktose kan ook ’n effek op die beheer van u bloedsuiker hê as u diabetes mellitus het.

2. Hoe om ZATYP TABLETS te drink

Moenie medisyne wat vir u voorgeskryf is vir enige ander persoon gee nie. Gebruik **ZATYP TABLETS** altyd presies soos wat u dokter vir u gesê het. Raadpleeg u dokter of apteker as u nie seker is nie.

U dokter sal vir u sê hoe lank u behandeling met **ZATYP TABLETS** sal duur.
Die totale dosis is 1,5 g wat as 500 mg daagliks vir 3 dae gegee moet word.
Vir seksueel oordraagbare siektes veroorsaak deur *Chlamydia trachomatis* of *Haemophilus ducreyi* is die dosis is 1 g gegee as ’n enkele dosis.
ZATYP TABLETS moet nie deur kinders wat minder as 45 kg weeg gedrink word nie. Vir kinders wat meer as 45 kg weeg, word die dosisse hier bo gewoonlik voorgeskryf.
Sê vir u dokter of apteker as u die indruk het dat die effek van **ZATYP TABLETS** te sterk of te swak is.
Gebruik van ZATYP TABLETS saam met voedsel en drank
ZATYP TABLETS kan met of sonder voedsel gedrink word. Die tablet moet heel met water afgesluk word.

As u meer ZATYP TABLETS gedrink het as wat u moes

Raadpleeg u dokter of apteker onmiddellik in geval van oordosering. As nie een beskikbaar is nie, kontak die naaste hospitaal of gifsentrum.

As u ’n dosis ZATYP TABLETS oorgeslaan het
Dit is belangrik dat u voortgaan om u medisyne te volgens die instruksies op die etiket te drink en dat u geen dosisse oorslaan nie. As u ’n dosis egter oorslaan, drink dit sodra as wat u onthou en drink dan die volgende dosis op die gewone tyd. Moenie ’n dubbele dosis drink om vir ’n vergete dosis op te maak nie.

3. Moontlike newe-effekte

ZATYP TABLETS kan newe-effekte veroorsaak.

Nie al die newe-effekte wat vir **ZATYP TABLETS** aangemeld is, is in hierdie blad opgeneem nie. As u algemene gesondheidstoestand vererger of as u enige newe-effekte ervaar terwyl u **ZATYP TABLETS** drink, moet u u dokter, apteker of ander gesondheidspraktisyn om advies raadpleeg.

Sê dadelik vir u dokter of gaan na die ongevalle-afdeling van u naaste hospitaal as u enige van die volgende opmerk:

- Swelling van die hande, voete, enkels, gesig, lippe, mond of keel wat probleme met sluk of asemhaling kan veroorsaak.
- Veluitslag of jeuk
- Diarree (los, vloeibare of waterige stoelgang)
- Buikpyn

Hierdie is almal ernstige newe-effekte. Dit mag wees dat u dringende mediese aandag nodig het.

Sê vir u dokter as u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:

- Buikongemak (pyn/krampe), diarree, naarheid
- Palpitasies (onreëlmatige hartklop)
- Torsade de Pointes (’n vorm van vinniger hartklop)
- Neutropenie (kortasemheid, moegheid, spierswakheid, onreëlmatige hartklop)

Die volgende newe-effekte kom minder dikwels of met onbekende frekwensie voor:

- Senuweeagtigheid, aggressiewe reaksie, agitasie, angs
- Orale kandidiase (wit, harige, seer tong en mond)
- Vaginale infeksie
- Duiseligheid (voel lighoofdig of ongebalanseerd)
- Sinkopee (floute of lighoofdigheid)
- Konvulsies (toevalle)
- Parestesie (tintelende sensasie)
- Versteuring en/of verlies van smaak/reuk
- Hipestesie (groter sensitiwiteit vir stimuli)
- Doofheid
- Tinnitus (gelui in die ore)
- Hipotensie (lae bloeddruk)
- Abnormale visie
- Oormatige winde, los stoelgang, braking
- Abnormale lewerfunksie
- Inflammasie van die niere
- Swart of teeragtige stoelgang

As u enige newe-effekte opmerk wat nie in hierdie blad genoem word nie, moet u u dokter of apteker asseblief in kennis stel.

Aanmeld van newe-effekte
Praat met u dokter, apteker of verpleegkundige as u newe-effekte kry. Dit sluit alle moontlike newe-effekte in wat nie in hierdie blad gelys word nie. U kan newe-effekte ook by SAHPRA via die “6.04 Adverse Drug Reaction Reporting Form” wat aanlyn by SAHPRA se publikasies gekry kan word: https://www.sahpra.org.za/Publications/Index/8 aanmeld. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van hierdie medisyne te gee.

