Klaribin Tablets
P1533504

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AUROGEN

SKEDULERINGSTATUS

S4

EIENDOMSNAAM (en doseervorm)

KLARIBIN TABLETS 250 mg (Tablet)
KLARIBIN TABLETS 500 mg (Tablet)

SAMESTELLING

KLARIBIN TABLETS 250 mg: Elke filmbedekte tablet bevat 250 mg klaritromisien. Suikervry.
KLARIBIN TABLETS 500 mg: Elke filmbedekte tablet bevat 500 mg klaritromisien. Suikervry.

Die ander bestanddele van die formulering is mikrokristallyne sellulose, kroskarmellose- natrium, povidoon, kolloïdale anhidriese silika, en magnesiumstearaat. **KLARIBIN TABLETS 250 mg** en **KLARIBIN TABLETS 500 mg** is met Opadry geel bedek wat bestaan uit hipromellose, propileenglikol, titaandioksied, hidroksipropielsellulose, vanillien, sorbiensuur en ysteroksied geel.

FARMAKOLOGIESE KLASSIFIKASIE

A 20.1.1 Breë- en mediumspektrum antibiotika

FARMAKOLOGIESE WERKING

Farmakodinamika:

Klaritromisien is 'n makroliede-antibiotikum. Dit oefen sy antibakteriële werking uit deur omkeerbaar aan die 50S ribosomale subeenheid van die 70S ribosoom van sensitiewe mikroörganismes te bind, waardeur bakteriële DNS-afhanklike proteïensintese geïnhibeer word. Klaritromisien besit aktiwiteit teen gram +ve en sommige gram -ve organismes. Die volgende is weerstandig:

- Eritromisien-weerstandige isolate van *Streptococcus pneumoniae*.
- Die voorkoms van weerstandigheid is hoër by penisillien-weerstandige stamme.
- Klaritromisien-weerstandige isolate van *H. pylori* het ontluik.
- Weerstandigheid ontwikkel vinnig in *Mycobacterium avium* wanneer klaritromisien as monoterapie gebruik word.

Farmakokinetika:

Klaritromisien word vinnig uit die spysverteringskanaal na orale toediening geabsorbeer, maar sy biobeskikbaarheid word van 55 % tot 50 % verminder as gevolg van vinnige eerste- verbygangmetabolisme. Piek plasmakonsentrasie kom ongeveer 2 uur na toediening voor. Die mate van absorpsie word relatief min deur kos beïnvloed. Klaritromisien kan dus met, of sonder kos, gegee word. Klaritromisien word deur die lewer gemetaboliseer na die aktiewe metaboliet, 14-hidroksiklaritromisien, asook na verskeie ander metaboliete. Beide klaritromisien en 14-hidroksiklaritromisien word wyd deur die liggaam versprei en bereik hoë intrasellulêre konsentrasies. Klaritromisien bereik egter nie beduidende vlakke in die serebrospinale vloeistof nie. Proteïenbinding van klaritromisien wissel van 40 % tot 70 % en is konsentrasie-afhanklik. Die eliminasie halfleeftye van klaritromisien en 14-hidroksi-klaritromisien is ongeveer 3 tot 7 en 5 tot 9 uur onderskeidelik. Langer halfleeftye word na groter dosisse waargeneem. Klaritromisien word deur renale en nie-renale roetes geëlimineer. Die hoeveelheid klaritromisien wat onveranderd in die urine uitgeskei word wissel van 20 % tot 40 % afhangende van die dosis wat toegedien word en die formulering. Tussen 10 % en 15 % van die dosis word in die urine uitgeskei as die 14-hidroksimetaboliet. Alhoewel die farmakokinetika van klaritromisien by pasiënte met hepatiese of renale disfunksie verander is, is dosisaanpassing nie nodig nie tensy 'n pasiënt ly aan ernstige renale disfunksie (kreatinienopruiming van <30 ml/min). Dit wil voorkom dat die eliminasie halfleeftye ook verleng is.

INDIKASIES

KLARIBIN word aangedui vir die behandeling van die volgende ligte tot matig ernstige bakteriële infeksies veroorsaak deur vatbare organismes:

- Onderste lugweginfeksies soos brongitis en pneumonie veroorsaak deur *S. pneumoniae, M. pneumoniae, M. catarrhalis,* of *H. influenzae*.
- Boonste lugweginfeksies soos faringitis en sinusitis as gevolg van *S. pyogenes*.
- Ligte tot matig ernstige akute otitis media as gevolg van *S. pneumoniae, M. catarrhalis* en *H. influenzae*.
- Vel- en sagteweefselinfeksies soos follikulitis, sellulitis of erisipelas as gevolg van *S. aureus*. Uitwissing van *Helicobacter pylori* wanneer dit in kombinasie met 'n protonpompinhibeerder en 'n ander antibiotikum gebruik word om die herhaling van duodenale ulkus te verminder.

KONTRA-INDIKASIES

- Hipersensitiwiteit teen klaritromisien of ander makroliede-antibiotika of enige komponent van **KLARIBIN**.
- Gelyktydige toediening van **KLARIBIN** saam met astemisool, sisapried en pimosied omdat dit QT-verlenging en kardiale disritmieë insluitend ventrikulêre tagikardie, fibrillasie en torsades de pointes mag veroorsaak (Sien "**INTERAKSIES**").
- Porfirie.
- Swangerskap (sien "**SWANGERSKAP EN LAKTASIE**").
- Gelyktydige toediening van **KLARIBIN** saam met ergotamien of dihidroergotamien omdat dit ergot-toksisiteit kan veroorsaak, gekenmerk deur vasospasma en iskemie van die ekstremiteite en sentrale senusisteem wat permanente weefselskade tot gevolg mag hê.
- HMG-KoA-reduktase-inhibeerders (statiene) soos lovastatien of simvastatien wat saam met klaritromisien geneem word, mag die risiko van rabdomiolise verhoog. Behandeling met statiene behoort tydens **KLARIBIN**-behandeling gestaak te word (sien "**WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS** " en "**INTERAKSIES**").
- Kolgisien is teenaangedui by pasiënte op **KLARIBIN** met renale of hepatiese inkorting wat P-glikoproteïen-inhibeerders of 'n sterk CYP3A4-inhibeerder neem (sien"**INTERAKSIES**").