4. Hoe om ZATYP TABLETS te bêre

HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS.
Bêre by of onder 25 °C.

- Bêre in die oorspronklike verpakking totdat dit vir gebruik benodig word.
- Moenie in ’n badkamer bêre nie.
- Moenie na die vervaldatum op die etiket gebruik nie.

Gee alle ongebruikte medisyne terug aan u apteker.
Ongebruikte medisyne moet nie in dreinering- of rioolstelsels (bv. toilette) gegooi word nie.

5. Inhoud van die pak en ander inligting

Wat ZATYP TABLETS bevat
Die aktiewe bestanddeel is asitromisiendihidraat
Anhidriese kalsiumwaterstoffosfaatdihidraat
Voorafgeswelde stysel
Natriumkruiskarmellose
Natriumlourielsulfaat
Magnesiumstearaat
Wit Opadry II 31K58902
Gesuiwerde water

Hoe ZATYP TABLETS lyk en die inhoud van die pakkie
ZATYP TABLETS 500 mg
Wit tot afwit, ovaalvormige filmbedekte bikonvekse tablette, met “6” & “7” weerskante van die breeklyn op die een kant en “D” op die ander kant gedruk.
Stulpstroke van helder PVC film-aluminiumfolie:
Asitromisien-tablette 500 mg word in bogenoemde stulpstroke verpak, en verder in gedrukte kartonne met die voubiljet volgens die goedgekeurde verpakkingsgrootte.
Vir 500 mg:
3’s: Bedrukte karton met 1 stulpstrook met 3 tablette.

NAAM, BESIGHEIDSADRES EN TELEFOONNOMMER VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT
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Phillip Engelbrechtlaan 53
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Johannesburg
Suid-Afrika

Hierdie blad is laas hersien op: 10 November 2020

Registrasienommer: 50/20.1.1/0755

Black A/s: 350 x 720 mm

AUROBINDO Packaging Development	Product Name: Zatyp Tablets	Component: Leaflet	Item Code: P1525981	Date & Time: 16.01.2021 & 4.00 PM
	Customer / Country: Auro_Gen_SA_Unit-7	Version No.: 03	Reason Of Issue: NEW	Reviewed / Approved by
Team Leader: Kiran	Dimensions: 350 x 720 mm	No. of Colours : 01		
Initiator: Bhogi				
Artist: Vision Graphic Designers	Pharmacode: 25981	25981		
Additional Information :				Sign / Date

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ZATYP TABLETS 500 mg film coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ZATYP TABLETS 500 mg film coated tablets

Each film coated tablet contains azithromycin dihydrate Ph.Eur 500 mg.

Contains sugar *lactose* monohydrate 15,4 mg).

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

ZATYP TABLETS 500 mg film coated tablets:

White to off-white, oval shaped, film coated biconvex tablets, debossed with "6" & "7" on either side of the score-line on one side and "D" on other side

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adults:

ZATYP TABLETS are indicated for mild to moderate infections caused by susceptible organisms; in lower respiratory tract infections including bronchitis due to *Haemophilus influenzae, 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/tonsilitis.

In sexually transmitted diseases in men and women, **ZATYP TABLETS** are indicated in the treatment of uncomplicated genital infections due to *Chlamydia trachomatis* and chancroid due to *Haemophilus ducreyi.*

Children 1 year and over: **ZATYP TABLETS** are indicated for pharyngitis/tonsilitis and otitis media caused by susceptible organisms in children over 45 kg.

4.2. Posology and method of administration

ZATYP TABLETS should be administered as a single daily dose with or without food.

ZATYP 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* or *Haemophilus ducreyi*, the dose is 1 g given as a single dose.

Special Populations

Use in patients with hepatic impairment

ZATYP TABLETS is contraindicated in patients with severe hepatic impairment (see Section 4.3)

Use in the elderly:

Normal adult dosage is recommended. Elderly patients may be more susceptible to development of Torsade de Pointes dysrhythmia than younger patients (see section 4.4).

Use in children:

Children over 45 kg - dose as per adults.

This formulation is not suitable for children under 45 kg.

Method of administration

Oral

4.3. Contraindications

ZATYP TABLETS is contraindicated in patients with a known hypersensitivity to azithromycin, erythromycin, any of the macrolide antibiotics, or to any excipient listed under section 6.1.

Because of the theoretical possibility of ergotism, **ZATYP TABLETS** and ergot derivatives should not be co-administered.

Use in hepatic impairment:

As the liver is the principal route of excretion of **ZATYP TABLETS,** it should not be prescribed in patients with hepatic diseases.

4.4. Special warnings and precautions for use

Hypersensitivity:

Serious allergic reactions, including angioedema and anaphylaxis and dermatologic reactions including Stevens-Johnson Syndrome, Acute Generalised Exanthematous Pustulosis (AGEP), Drug with Eosinophilic and systemic symptoms ((DRESS) and toxic epidermal necrolysis have been reported. Some of these reactions with **ZATYP TABLETS** have resulted in recurrent symptoms and required a longer period of observation and treatment. If an allergic reaction occurs, **ZATYP TABLETS** should be discontinued and appropriate therapy should be instituted. Medical practitioners should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Hepatotoxicity:

Since the liver is the principal route of elimination for azithromycin, **ZATYP TABLETS** should not be used in patients with hepatic disease (see Section 4.3).

Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis and hepatic failure, some of which have resulted in death, have been reported. Discontinue **ZATYP TABLETS** immediately if signs and/or symptoms of hepatitis occur.

Ergot derivatives:

In patients receiving ergot derivatives, ergotism has been precipitated by co-administration of some macrolide antibiotics. There is no data concerning the possibility of an interaction between ergot and **ZATYP TABLETS.** However, because of the theoretical possibility of ergotism**, ZATYP TABLETS** and ergot derivatives should not be co-administered (see section 4.3).

Superinfection:

Observation for signs of superinfection with non-susceptible organisms, including fungi is recommended.

Pseudomembranous colitis:

Pseudomembranous colitis has been reported and may range in severity from mild to life-threatening.

Therefore, it is important to consider this diagnosis in patients with diarrhoea subsequent to administration of **ZATYP TABLETS.**

***Clostridium difficile*-associated diarrhoea:**

Clostridium difficile-associated diarrhoea *(CDAD)* due to overgrowth of *Clostridium difficile* in the gut, has been reported with use of **ZATYP TABLETS,** and may range in severity from mild diarrhoea to fatal colitis.

If CDAD is suspected or confirmed, ongoing **ZATYP TABLETS** use should be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *Clostridium difficile* and surgical evaluation should be instituted as clinically indicated.

Renal impairment:

In patients with a creatinine clearance < 30 mg/ml, a 33 % increase in systemic exposure to **ZATYP TABLETS** was observed (see section 5.2). Acute renal failure and interstitial nephritis have been reported (see section 4.8).

Prolongation of the QT interval:

Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac dysrhythmia and Torsade de Pointes, have been seen in treatment with other macrolides including **ZATYP TABLETS** (see section 4.8). Prescribers should specifically consider the risk of QT prolongation, which can be fatal in at-risk groups including:

- Patients with congenital or documented QT prolongation
- Patients currently receiving treatment with other active substances known to prolong QT interval such as antidysrhythmics of classes IA and III; antipsychotic medicines: antidepressants; and fluoroquinolones.
- Patients with electrolyte disturbance, particularly in cases of hypokalaemia and hypomagnesaemia.
- Patients with clinically relevant bradycardia, cardiac dysrhythmia or cardiac insufficiency.
- Elderly patients: elderly patients may be more susceptible to medicine-associated effects on the QT interval.
- Myasthenia gravis

Exacerbation of symptoms of myasthenia gravis and new-onset of myasthenia syndrome have been reported in patients receiving azithromycin therapy.

- **Use in children under 1 year of age:**

The safety and efficacy of **ZATYP TABLETS** in children less than 1 year have not been established

Lactose intolerance:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicine.

Contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

4.5. Interaction with other medicines and other forms of interaction

Ergot derivatives:

Because of the theoretical possibility of ergotism, **ZATYP TABLETS** and ergot derivatives should not be co-administered (see section 4.3 and section 4.4).

Cetirizine:

In healthy volunteers, co-administration of a 5-day regimen of azithromycin with cetirizine 20 mg at steady-state resulted in no pharmacokinetic interaction and no significant changes in the QT interval. Azithromycin does not interact significantly with the hepatic cytochrome P450 system. It is not believed to be associated with the pharmacokinetic medicine interactions seen with erythromycin. Hepatic cytochrome P450 induction or inactivation via cytochrome-metabolite complex does not occur with azithromycin.

Pharmacokinetic studies have been conducted between azithromycin and the following medicines known to undergo significant cytochrome P450 mediated metabolism:

Atorvastatin:

Co-administration of atorvastatin (10 mg daily) and azithromycin (500 mg daily) did not alter the plasma concentrations of atorvastatin (based on a HMG CoA reductase inhibition assay). However, post-marketing cases of rhabdomyolysis in patients receiving azithromycin with statins have been reported.