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS

- **KLARIBIN** word deur die lewer gemetaboliseer en in die faeces via die gal uitgeskei. Omsigtigheid behoort uitgeoefen te word by pasiënte met ingekorte hepatiese funksie. Hepatiese disfunksie, insluitend verhoogde lewerensieme en hepatosellulêre en/of cholestatiese hepatitis, met of sonder geelsug is met **KLARIBIN** aangemeld. Hierdie hepatiese disfunksie mag ernstig wees en is gewoonlik omkeerbaar. In sommige gevalle is lewerversaking met noodlottige gevolge aangemeld en is oor die algemeen geassosieer met ernstige onderliggende en/of gelyktydige medikasies. Staak **KLARIBIN** onmiddellik indien tekens en simptome van hepatitis, soos anoreksie, geelsug, donker urine, pruritus of teer buik voorkom.
- Inkorting van renale funksie (ernstig) - Die eliminasie van **KLARIBIN** is verminder by pasiënte met inkorting van renale funksie, veral dié met 'n kreatinienopruiming van <30 ml/min. Die dosis van **KLARIBIN** behoort gehalveer te word of die doseringsinterval moet verdubbel word by pasiënte met 'n kreatinienopruiming van <30 ml/min.
- Rabdomiolise is aangemeld met gelyktydige gebruik van **KLARIBIN** en die HMG-KoAreduktase-inhibeerders, bv. simvastatien, atorvastatien, rosuvastatien en lovastatien. Gelyktydige gebruik van klaritromisien saam met lovastatien of simvastatien is teenaangedui (Sien "**INTERAKSIES**" en "**KONTRA-INDIKASIES**").
- Rifabutien en rifampisien - Mag serumkonsentrasies van **KLARIBIN** met >50 % verminder. Daar is aangemeld dat gelyktydige toediening 'n hoër voorkoms van uveïtis veroorsaak in vergelyking met rifabutien op sy eie (Sien "**INTERAKSIES**").
- Teofillien - Die area onder die plasmakonsentrasie-tyd-kurwe is verhoog. Monitering van teofillienserumkonsentrasies word aanbeveel (Sien "**INTERAKSIES**").
- Kruisweerstand tussen **KLARIBIN** en ander makroliede, linkomisien en klindamisien is aangemeld.
- Langtermyn gebruik van **KLARIBIN** mag kolonisasie met verhoogde getalle van nievatbare bakterieë en swamme veroorsaak. Indien superinfeksies voorkom, behoort toepaslike terapie ingestel te word.
- Pseudomembraneuse kolitis is met makroliede soos **KLARIBIN** aangemeld en mag in erns wissel van lig tot lewensbedreigend. Behandeling met antibakteriële medisyne verander die normale flora van die kolon wat tot oormatige groei van *Clostridium difficile* mag lei. *Clostridium difficile*-geassosieerde diarree (CDAD) is met die gebruik van **KLARIBIN** aangemeld en mag wissel in erns van matige tot fatale kolitis. CDAD moet as diagnose oorweeg word in alle pasiënte wat met diarree presenteer tydens en na die toediening van **KLARIBIN**. 'n Noukeurige mediese geskiedenis is noodsaaklik omdat daar gerapporteer is dat CDAD twee maande na die toediening van 'n antibakteriële middel voorgekom het (sien "**NEWE-EFFEKTE**").
- Indien CDAD sou voorkom, behoort **KLARIBIN** dadelik gestaak, 'n mediese praktisyn geraadpleeg en 'n toepaslike terapie ingestel te word. Anti-peristaltiese medisyne is teenaangedui in hierdie situasie.
- Verergering van simptome van myasthenia gravis is aangemeld in pasiënte wat **KLARIBIN**-terapie ontvang het.
- Omsigtigheid word aanbeveel ten opsigte van gelyktydige toediening van klaritromisien en triasoolbensodiasepiene soos alprasolam, midasolam en triasolam (sien "**INTERAKSIES**").
- Weens die ontluikende weerstand van *Streptococcus pneumoniae* teen makroliede, is dit belangrik dat sensitiwiteitstoetse uitgevoer word wanneer **KLARIBIN** voorgeskryf word vir gemeenskapsverworwe pneumonie. In die geval van hospitaal-verworwe pneumonie, behoort **KLARIBIN** in kombinasie met bykomstige toepaslike antibiotika gebruik te word.
- Vel- en sagte weefselinfeksies word meestal veroorsaak deur *S. aureus* en *S. pyogenes*, wat beide weerstandig teen makroliede mag wees.
- **KLARIBIN** behoort met versigtigheid gebruik te word wanneer dit saam met medisyne toegedien word wat die sitochroom CYP3A4-ensiem induseer (sien "**INTERAKSIES**").
- Die gelyktydige gebruik van **KLARIBIN** en orale hipoglisemiese middels en/of insulien kan beduidende hipoglisemie veroorsaak. Met sekere hipoglisemiese medisyne soos nateglinied, pioglitasoon en repaglinied, mag inhibisie van CYP3A4 deur **KLARIBIN** 'n rol speel en dit kan hipoglisemie veroorsaak as dit gelyktydig gebruik word. Versigtige monitering van glukose word aanbeveel.
- Daar bestaan 'n risiko van ernstige bloeding en beduidende verhogings in INR en protrombientyd as **KLARIBIN** saam met warfarien toegedien word. INR en protrombientyd behoort dikwels gemoniteer te word.
- Behandeling met **KLARIBIN** behoort gestaak te word indien enige tekens van hepatiese disfunksie ontwikkel. Hepatiese disfunksie is gewoonlik omkeerbaar, maar dit kan ernstig wees. In seldsame gevalle is lewerversaking met noodlottige gevolge aangemeld, wat gewoonlik met ander ernstige onderliggende siektes en/of gelyktydige medisyne geassosieer was. Geïsoleerde gevalle van verhoogde serumkreatinien is aangemeld, maar 'n assosiasie met **KLARIBIN** is nie vasgestel nie.
- Berigte van hipoglisemie het voorgekom, waarvan sommige by pasiënte op gelyktydige orale hipoglisemiese middels of insulien was, voorgekom het.
- Nadelige effekte in immuungekompromitteerde pasiënte wat met hoër dosisse **KLARIBIN** oor lang tydperke behandel is, het naarheid, braking, smaakperversie, abdominale pyn, diarree, veluitslag, winderigheid, hoofpyn, gehoorversteuring, AST- en ALT-verhogings, verhoogde BUN-vlakke en abnormaal lae witbloedsel- en plaatjietellings ingesluit. Addisionele lae-frekwensie insidente het dispnee, slaaploosheid en droë mond ingesluit.

Effekte op die vermoë om te bestuur en masjiene te gebruik

Die potensiaal vir duiseligheid, vertigo, verwarring en disoriëntasie moet in ag geneem word voordat pasiënte op **KLARIBIN** bestuur of masjiene gebruik.

INTERAKSIES

- Gelyktydige gebruik van **KLARIBIN** saam met die volgende medisyne is teenaangedui: kolgisien, HMG-KoA-reduktase-inhibeerders en ergotalkaloïede (sien "**KONTRAINDIKASIES**").
- Astemisool, sisapried en pimosied het kardiale disritmieë, insluitend QTc-interval-verlenging, ventrikulêre disritmie, ventrikulêre tagikardie, ventrikulêre fibrillasie en torsades de pointes veroorsaak. Fataliteite het voorgekom. Die mees waarskynlike oorsaak is die inhibisie van metabolisme van hierdie medisyne deur **KLARIBIN** (sien "**KONTRA-INDIKASIES**").
- Induseerders van sitochroom P450 wat die konsentrasie van klaritromisien mag affekteer - Induseerders van CYP3A4 (soos rifampisien, fenitoïen, karbamasepien, fenobarbital, St John se kruid) mag die metabolisme van **KLARIBIN** verhoog en sub-terapeutiese vlakke van **KLARIBIN** veroorsaak wat dan tot verminderde doeltreffendheid mag lei.
- Die volgende medisyne mag die sirkulerende konsentrasies van klaritromisien beïnvloed.

KLARIBIN-dosisaanpassing of oorweging van alternatiewe behandelings mag nodig wees:

- Sterk induseerders van die sitochroom P450 metabolisme sisteem soos efavirens, nevirapien, rifampisien, rifabutien en rifapentien mag die metabolisme van **KLARIBIN** versnel en dus die plasmavlakke van klaritromisien verlaag, terwyl dit die vlakke van die aktiewe metaboliet, 14-OH-klaritromisien verhoog. Omdat die mikrobiologiese aktiwiteit van klaritromisien en 14-OH-klaritromisien verskillend is vir verskillende bakterieë, kan die beoogde terapeutiese effek moontlik tydens gelyktydige toediening van **KLARIBIN** en ensieminduseerders belemmer word.
- **KLARIBIN**-blootstelling mag deur etravirien verminder word: maar konsentrasies van die aktiewe metaboliet, 14-OH-klaritromisien, is verhoog. Omdat 14-OH-klaritromisien verminderde aktiwiteit teen *Mycobacterium avium complex* (MAC) het, mag die algehele aktiwiteit teen hierdie patogeen verander word.
- Inhibeerders van sitochroom P450 wat die konsentrasie van klaritromisien mag beïnvloed:
- Gelyktydige toediening van flukonasool en **KLARIBIN** mag lei tot verhogings in die gemiddelde ewewigstoestand minimum klaritromisienkonsentrasie en area onder die kurwe. Ewewigstoestand konsentrasies van die aktiewe metaboliet, 14-OH-klaritromisien word nie beduidend verhoog nie. Dosisaanpassing van **KLARIBIN** is nie nodig nie.
- Beide klaritromisien en atasanavir is substrate en inhibeerders van CYP3A en daar is bewyse van 'n twee-rigting interaksie. Gelyktydige toediening van **KLARIBIN** saam met atasanavir en sakinavir mag lei tot 'n groot toename in die blootstelling aan klaritromisien en verhogings in die plasmakonsentrasies van atasanavir en sakinavir. Vir pasiënte op atasanavir met renale inkorting, behoort dieselfde dosisverminderings soos met ritonavir gevolg te word.
- Gelyktydige toediening van **KLARIBIN** en itrakonasool mag beide se plasmavlakke verhoog. Pasiënte op albei van hierdie medisyne behoort gemoniteer te word vir tekens of simptome van verhoogde of verlengde farmakologiese effek.
- Medisyne wat deur die sitochroom P450 ensiemsisteem (CYP3A4) gemetaboliseer word, mag deur **KLARIBIN** as 'n ensieminhibeerder geaffekteer word, byvoorbeeld: alprasolam, siklosporien, disopiramied, ergotalkaloïede, karbamasepien, metielprednisoloon, midasolam, omeprasool, kinidien, sildenafiel, simvastatien, takrolimus, triasolam, vinblastien, fenitoïen, en valproaat - **KLARIBIN** mag dus met verhoogde vlakke van hierdie medisyne geassosieer word. Serumkonsentrasies van hierdie medisyne mag monitering benodig veral medisyne met 'n klein veiligheidsgrens soos teofillien en karbamasepien. Rabdomiolise is aangemeld met gelyktydige gebruik van **KLARIBIN** en die HMG-KoA-reduktase-inhibeerders, bv. simvastatien en lovastatien (Sien "**WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**" en "**KONTRA-INDIKASIES**").
- Gelyktydige gebruik van **KLARIBIN** en medisyne wat QT-verlenging, kardiale disritmieë of torsades de pointes veroorsaak, behoort met versigtigheid gebruik te word. Die serumvlakke van kinidien of disopiramied en EKGs behoort tydens terapie met **KLARIBIN** gemoniteer te word.
- Gelyktydige toediening van klaritromisien en orale of IV toediening van midasolam verhoog onderskeidelik die midasolam AOK 7- en 2,7-voudig. Gelyktydige toediening van **KLARIBIN** saam met orale midasolam behoort vermy te word en met IV midasolam behoort die pasiënt noukeurig gemoniteer te word. Dieselfde voorsorgmaatreëls behoort ook toegepas te word op ander bensodiasepiene wat deur CYP3A4 gemetaboliseer word, insluitend alprasolam en triasolam. Nadelige SSS-effekte soos lomerigheid en verwarring het voorgekom.
- Gelyktydige gebruik van **KLARIBIN** en kolgisien veral by bejaardes, wat in sommige gevalle voorgekom het in pasiënte met renale ontoereikendheid, mag kolgisientoksisiteit veroorsaak. Sterftes is in sommige van hierdie pasiënte aangemeld (sien "**KONTRA-INDIKASIES**").
- Gelyktydige toediening van klaritromisien en fosfodiësterase-tipe-5- (PDE5)inhibeerders mag tot verhoogde (PDE5) inhibeerder blootstelling lei. Vermindering van die doserings van sildenafiel, tadalafiel en vardenafiel behoort oorweeg te word wanneer hierdie medisyne saam met **KLARIBIN** toegedien word.
- Vermindering in die dosering van tolterodien mag nodig wees in die teenwoordigheid van CYP3A4-inhibeerders soos **KLARIBIN** in die subgroep van pasiënte by wie die CYP2D6-ensiem ontbreek.
- Gelyktydige toediening van omeprasool en **KLARIBIN** het tot verhogings in die gemiddelde ewewigstoestand konsentrasie en area onder die kurwe van omeprasool gelei. Die gastriese pH verhoog. Die konsentrasie van klaritromisien (soos in **KLARIBIN**) neem ook toe in gastriese weefsel en slym, en tot 'n mindere mate in plasma gedurende die gebruik van omeprasool.
- Omdat verhoogde serumvlakke aangemeld is met fenitoïen en valproaat in kombinasie met CYP3A4-inhibeerders, insluitend klaritromisien, word bepalings van serumvlakke aanbeveel vir hierdie medisyne wanneer dit gelyktydig met **KLARIBIN** toegedien word.
- Hipotensie bradidisritmieë en laktiese asidose is waargeneem by pasiënte wat klaritromisien (soos in **KLARIBIN**) en verapamiel gelyktydig geneem het.
- Rifabutien en rifampisien - Mag serumkonsentrasies van **KLARIBIN** met >50 % verminder. Daar word berig dat gelyktydige toediening 'n hoër voorkoms van uveïtis veroorsaak in vergelyking met rifabutien alleen (Sien "**WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**").
- Teofillien en karbamasepien - Die area onder die plasmakonsentrasie-tydkurwes is verhoog met gelyktydige gebruik saam met **KLARIBIN**. Monitering van die serumkonsentrasies van hierdie medisyne word aanbeveel (Sien "**WAARSKUWINGS EN SPESIAL VOORSORGMAATREËLS**").
- Antikoagulante soos warfarien - **KLARIBIN** mag die effekte van warfarien versterk. Protrombientyd of INR behoort noukeurig gemoniteer te word.
- Digoksien - Daar kon aangedui word dat **KLARIBIN** die serumkonsentrasies van digoksien verhoog het en tot digoksientoksisiteit, insluitend fatale disritmieë, gelei het. Monitering van die serumkonsentrasies van digoksien word aanbeveel.
- Sidovudien - 'n Afname in die ewewigstoestand konsentrasie van sidovudien mag voorkom. Dosisse van sidovudien en **KLARIBIN** behoort ten minste 4 uur uitmekaar geneem te word.