Efavirenz:

Co-administration of a 600 mg single dose of azithromycin and 400 mg efavirenz daily for 7 days did not result in any clinically significant pharmacokinetic interactions.

Fluconazole:

Co-administration of a single dose of 1200 mg **ZATYP TABLETS** did not alter the pharmacokinetics of a single dose of 800 mg fluconazole. Total exposure and half-life of **ZATYP TABLETS** were unchanged by the co-administration of fluconazole, however, a clinically insignificant decrease in C_{max} (18 %) **of ZATYP TABLETS** was observed.

Indinavir:

Co-administration of a single dose of 1200 mg **ZATYP TABLETS** had no statistically significant effect on the pharmacokinetics of indinavir administered as 800 mg three times daily for 5 days.

Midazolam:

In healthy volunteers, co-administration of **ZATYP TABLETS** 500 mg/day for 3 days did not cause clinically significant changes in the pharmacokinetic properties and pharmacodynamics properties of a single 15 mg dose of midazolam.

Nelfinavir:

Co-administration **of ZATYP TABLETS** (1200 mg) and nelfinavir at steady state (750 mg three times daily) resulted in increased azithromycin concentrations. No clinically significant adverse effects were observed and although a dose adjustment of **ZATYP TABLETS** is not recommended when administered in combination with nelfinavir, close monitoring for known side effects of **ZATYP TABLETS** is warranted.

Sildenafil:

In normal healthy male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC and C_{max}, of sildenafil or its major circulating metabolite.

Triazolam:

In 14 healthy volunteers, co-administration of azithromycin 500 mg on day 1 and 250 mg on day 2 with 0,125 mg triazolam on day 2 had no significant effect on any of the pharmacokinetic variables for triazolam compared to triazolam and placebo.

Trimethoprim/sulfamethoxazole:

Co-administration of trimethoprim/sulfamethoxazole (160 mg/800 mg) for 7 days with azithromycin 1 200 mg on day 7 had no significant effect on peak concentrations, total exposure or urinary excretion of either trimethoprim or sulfamethoxazole. Azithromycin serum concentrations were similar to those seen in other studies.

Special administration advised with the following:

Antacids:

In a pharmacokinetic study investigating the effects of simultaneous administration of antacids azithromycin, no effect on overall bioavailability was seen although peak serum concentrations were reduced by approximately 24 %. In patients receiving both **ZATYP TABLETS** and antacids, the medicines should not be taken simultaneously. **ZATYP TABLETS** should be taken at least 1 hour before or 2 hours after an antacid.

Cimetidine:

A single dose of cimetidine administered 2 hours before **ZATYP TABLETS** had no effect on the pharmacokinetics of **ZATYP TABLETS**.

No pharmacokinetic interactions were reported in studies of ZATYP TABLETS co-administered with:

- Carbamazepine, methylprednisolone, didanosine (dideoxyinosine), theophylline, rifabutin (however co administration **ZATYP TABLETS** and rifabutin was associated with the development of neutropenia. A causal relationship to its **ZATYP TABLETS** has not been established (see section 4.8)
- Zidovudine (single 1 000 mg doses and multiple 1200 mg or 600 mg doses of azithromycin had little effect on the plasma pharmacokinetics or urinary excretion of zidovudine or its glucuronide metabolite. However, administration of azithromycin increased the concentrations of phosphorylated zidovudine, the clinically active metabolite, in peripheral blood mononuclear cells. The clinical significance of this finding is unclear, but it may be of benefit to patients).

Special precautionary monitoring is advised with the following:

Ciclosporin:

In a pharmacokinetic study with healthy volunteers that were administered a 500 mg/day oral dose of azithromycin for 3 days and were then administered a single 10 mg/kg oral dose of ciclosporin, the resulting ciclosporin C_{max} and AUC_{0-5} were found to be significantly elevated (C_{max} increase by 24 % and AUC_{0-5} was 5 107 and 4 210 µg.h/mL with and without azithromycin, respectively, p ≤ 0,05). Consequently, caution should be exercised before co-administration of these two medicines. If co-administration is necessary, ciclosporin levels should be monitored and the dose adjusted accordingly.

P-glycoprotein substrates:

Concomitant administration of **ZATYP TABLETS** with P-glycoprotein substrates such as digoxin or dabigatran, has been reported to result in increased serum levels of the P-glycoprotein substrate. Therefore, if **ZATYP TABLETS** and P-glycoprotein substrates such as digoxin or dabigatran are administered concomitantly, the possibility of elevated serum medicine concentrations should be considered. Clinical monitoring and serum monitoring of digoxin levels during treatment with **ZATYP TABLETS** and after its discontinuation are necessary. 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 **ZATYP TABLETS,** a related azalide antibiotic, and digoxin the possibility of raised digoxin levels should be borne in mind.

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. However there have been reports received in the post-marketing period of potentiated anticoagulation subsequent to co-administration of **ZATYP TABLETS** and warfarin. Although a causal relationship has not been established, consideration should be given to the frequency of monitoring prothrombin time when **ZATYP TABLETS** is used in patients receiving coumarin-type oral anticoagulants.

4.6. Fertility, pregnancy and lactation

The safety and efficacy of **ZATYP TABLETS** in pregnancy and lactation have not been established.

Pregnancy

Animal reproduction studies have been performed at doses up to moderately maternally toxic dose concentrations. In these studies, no evidence of harm to the foetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, **ZATYP TABLETS** should be used during pregnancy only if clearly needed.

Lactation

Azithromycin has been reported to be secreted into human breast milk, but there are no adequate and well controlled clinical studies in nursing women that have characterized the pharmacokinetics of azithromycin excretion into human breast milk.

ZATYP TABLETS should only be used in lactating women where adequate alternatives are not available.

4.7. Effects on ability to drive and use machines

Side effects such as dizziness, convulsions, vertigo, somnolence, and syncope have been reported with usage of **ZATYP TABLETS**. These side effects may affect a patient's ability to drive or operate machinery.

4.8. Undesirable effects

a. Tabulated list of adverse reactions

System organ class	Side effects
Blood and lymphatic system disorders	
Less frequent	Neutropenia
Immune system disorders	
Less frequent	Angioedema
Eye disorders	
Less frequent	Abnormal vision
Ear and labyrinth disorders	
Less frequent	Hearing impairment including hearing loss, deafness and/or tinnitus
Cardiac disorders	
Less frequent	Chest pains, dysrhythmias including ventricular tachycardia, palpitations, QT prolongation, Torsade de Pointes
Gastrointestinal disorders	
Frequent	Abdominal discomfort (pain/cramps), diarrhoea, nausea
Less frequent	Flatulence: loose stools, vomiting
Less frequent	Malaena
Hepatobiliary disorders	
Less frequent	Abnormal liver function
Skin and subcutaneous tissue disorders	
Less frequent	Rash
Less frequent	Allergic reactions
Renal and urinary disorders	
Less frequent	Nephritis

In post-marketing experience, the following additional undesirable effects have been reported with frequency unknown:

System organ class	Side effects
Infections and infestations	Moniliasis, vaginitis
Blood and lymphatic system disorders	Thrombocytopenia
Immune system disorders	Anaphylaxis
Metabolism and nutrition disorders	Anorexia
Psychiatric disorders	Nervousness, aggressive reaction, agitation, anxiety
Nervous system disorders	Dizziness, convulsions, headache, hyperactivity, hypoesthesia, paraesthesia, somnolence, syncope, taste/smell perversion and/or loss
Ear and labyrinth disorders	Deafness, tinnitus, impaired hearing, vertigo
Cardiac disorders	Palpitations, dysrhythmias including ventricular tachycardia, QT prolongation, Torsade de Pointes
Vascular disorders	Hypotension

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the '6.04 Adverse Drug Reactions Reporting Form'. Found under SAHPRA's publications: https://www/sahpra.org.za/Publications/Index/8

4.9. Overdose

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. Typical symptoms of over dosage with macrolide antibiotics include hearing loss, severe nausea, vomiting and diarrhoea. General supportive measures are indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Azithromycin is an azalide, a subclass of the macrolide antibiotics. Chemically it is derived by insertion of a nitrogen atom into the lactone ring of erythromycin A. The chemical name of azithromycin is 9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A. The molecular weight is 749,0. Azithromycin binds to the 23S rRNA of the 50S ribosomal subunit. It blocks protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting the assembly of the 50S ribosomal subunit.

Cardiac electrophysiology:

QTc interval-prolongation was studied in a randomised, placebo-controlled parallel trial in 116 healthy subjects who received either chloroquine (1 000 mg) alone or in combination with azithromycin (500 mg, 1 000 mg, and 1 500 mg once daily). Co-administration of azithromycin significantly increased the QTc interval in a dose- and concentration-dependent manner. In comparison to chloroquine alone, the maximum mean (95 % upper confidence bound) increases in QTcF were 5 (10) ms, 7 (12) ms and 9 (14) ms with the co-administration of 500 mg, 1 000 mg and 1 500 mg azithromycin, respectively.