SWANGERSKAP EN LAKTASIE

Die veiligheid en doeltreffendheid in swangerskap en laktasie is nie vasgestel nie. **KLARIBIN** word in borsmelk uitgeskei.

KLARIBIN behoort nie tydens swangerskap gebruik te word nie, omdat die gebruik daarvan met embriotoksisiteit by diere geassosieer is.

DOSIS EN GEBRUIKSAANWYSINGS

Kinders:
Die veiligheid en doeltreffendheid in suigelinge onder die ouderdom van 6 maande is nie vasgestel nie. Hierdie formulering is nie gekik vir gebruik by kinders jonger as 12 jaar nie.

Volwassenes en kinders ouer as 12 jaar: 250 mg twee keer daagliks. In meer ernstige infeksies, mag die dosis tot 500 mg twee keer daagliks verhoog word.

Renale inkorting:
Kreatinienopruiming (> 30 ml/min): Verminder dosis met die helfte, d.i. 250 mg een keer daagliks of 250 mg twee keer daagliks vir ernstige infeksies. Beperk die duur van behandeling tot 14 dae. **Uitwissing van *H. pylori***

Volwassenes:
500 mg twee keer daagliks in kombinasie met 'n toepaslike antibiotikum en 'n suur-verlagende middel vir 7 tot 10 dae. Die veiligheid en doeltreffendheid van **KLARIBIN** in kombinasie met protonpompinhibeerders behalwe omeprasool is nie vasgestel nie.

Gelyktydige gebruik van ritonavir

Die metabolisme van **KLARIBIN** word geïnhibeer. Geen dosisvermindering van **KLARIBIN** is nodig by pasiënte met normale renale funksie. Pasiënte met inkorting van renale funksie het 'n verlaging in die dosis van **KLARIBIN** nodig, soos volg:

- Kreatinienopruiming 30 tot 60 ml/min - Verminder dosis met 50 %.
- Kreatinienopruiming <30 ml/min - Verminder dosis met 75 %. Moenie 'n dosis van 1 g/dag tydens gelyktydige toediening van **KLARIBIN** en ritonavir oorskry nie. Daar is gesuggereer dat ander MIV-protease-inhibeerders en nie-nukleosied omkeringstranskriptase-inhibeerders 'n soortgelyke effek op **KLARIBIN** mag hê. **KLARIBIN** mag met, of sonder maaltye, geneem word.

NEWE-EFFEKTE

Infeksies en infestasie:
Minder frekwent: Orale candidiase, gastroënteritis, vaginale infeksie, pseudomembraneuse kolitis, erisipelas, eritrasma.

Bloed- en limfatiese sisteemversteurings:
Minder frekwent: Leukopenie, trombositopenie, agranulositose.

Immuunsisteemversteurings:
Minder frekwent: Allergiese reaksies, anafilakse.

Endokriene versteurings:
Minder frekwent: Hipoglisemie.

Metabolisme en voedingversteurings:
Minder frekwent: Anoreksie, verminderde aptyt, hipoglismie.

Psigiatriese versteurings:
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: Angs, slaaploosheid, hallusinasies, slegte drome, depersonalisasie, psigotiese versteuring, depressie.

Senusisteemversteurings:
Frekwent: Hoofpyn. *Die volgende newe-effekte is aangemeld en die frekwensies is onbekend:* Duiseligheid, vertigo, disoriëntasie, verwarring, konvulsies, tremor, parosmie, anosmie, disgeusie en ageusie.

Oor- en doolhofversteurings:
Minder frekwent: Gehoorverlies, vertigo en tinnitus.

Kardiale versteurings:
Minder frekwent: QT-verlenging, ventrikulêre tagikardie, torsades de pointes en hartkloppings.

Respiratoriese, torakale en mediastinale versteurings:
Minder frekwent: Epistakse.

Gastroïntestinale versteurings:
Frekwent: Naarheid, braking, abdominale pyn, abnormale smaak, diarree. *Minder frekwent*: Glossitis, stomatitis, orale candidiase, verkleuring van die tong, verkleuring van die tande, pseudomembraneuse kolitis (abdominale krampe of pyn, teerheid, ernstige, waterige diarree wat ook bloederig mag wees, koors), dispepsie, gastroïntestinale refluks, gastritis, proktalgie, hardlywigheid, droë mond, eruktasie en akute pankreatitis.

Hepatobiliêre versteurings:
Minder frekwent: Toename in lewerensieme, hepatosellulêre en/of cholestatiese hepatitis (met of sonder geelsug), en lewerversaking.

Vel- en onderhuidse weefselversteurings:
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: Hiperhidrose, pruritus, ligte velerupsies, aknee, urtikarie, Stevens-Johnson-sindroom, toksiese epidermale nekrolise, geneesmiddeluitslag met eosinofilie en sistemiese simptome (DRESS) en Henoch-Schönlein se purpura.

Muskuloskeletale, bindweefsel- en beenversteurings:
Minder frekwent: Mialgie, rabdomiolise en miopatie.

Renale en urinêre versteurings:
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: Interstisiële nefritis en nierversaking.

Algemene versteurings en toestande by die toedieningsplek:
Minder frekwent: Astenie.

Ondersoeke:
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: Verhoogde INR en verlengde protrombientyd, abnormale globulienverhouding.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN Sien **"NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS".**

Simptome van oordosis

Inname van groot hoeveelhede **KLARIBIN** kan verwag word om gastroïntestinale simptome te veroorsaak. Nadelige reaksies wat oordosis begelei, behoort behandel te word deur die vinnige eliminasie van ongeabsorbeerde medisyne en ondersteunende maatreëls. Veranderde geestestoestand, paranoïede gedrag, hipokalemie en hipoksie mag voorkom.

Behandeling van oordosis

Behandeling is simptomaties en ondersteunend. Daar word nie verwag dat **KLARIBIN** merkbaar deur hemodialise of dialise beïnvloed sal word nie.

IDENTIFIKASIE

KLARIBIN TABLETS 250 mg: Ligte geelkleurige, ovaalvormige, bikonvekse filmbedekte tablette, met 'D' gedebosseleer op een kant en '62' op die ander kant.

KLARIBIN TABLETS 500 mg: Ligte geelkleurige, ovaalvormige, bikonvekse filmbedekte tablette, met 'D' gedebosseleer op een kant en '63' op die ander kant.

AANBIEDING

KLARIBIN TABLETS 250 mg:

1. **PVC/PVdC Stulpverpakking:**
Tablette word verpak in helder 250 mikron PVC wat met 60 gvm PVdC-film bedek is en gedrukte aluminiumfoelie, met 'n 6-8 gvm hitte-seël vernis. Verpakkingsgrootte: 10e - Elke karton bevat 1 stulpverpakking van 10 tablette. 14s - Elke karton bevat 1 stulpverpakking van 14 tablette.