Efflux pumps occur in a number of bacteria, including Gram-negatives, such as *Haemophilus influenzae* (where they may determine intrinsically higher MICs) and staphylococci. In streptococci and enterococci, an efflux pump that recognises 14 - and 15-membered macrolides (which include, respectively, erythromycin and azithromycin) is encoded by *mef*(A) genes.

Azithromycin demonstrates cross-resistance with erythromycin-resistant Gram-positive organisms.

Ribosomal modifications determine cross-resistance with other classes of antibiotics whose ribosomal binding sites overlap that of the macrolides: the lincosamides (including clindamycin), and the streptogramins B (which include, for example, the quinupristin component of quinupristin/dalfopristin). A decrease in macrolide susceptibility over time has been noted in particular in *Streptococcus pneumoniae* and *Staphylococcus aureus*, and has also been observed in *viridans streptococci* and in *Streptococcus agalactiae*.

Azithromycin has *in vitro* activity against:

- Aerobic and facultative Gram-positive bacteria (erythromycin-susceptible organisms).
- Aerobic and facultative Gram-negative bacteria.

In vitro resistance to azithromycin:

Azithromycin-resistant organisms are encountered relatively frequently among aerobic and facultative Gram-positive bacteria, in particular among methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin- resistant *Streptococcus pneumoniae* (PRSP).

Pseudomonas spp. and most *Enterobacteriaceae* are inherently resistant to azithromycin, although azithromycin has been used to treat *Salmonella enterica*, *Pneumocystis jirovecii* and *Toxoplasma gondii* infections.

In vitro sensitivity does not necessarily imply *in vivo* efficacy.

5.2. Pharmacokinetic properties

Absorption

Following oral administration in humans, azithromycin is widely distributed throughout the body; bioavailability is approximately 37 %. No significant decrease in bioavailability was observed when azithromycin was administered with a meal. The time taken to peak plasma levels is 2 - 3 hours.

In patients hospitalised with community acquired pneumonia receiving single daily one-hour intravenous infusions for 2 to 5 days of 500 mg azithromycin at a concentration of 2 mg/mL, the mean C_{max} ± S.D. achieved was 3,63 ± 1,60 µg/mL, while the 24-hour trough level was 0,20 ± 0,15 µg/mL, and the AUC_{24} was 9,60 ± 4,80 µg·h/mL. The mean C_{max}, 24-hour trough and AUC_{24} values were 1,14 ± 0,14 µg/mL, 0,18 ± 0,02 µg , and 8,03 ± 0,86 µg/mL, respectively, in normal volunteers receiving a 3-hour intravenous infusion of 500 mg azithromycin at a concentration of 1 mg/mL.

Distribution

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) indicating that the medicine is highly tissue bound. Concentrations in target tissues such as lung, tonsil and prostate exceed the MIC_{90} for likely pathogens after a single dose of 500 mg

Elimination

Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2 to 4 days.

Approximately 12 % of an intravenously administered dose is excreted in the urine over 3 days as azithromycin, the majority in the first 24 hours. Biliary excretion of azithromycin is a major route of elimination for unchanged medicine following oral administration. Very high concentrations of unchanged medicine have been found in human bile, together with 10 metabolites, formed by N- and O-demethylation, by hydroxylation of the desosamine and aglycone rings, and by cleavage of the cladinose conjugate. Comparison of HPLC and microbiological assays in tissues suggests that metabolites play no part in the microbiological activity of azithromycin.

In a multiple-dose study in 12 normal volunteers utilising a 500 mg (1 mg/mL) one-hour intravenous dosage regimen for five days, the amount of administered azithromycin dose excreted in urine in 24 hours was about 11 % after the 1st dose and 14 % after the 5th dose. These values are greater than the reported 6 % excreted unchanged in urine after oral administration of azithromycin.

The pharmacokinetics of azithromycin in adult patients with mild-to-moderate renal impairment (GFR 10 - 80 mL/min) were not affected following a single 1 g dose of immediate release azithromycin. Statistically significant differences in AUC_{0-120} (8,8 mg·h/mL vs. 11,7 mg·h/mL), Cmax (1,0 mg/mL vs. 1,6 mg/mL) and CLr (2,3 mL/min/kg vs. 0,2 mL/min/kg) were observed between the group with severe renal impairment (GFR < 10 mL/min) and the group with normal renal function.

Hepatic insufficiency:

In patients with mild (Class A) to moderate (Class B) hepatic impairment, there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to normal hepatic function. The urinary clearance of azithromycin appears to increase in these patients, perhaps to compensate for reduced hepatic clearance. Azithromycin has not been studied and should not be used in patients with severe hepatic impairment.