2. **HDPE-Houer Verpakking:**
Tablette word verpak in 'n 100 ml wit HDPE-houer met 'n 38 mm nek-afwerking (OFC 113 ml) met 'n 38 mm-400RS wit sluitstuk met 'n induksie seël pluisie. Verpakkingsgrootte: -100s- Een HDPE-houer van 100 tablette.

KLARIBIN TABLETS 500 mg:

1. **PVC/PVdC Stulpverpakking:**
Tablette word verpak in helder 250 mikron PVC wat met 60 gvm PVdC-film bedek is en gedrukte aluminiumfoelie, met 'n 6-8 gvm hitte-seël vernis. Verpakkingsgrootte: 10e - Elke karton bevat 1 stulpverpakking van 10 tablette. 14s - Elke karton bevat 1 stulpverpakking van 14 tablette.

2. **HDPE-Houer Verpakking:**
Tablette word verpak in 'n 120 ml wit HDPE-houer met 'n 38 mm nek-afwerking (OFC 138 ml) met 'n 38 mm-400RS wit sluitstuk met 'n induksie seël pluisie. Verpakkingsgrootte: 100s- Een HDPE-houer van 100 tablette.

BERGINGSINSTRUKSIES

Bewaar by of benede 25 oC.

Beskerm teen vog.

Hou die HDPE-houers dig gesluit.

Hou die stulpverpakkings in die karton totdat dit vir gebruik benodig word.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS

KLARIBIN TABLETS 250 mg: 42/20.1.1/0852

KLARIBIN TABLETS 500 mg: 42/20.1.1/0853

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

Aurogen South Africa (Edms) Bpk
Woodhill Kantoorpark, Gebou Nr. 1 Eerste Vloer
Phillip Engelbrechtlaan 53,
Meyersdal, Uitbr. 12, Johannesburg,
1448, Suid Afrika.

DATUM VAN PUBLIKASIE VAN DIE VOUBILJET

Datum van registrasie:
01 Julie 2014

Datum van hersiening:
01 Januarie 2023

✂ DETACH BEFORE DISPENSING

S4

KLARIBIN TABLETS 250 mg (Tablet)
KLARIBIN TABLETS 500 mg (Tablet)

Klaritromisien

Lees hierdie hele brosjure versigtig voordat jy begin om KLARIBIN te neem.
- Hou hierdie brosjure. Jy mag dit weer moet lees.
- Indien jy verdere vrae het, vra asseblief jou dokter of jou apteker daaroor.
- **KLARIBIN** is vir jou persoonlik voorgeskryf en jy behoort nie jou medisyne met ander persone te deel nie. Dit kan hulle skade aandoen, al is hulle simptome dieselfde as joune.

1. WAT KLARIBIN BEVAT

Die aktiewe stof is klaritromisien.

KLARIBIN TABLETS 250 mg: Elke filmbedekte tablet bevat 250 mg klaritromisien. Suikervry.
KLARIBIN TABLETS 500 mg: Elke filmbedekte tablet bevat 500 mg klaritromisien. Suikervry.

Die ander bestanddele is sellulose mikrokristallyn, kroskarmellose-natrium, magnesiumstearaat, Opadry geel (hipromellose, propileenglikol, titaandioksied, hidroksipropielsellulose, vanillien, sorbiensuur en ysteroksied geel), povidoon en silika kolloïdaal anhidries.

2. WAAROOR KLARIBIN GEBRUIK WORD

KLARIBIN word aangedui vir die simptomatiese behandeling van:
- Borsinfeksies soos brongitis en longontsteking.
- Keel- en sinusinfeksies soos faringitis en sinusitis.
- Ligte tot matig ernstige akute otitis media (infeksie van die middeloor).
- Vel- en sagte weefselinfeksies.
- Uitwissing van *Helicobacter pylori* (die bakterie wat verantwoordelik is vir die ontstaan van gastriese of duodenale ulkusse) wanneer dit in kombinasie met 'n protonpompinhibeerder en 'n ander antibiotikum gebruik word om die herhaling van duodenale ulkus te verminder.

3. VOORDAT JY KLARIBIN NEEM

Moenie KLARIBIN neem nie:
- Indien jy 'n hipersensitiwiteit teen klaritromisien of enige makroliedeantibiotika of enige ander komponent van die formulering het.
- Indien jy astemisool, sisapried of pimosied neem.
- Indien jy aan porfirie ly.
- Indien jy swanger is.
- Indien jy ergotamien of dihidroergotamien neem wat algemeen gebruik word om migraine te behandel, omdat die kombinasie met **KLARIBIN** vernouing van die bloedvate kan veroorsaak wat 'n afname in die suurstoftoevoer na die brein en hande en voete kan veroorsaak wat uiteindelik weefselskade tot gevolg kan hê.
- Indien jy statiene neem, bv. simvastatien en lovastatien, medisyne wat gebruik word om hoë cholesterol te behandel, omdat dit die risiko van rabdomiolise, die afbraak van beskadigde spierweefsel, kan verhoog.
- Indien jy kolgisien neem, 'n medisyne wat gebruik word om jig te behandel.

Neem spesiale sorg met KLARIBIN:
- Indien jy aan lewerprobleme ly. Indien jy vergeling van die vel en die wit dele van die oë ontwikkel, en aan abdominale pyn en teerheid, donker urine en erg jeukerige vel ly, behoort jy dadelik die inname van **KLARIBIN** te staak.
- Indien jy aan nierprobleme ly - die eliminasie van **KLARIBIN** is verminder by pasiënte met inkorting van nierfunksie, veral dié met 'n kreatinienopruiming van <30 ml/min.
- Indien jy rifabutien en/of rifampisien neem, omdat die kombinasie 'n afname van **KLARIBIN** in jou bloed sal veroorsaak. Daar word aangemeld dat gelyktydige toediening 'n hoër voorkoms van uveïtis, 'n inflammasie van deel van die oog, veroorsaak in vergelyking met wanneer rifabutien alleen geneem word.
- Indien jy teofillien neem, 'n medisyne wat gebruik word om jou lugweë oop te maak sodat jy beter kan asemhaal.
- Indien jy erge diarree ondervind as gevolg van **KLARIBIN**, mag jy aan pseudomembraneuse kolitis ly.
- Indien jy bensodiasepiene, bv. midasolam, triasolam of alprasolam neem, medisyne wat gebruik word as spierverslappers en om angs te behandel.
- Indien jy medisyne soos insulien neem wat bloedglukose verlaag, omdat dit hipoglisemie kan veroorsaak, waar jou bloedglukosevlak te veel daal.

Neem van KLARIBIN saam met kos en drank:
Jy mag **KLARIBIN** met, of sonder kos, neem.

Swangerskap en Borsvoeding:
Indien jy swanger is of jou baba borsvoed, behoort jy nie **KLARIBIN** te neem nie omdat die veiligheid en doeltreffendheid in swangerskap en borsvoeding nie vasgestel is nie. **KLARIBIN** word in borsmelk uitgeskei.

Indien jy swanger is of jou baba borsvoed, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir advies raadpleeg voordat jy **KLARIBIN** neem.

Bestuur en gebruik van masjiene:
Moenie bestuur of masjiene gebruik nie, voordat jy weet hoe **KLARIBIN** jou sal affekteer.

Neem van ander medisyne saam met KLARIBIN:
- Jy behoort **KLARIBIN** nie saam met kolgisien (medisyne vir jig), statiene (medisyne vir hoë cholesterol) of migraine-medikasies te neem nie.
- Die inname van **KLARIBIN** saam met astemisool, sisapried of pimosied mag onreëlmatige hartritmes veroorsaak en kan fataal wees.
  - Medisyne soos rifampisien, fenitoïen, karbamasepien, fenobarbital, efavirens, etravirien, en St. John se kruid mag die metabolisme van **KLARIBIN** verhoog en dus sy doeltreffendheid verminder.
  - Swamwerende middels soos flukonasool en itrakonasool en antiretrovirale middels soos atasanavir en sakinavir mag die bloedkonsentrasie van **KLARIBIN** verhoog.
  - Ander medisyne wat deur **KLARIBIN** geaffekteer mag word, sluit siklosporien, disopiramied, karbamasepien, metielprednisoloon, omeprasool, kinidien, sildenafiel, takrolimus, triasolam, vinblastien, digoksien, sidovudien, fenitoïen, en valproaat, in.
  - Indien jy warfarien neem of enige ander medisyne wat die bloed verdun.
  - Indien jy immuungekompromitteerd is en met hoër dosisse **KLARIBIN** vir 'n lang tydperk behandel is, mag jy die volgende ondervind: naarheid, braking, smaakperversie, abdominale pyn, diarree, veluitslag, winderigheid, hoofpyn, en gehoorversteuring.

Jy moet altyd jou gesondheidsorgdeskundige vertel indien jy enige ander medisyne neem. (Dit sluit komplementêre of tradisionele medisyne in).

4. HOE OM KLARIBIN TE NEEM

Neem **KLARIBIN** altyd presies volgens jou dokter se instruksies. Jy behoort met jou dokter of apteker te gesels indien jy nie seker is nie. Indien jy onder die indruk verkeer dat die effek van **KLARIBIN** te sterk of te swak is, gesels met jou dokter of apteker daaroor.

Kinders:
Die veiligheid en doeltreffendheid in suigelinge onder die ouderdom van 6 maande is nie vasgestel nie. **KLARIBIN** is nie gekik vir gebruik by kinders jonger as 12 jaar nie.

Volwassenes en kinders ouer as 12 jaar:
250 mg twee keer daagliks. In meer ernstige infeksies, mag die dosis tot 500 mg twee keer daagliks verhoog word.

KLARIBIN kan met of sonder kos geneem word. Jou dokter sal 'n toepaslike dosis volgens jou toestand voorskryf.

Indien jy meer KLARIBIN neem as wat jy behoort te neem:

In 'n geval van oordosis, raadpleeg jou dokter of apteker. Indien beide nie beskikbaar is nie, moet jy die naaste hospitaal of gifbeheersentrum kontak.

Indien jy vergeet om KLARIBIN te neem:
Moenie 'n dubbele dosis neem om op te maak vir vergete individuele dosisse nie.

5. MOONTLIKE NEWE-EFFEKTE

KLARIBIN kan newe-effekte veroorsaak. Indien jy enige van die volgende simptome ondervind, staak inname van

KLARIBIN en vertel jou dokter dadelik daarvan:
- Allergiese reaksie waar jy probleme het om asem te haal
- Duiseligheid, versteurde visie of floutes omdat jy lae bloedglukosevlakke mag hê.
- Onreëlmatige hartslae, byvoorbeeld te vinnig of te stadig.
- Ernstige afskilferende veluitslag wat na jou mond of oë mag versprei.
- Vergeling van jou vel en die wit dele van die oë, donker urine of 'n pynlike, teer buik omdat jy geelsug mag hê. Indien jy enige van die volgende simptome ondervind, moet jy jou dokter so gou as moontlik daarvan vertel:
- Abdominale krampe of pyn, teerheid, ernstige, waterige diarree wat ook bloederig mag wees, koors
- Konvulsies
- Disoriëntasie
- Spierpyn Dit is almal ernstige newe-effekte. Jy het moontlik dringende mediese aandag nodig. Vertel jou dokter indien jy van enige van die volgende bewus word:
- Orale sproei, of 'n vaginale infeksie
- Verminderde aptyt
- Angs
- Slaaploosheid
- Hallusinasies
- Slegte drome
- Depersonalisasie
- Depressie
- Duiseligheid
- Vertigo
- Verwarring
- Tremor
- Gehoorverlies
- Tinnitus (gesuis in die ore)
- Naarheid
- Braking
- Spierpyn

Nie alle newe-effekte wat vir **KLARIBIN** aangemeld is, word in hierdie brosjure ingesluit nie. Indien jou algemene gesondheid sou vererger of as jy enige nadelige effekte ondervind terwyl jy hierdie medisyne neem, moet jy asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir advies raadpleeg.

6. BERGING EN WEGDOENING VAN KLARIBIN

Bewaar alle medisyne buite bereik van kinders.

Bewaar by of benede 25 C.

Beskerm teen vog.

Hou die HDPE-houers dig gesluit.

Hou die stulpverpakkings in die karton totdat hulle vir gebruik benodig word.

Gee alle ongebruikte medisyne terug aan jou apteker. Moenie ongebruikte medisyne in dreine of rioolsisteme (bv. toilette) weggooi nie.

7. AANBIEDING VAN KLARIBIN

KLARIBIN TABLETS 250 mg:

1. **PVC/PVdC Stulpverpakking:**
Tablette word verpak in helder 250 mikron PVC wat met 60 gvm PVdC-film bedek is en gedrukte aluminiumfoelie, met 'n 6-8 gvm hitte-seël vernis. Verpakkingsgrootte: 10e - Elke karton bevat 1 stulpverpakking van 10 tablette. 14s - Elke karton bevat 1 stulpverpakking van 14 tablette.

2. **HDPE-Houer Verpakking:**
Tablette word verpak in 'n 100 ml wit HDPE-houer met 'n 38 mm nek-afwerking (OFC 113 ml) met 'n 38 mm-400RS wit sluitstuk met 'n induksie seël pluisie. Verpakkingsgrootte: 100s- Een HDPE-houer van 100 tablette.

KLARIBIN TABLETS 500 mg:

1. **PVC/PVdC Stulpverpakking:**
Tablette word verpak in helder 250 mikron PVC wat met 60 gvm PVdC-film bedek is en gedrukte aluminiumfoelie, met 'n 6-8 gvm hitte-seël vernis. Verpakkingsgrootte: 10e - Elke karton bevat 1 stulpverpakking van 10 tablette. 14s - Elke karton bevat 1 stulpverpakking van 14 tablette.

2. **HDPE-Houer Verpakking:**
Tablette word verpak in 'n 120 ml wit HDPE-houer met 'n 38 mm nek-afwerking (OFC 138 ml) met 'n 38 mm-400RS wit sluitstuk met 'n induksie seël pluisie. Verpakkingsgrootte: 100s- Een HDPE-houer van 100 tablette.