Elderly:

Elderly volunteers (> 65 years) had slightly higher AUC values than younger volunteers (< 40 years) after a 5-day regimen, but these are not considered clinically significant, and hence no dose adjustment is recommended.

5.3 Preclinical safety data

Not applicable

Environmental Risk Assessment

ZATYP TABLETS is a well-established active ingredient used in pharmaceutical preparations for human use. Given the anticipated pattern of use and disposal of the product, the environmental exposure of the active substance and metabolites are expected to be very limited. The use of **ZATYP TABLETS** is not considered warranting any environmental concerns or requiring any special product labelling.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Azithromycin Dihydrate
Calcium Hydrogen Phosphate, Anhydrous
Starch, Pregelatinised
Croscarmellose Sodium
Sodium Lauryl Sulfate
Magnesium Stearate
Opadry II 31K58902 white
Purified water

6.2. Incompatibilities

Not applicable

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store at or below 25 °C.
Keep in original packaging until required for use.
KEEP OUT OF REACH OF CHILDREN.

6.5. Nature and contents of container

***Clear* PVC Film- Aluminium foil blister pack:**

ZATYP TABLETS are packed in above blisters shall be further packed in pre-printed cartons with patient information leaflet according to the approved pack size.

For 500 mg:

3's: Printed cardboard carton containing 1 blister of 3 tablets each.

6.6. Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

AUROGEN SOUTH AFRICA (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8. REGISTRATION NUMBER

50/20.1.1/0755

9. DATE OF FIRST AUTHORISATION

10 NOVEMBER 2020

P/1525681

SCHEDULING STATUS

S4

PATIENT INFORMATION LEAFLET

ZATYP TABLETS (500 mg)

Azithromycin Dihydrate

Contains Sugar (Lactose Monohydrate 15,4 mg)

Read all of this leaflet carefully before you start taking ZATYP TABLETS

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- **ZATYP TABLETS** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet:

1. What **ZATYP TABLETS** is and what it is used for.
2. What you need to know before you use **ZATYP TABLETS.**
3. How to use **ZATYP TABLETS.**
4. Possible side effects.
5. How to store **ZATYP TABLETS.**
6. Contents of the pack and other information.

What ZATYP TABLETS is and what it is used for

ZATYP TABLETS is an antibiotic which belongs to a group of antibiotics called macrolides. It is used to treat infections caused by bacteria and other micro-organisms.

ZATYP TABLETS is usually prescribed to treat respiratory tract infections such as inflammation of the bronchi, lung infection, tonsilitis, inflammation of the pharynx, sinusitis and ear infections, skin and soft tissue infections (such as abscess), or sexually transmitted diseases such as chancroid (painful sores on the genitalia) or those caused by an organism called Chlamydia.

1. What you need to know before you take ZATYP TABLETS

Do not take ZATYP TABLETS :

- If you are hypersensitive (allergic) to azithromycin, erythromycin or any macrolide antibiotic or any of the other ingredients of **ZATYP TABLETS.**
- If you are taking any ergot derivatives, which are used for the treatment of migraines and cluster headaches. These medicines, when taken with **ZATYP TABLETS** can cause a condition in the body called ergotism,
- If you are suffering from or have ever suffered from liver disease.

Warnings and Special Precautions

Take special care with ZATYP TABLETS

Your doctor needs to know before you take **ZATYP TABLETS** if you have had any of the following:

- Liver problems: your doctor may need to monitor your liver function or stop the treatment
- If you are taking any ergot derivatives such as ergotamine (used to treat migraine) as these medicines should not be taken together with **ZATYP TABLETS**
- Kidney problems
- Heart conditions
- If you suffer from an autoimmune, neuromuscular disease called myasthenia gravis, your symptoms may become worse, when taking **ZATYP TABLETS.**

Tell your doctor immediately if you feel irregular heart beating in your chest or have an abnormal heartbeat when taking **ZATYP TABLETS**.

If you develop diarrhoea or loose stools during or after treatment, tell your doctor at once. Do not take any medicine to treat your diarrhoea without first checking with your doctor. If your diarrhoea continues, tell your doctor as soon as possible.

Tell your doctor if you develop serious skin reactions or new infections.

Taking other medicines with ZATYP TABLETS :

Always tell your healthcare professional if you are taking any other medicine (this includes complementary or traditional medicines). See **Do not take ZATYP TABLETS**.