8. IDENTIFIKASIE VAN KLARIBIN

KLARIBIN TABLETS 250 mg: Ligte geelkleurige, ovaalvormige, bikonvekse filmbedekte tablette, met 'D' gedebosseleer op een kant en '62' op die ander kant.
KLARIBIN TABLETS 500 mg: Ligte geelkleurige, ovaalvormige, bikonvekse filmbedekte tablette, met 'D' gedebosseleer op een kant en '63' op die ander kant.

9. REGISTRASIENOMMER/ VERWYSINGSNOMMER

KLARIBIN TABLETS 250 mg: 42/20.1.1/0852
KLARIBIN TABLETS 500 mg: 42/20.1.1/0853

10. NAAM EN ADRES VAN DIE REGISTRASIEHOUER

Aurogen South Africa (Edms) Bpk
Woodhill Kantoorpark, Gebou Nr. 1 Eerste Vloer
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1448, Suid Afrika.

11 DATUM VAN PUBLIKASIE

Datum van registrasie:
01 Julie 2014

Datum van hersiening:
01 Januarie 2023

SCHEDULING STATUS

S4

PROPRIETARY NAME (and dosage form)

KLARIBIN TABLETS 250 mg (Tablet)
KLARIBIN TABLETS 500 mg (Tablet)

COMPOSITION

KLARIBIN TABLETS 250 mg: Each film-coated tablet contains 250 mg clarithromycin. Sugar free.
KLARIBIN TABLETS 500 mg: Each film-coated tablet contains 500 mg clarithromycin. Sugar free.

The other ingredients of the formulation are microcrystalline cellulose, croscarmellose sodium, povidone, colloidal anhydrous silica, and magnesium stearate. **KLARIBIN TABLETS 250 mg** and **KLARIBIN TABLETS 500 mg** are coated with Opadry yellow which is composed of hypromellose, propylene glycol, titanium dioxide, hydroxypropylcellulose, vanillin, sorbic acid and iron oxide yellow.

PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION

Pharmacodynamics:

Clarithromycin is a macrolide antibiotic. It exerts its antibacterial action by binding reversibly to the 50S ribosomal subunit of the 70S ribosome of sensitive micro organisms, thereby inhibiting bacterial RNA-dependant protein synthesis. Clarithromycin has activity against gram +ve and some gram –ve organisms. The following are resistant:

- Erythromycin-resistant isolates of *Streptococcus pneumoniae.*
- Incidence of resistance is higher among penicillin-resistant strains.
- Clarithromycin-resistant isolates of *H. pylori* have emerged.
- Resistance develops rapidly in *Mycobacterium avium* when clarithromycin is used as monotherapy.

Pharmacokinetics:

Clarithromycin is absorbed rapidly from the gastro-intestinal tract after oral administration, but its bioavailability is reduced to 50 % from 55 % because of rapid first-pass metabolism. Peak plasma concentration occurs approximately 2 hours after administration. The extent of absorption is relatively unaffected by food. Clarithromycin may therefore be given with or without food. Clarithromycin is metabolised by the liver to the active metabolite, 14-hydroxyclarithromycin, as well as to several other metabolites. Both clarithromycin and 14-hydroxyclarithromycin are distributed widely throughout the body and achieve high intracellular concentrations. Clarithromycin does not achieve significant levels in the cerebrospinal fluid. Protein binding of clarithromycin ranges from 40 % to 70 % and is concentration-dependent. The elimination half-lives of clarithromycin and 14-hydroxyclarithromycin are approximately 3 to 7 and 5 to 9 hours respectively. Longer half-lives are observed after larger doses. Clarithromycin is eliminated by renal and non-renal routes. The amount of clarithromycin excreted unchanged in the urine ranges from 20 % to 40 %, depending on the dose administered and the formulation. Between 10 % and 15 % of the dose is excreted in the urine as the 14-hydroxy metabolite. Although the pharmacokinetics of clarithromycin is altered in patients with hepatic or renal dysfunction, dosage adjustment is not necessary unless a patient has severe renal dysfunction (creatinine clearance of <30 ml/min). The elimination half-lives also appear to be lengthened.

INDICATIONS

KLARIBIN is indicated for the treatment of the following mild to moderately severe bacterial infections caused by susceptible organisms:

- Lower respiratory tract infections such as bronchitis and pneumonia caused by *S. pneumoniae*, *M. pneumoniae*, *M. catarrhalis*, or *H. influenzae.*
- Upper respiratory tract infections such as pharyngitis and sinusitis due to *S. pyogenes.*
- Mild to moderately severe acute otitis media due to *S. pneumoniae, M. catarrhalis* and *H. influenzae.*
- Skin and soft tissue infections such as folliculitis, cellulitis or erysipelas due to *S. aureus.*

Eradication of *Helicobacter pylori* when used in combination with a proton pump inhibitor and another antibiotic to decrease recurrence of duodenal ulcer.

CONTRA-INDICATIONS

- Hypersensitivity to clarithromycin or other macrolide antibiotics or to any component of **KLARIBIN**.
- Concomitant administration of **KLARIBIN** with astemizole, cisapride and pimozide as this may result in QT prolongation and cardiac dysrhythmias including ventricular tachycardia, fibrillation and torsades de pointes (See **"INTERACTIONS"**).
- Porphyria.
- Pregnancy (see **"PREGNANCY AND LACTATION")**
- Concomitant administration of **KLARIBIN** with ergotamine or dihydroergotamine as this may result in ergot toxicity characterised by vasospasm and ischaemia of the extremities and central nervous system resulting in permanent tissue damage.
- HMG-CoA reductase inhibitors (statins) such as lovastatin or simvastatin taken with clarithromycin may increase the risk of rhabdomyolysis. Treatment with statins should be discontinued during **KLARIBIN** treatment (see **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"INTERACTIONS"**).
- Colchicine is contra-indicated in patients on **KLARIBIN** with renal or hepatic impairment who are taking P-glycoprotein inhibitors or a strong CYP34A inhibitor (see **"INTERACTIONS"**).