Tell your doctor before taking **ZATYP TABLETS** if you are taking any of the medicines listed below:

- Ergot or ergotamine (used to treat migraines) (see Take special care with **ZATYP TABLETS**)
- Antacids (for indigestion)
- Ciclosporin (used to suppress the immune system to prevent and treat rejection of a transplanted organ or bone marrow)
- Digoxin (used to treat heart failure)
- Warfarin or any similar medicine to prevent blood clots

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before you start taking **ZATYP TABLETS.**

The safety and efficacy of **ZATYP TABLETS** in pregnancy and breastfeeding have not been established.

Driving and using machines

ZATYP TABLETS may cause dizziness, convulsions, vertigo, increased sleepiness and temporary loss of consciousness, which may affect your ability to drive and operate machinery.

Important information about some of the ingredients of ZATYP TABLETS

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Lactose may also have an effect on the control of your blood sugar if you have diabetes mellitus.

2. How to take ZATYP TABLETS

Do not share medicines prescribed for you with any other person. Always take **ZATYP TABLETS** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Your doctor will tell you how long your treatment with **ZATYP TABLETS** will last.

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* or *Haemophilus ducreyi*, the dose is 1 g given as a single dose.

ZATYP TABLETS should not be taken by children weighing less than 45 kg. For children weighing more than 45 kg the doses mentioned above are usually prescribed.

If you have the impression that the effect of **ZATYP TABLETS** is too strong or too weak, tell your doctor or pharmacist.

Taking ZATYP TABLETS with food and drink

ZATYP TABLETS may be taken with or without food. They must be taken whole with water.

If you take more ZATYP TABLETS than you should

In the event of overdosage, consult your doctor or pharmacist without delay. If neither is available, contact the nearest hospital or poison control centre.

If you missed a dose of ZATYP TABLETS

It is important that you continue to take your medicine according to the instructions on the label and that you do not miss any doses. However, if you do miss a dose, take it as soon as you remember and take the next dose at the normal time. Do not take a double dose to make up for a forgotten dose.

3. Possible side effects

ZATYP TABLETS can have side effects.

Not all side effects reported for **ZATYP TABLETS** are included in this leaflet. Should your general health worsen or if you experience any unforeseen effects while taking **ZATYP TABLETS**, please consult your doctor, pharmacist or other healthcare professional for advice.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Swelling of the hands, feet, ankles, face, lips, and mouth or throat, which may cause difficulty in swallowing or breathing
- Rash or itching
- Diarrhoea (loose, liquid or watery stools)
- Abdominal pain

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- Abdominal discomfort (pain/cramps), diarrhoea, nausea
- Palpitations (irregular heartbeats)
- Torsade de Pointes (a form of irregular heartbeat)
- Neutropenia (shortness of breath, fatigue, muscle weakness, irregular heartbeat).

The following side effects occur less frequently or with an unknown frequency:

- Nervousness, aggressive reaction, agitation, anxiety
- Oral candidiasis (white, furry, sore tongue and mouth)
- Vaginal infection
- Dizziness (feeling of lightheaded or unbalanced)
- Syncope (fainting or light headedness)
- Convulsion (seizures)
- Paraesthesia (tingling)
- Taste/smell perversion and/or loss
- Hypoaesthesia (increase in sensitivity to stimuli)
- Deafness
- Tinnitis (ringing in the ears)
- Hypotension (low blood pressure)
- Abnormal vision
- Excessive gas, loose stools, vomiting
- Abnormal liver function
- Kidney inflammation
- Black or tarry faeces

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects via the "Adverse Drug Reporting Form", found online under SAHPRA "https://www.sahpra.org.za/Publications/Index/8" By reporting side effects, you can help provide more information on the safety of this medicine.

4. How to store ZATYP TABLETS

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Store at or below 25 °C.

- Keep in original packaging until required for use.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

5. Contents of the pack and other information

What ZATYP TABLETS contains

The active substance is Azithromycin Dihydrate
Calcium Hydrogen Phosphate, Anhydrous
Starch, Pregelatinised
Croscarmellose Sodium
Sodium Lauryl Sulfate
Magnesium Stearate
Opadry II 31K58902 white
Purified water

What ZATYP TABLETS looks like and contents of the pack

ZATYP TABLETS 500 mg

White to off-white, oval shaped, film coated biconvex tablets, debossed with "6" & "7" on either side of the score-line on one side and "D" on other side

Clear PVC Film- Aluminium foil blister pack:

Azithromycin tablets 500 mg are packed in above blisters shall be further packed in preprinted cartons with package leaflet according to the approved pack size.

For 500 mg:

3's: Printed cardboard carton containing 1 blister of 3 tablets each.

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