WARNINGS AND SPECIAL PRECAUTIONS

- **KLARIBIN** is metabolised by the liver and excreted in faeces via the bile. Caution should be exercised in patients with impaired hepatic function. Hepatic dysfunction, including increased liver enzymes and hepato-cellular and/or cholestatic hepatitis, with or without jaundice, has been reported with **KLARIBIN**. This hepatic dysfunction may be severe and is usually reversible. In some instances hepatic failure with fatal outcome has been reported and generally has been associated with serious underlying and/or concomitant medications. Discontinue **KLARIBIN** immediately if signs and symptoms of hepatitis occur, such as anorexia, jaundice, dark urine, pruritus or tender abdomen.
- Renal function impairment (severe) - The elimination of **KLARIBIN** is reduced in patients with renal function impairment, especially those with a creatinine clearance of <30 ml/min. The dose of **KLARIBIN** should be halved or the dosing interval doubled in patients with a creatinine clearance of <30 ml/min.
- Rhabdomyolysis has been reported with concomitant use of **KLARIBIN** and the HMG-CoA reductase inhibitors e.g. simvastatin, atorvastatin, rosuvastatin and lovastatin. Concomitant use of clarithromycin with lovastatin or simvastatin is contra-indicated (See **"INTERACTIONS"** and **"CONTRA-INDICATIONS"**).
- Rifabutin and rifampicin - May decrease serum concentration of **KLARIBIN** by >50 %. Coadministration has been reported to cause a higher incidence of uveitis compared to rifabutin alone (See **"INTERACTIONS"**).
- Theophylline - The area under the plasma concentration-time curve is increased. Monitoring of theophylline serum concentrations is recommended (See **"INTERACTIONS"**).
- Cross-resistance between **KLARIBIN** and other macrolides, lincomycin and clindamycin have been reported.
- Long term use of **KLARIBIN** may result in colonisation with increased numbers of nonsusceptible bacteria and fungi. If super-infections occur, appropriate therapy should be instituted.
- Pseudomembranous colitis has been reported with macrolides such as **KLARIBIN** and may range in severity from mild to life threatening. Treatment with antibacterial medicines alters the normal flora of the colon, which may lead to overgrowth of *Clostridium difficile. Clostridium difficile* associated diarrhoea (CDAD) has been reported with the use of **KLARIBIN** and may range in severity from mild to fatal colitis. CDAD must be considered as diagnosis in all patients who present with diarrhoea during or subsequent to the administration of **KLARIBIN**. Careful medical history is necessary since CDAD has been reported to occur two months after the administration of an antibacterial agent (see **"SIDE EFFECTS"**).
- Should CDAD occur, **KLARIBIN** should immediately be discontinued, a medical practitioner be consulted and an appropriate therapy initiated. Antiperistaltic medicines are contra-indicated in this situation.
- Exacerbation of symptoms of myasthenia gravis has been reported in patients receiving **KLARIBIN** therapy.
- Caution is advised regarding concomitant administration of clarithromycin and triazolobenzodiazepines such as alprazolam, midazolam and triazolam (see **"INTERACTIONS"**).
- In view of the emerging resistance of *Streptococcus pneumoniae* to macrolides, it is important that sensitivity testing be performed when prescribing **KLARIBIN** for community acquired pneumonia. In hospital-acquired pneumonia, **KLARIBIN** should be used in combination with additional appropriate antibiotics.
- Skin and soft tissue infections are most often caused by *S. aureus* and *S. pyogenes*, both of which may be resistant to macrolides.
- **KLARIBIN** should be used with caution when administered concurrently with medicines that induce the cytochrome CYP3A4 enzyme (see **"INTERACTIONS"**)
- The concomitant use of **KLARIBIN** and oral hypoglycaemic agents and/or insulin can result in significant hypoglycaemia. With certain hypoglycaemic medicines such as nateglinide, pioglitazone and repaglinide, inhibition of CYP3A4 by **KLARIBIN** may be involved and could cause hypoglycaemia when used concomitantly. Careful monitoring of glucose is recommended.
- There is a risk of serious haemorrhage and significant elevations in INR and prothrombin time when **KLARIBIN** is co-administered with warfarin. INR and prothrombin times should be monitored frequently.
- Treatment with **KLARIBIN** should be discontinued if any signs of hepatic dysfunction develop. Hepatic dysfunction is usually reversible, but may be severe. In rare instances, hepatic failure with fatal outcome has been reported, usually associated with other serious underlying diseases and/or concomitant medicines. Isolated cases of increased serum creatinine have been reported, but an association with **KLARIBIN** has not been established.
- There have been reports of hypoglycaemia, some of which occurred in patients on concomitant oral hypoglycaemics or insulin.
- Adverse effects in immunocompromised patients treated with higher doses of **KLARIBIN** over long periods include nausea, vomiting, taste perversion, abdominal pain, diarrhoea, rash, flatulence, headache, hearing disturbance, AST and ALT elevations, elevated BUN levels and abnormally low white blood cell and platelet counts. Additional low-frequency events included dyspnoea, insomnia and dry mouth.

Effects on the ability to drive and use machinery

The potential for dizziness, vertigo, confusion and disorientation should be taken into account before patients on **KLARIBIN** drive or use machinery.

INTERACTIONS

- Concomitant use of **KLARIBIN** with the following medicines are contra-indicated: colchicine, HMG-CoA reductase inhibitors and ergot alkaloids (see **"CONTRA-INDICATIONS"**).
- Astemizole, cisapride and pimozide has resulted in cardiac dysrhythmias, including QTcinterval prolongation, ventricular dysrhythmia, ventricular tachycardia, ventricular fibrillation and torsade de pointes. Fatalities have occurred. The most likely cause is the inhibition of metabolism of these medicines by **KLARIBIN** (see "**CONTRAINDICATIONS"**).
- Inducers of cytochrome P450 which may affect the concentration of clarithromycin – Inducers of CYP3A4 (such as rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort) may increase the metabolism of **KLARIBIN** and may result in subtherapeutic levels of **KLARIBIN**, leading to reduced efficacy.
- The following medicines may affect the circulating concentrations of clarithromycin. **KLARIBIN** dosage adjustment or consideration of alternative treatments may be required:
- Strong inducers of cytochrome P450 metabolism system such as efavirenz, nevirapine, rifampicin, rifabutin and rifapentine may accelerate the metabolism of **KLARIBIN** and thus lower the plasma levels of clarithromycin, while increasing the levels of the active metabolite, 14-OH-clarithromycin. Since the microbiological activities of clarithromycin and 14-OH-clarithromycin are different for different bacteria, the intended therapeutic effect could be impaired during concomitant administration of **KLARIBIN** and enzyme inducers.
- **KLARIBIN** exposure may be decreased by etravirine: however concentrations of the active metabolite, 14-OH-clarithromycin, were increased. Because 14-OHclarithromycin has reduced activity against *Mycobacterium avium complex* (MAC), overall activity against this pathogen may be altered.
- Inhibitors of cytochrome P450 which may affect the concentration of clarithromycin:
- Concomitant administration of fluconazole and **KLARIBIN** may lead to increases in the mean steady-state minimum clarithromycin concentration and area under the curve. Steady state concentrations of the active metabolite, 14-OH-clarithromycin are not significantly increased. **KLARIBIN** dose adjustment is not necessary.
- Both clarithromycin and atazanavir are substrates and inhibitors of CYP3A and there is evidence of a bidirectional interaction. Co-administration of **KLARIBIN** with atazanavir and saquinavir may result in a large increase to the exposure to clarithromycin and increases in the plasma concentrations of atazanavir and saquinavir. For patients on atazanavir with renal impairment, the same dose reductions should be followed as with ritonavir.
- Co-administration of **KLARIBIN** and itraconazole may increase each other's plasma levels. Patients on both these medicines should be monitored for signs or symptoms of increased or prolonged pharmacological effect.
- Medicines metabolised by the cytochrome P450 enzyme system (CYP3A4) may be affected by **KLARIBIN** as an enzyme inhibitor for example: alprazolam, ciclosporin, disopyramide, ergot alkaloids, carbamazepine, methylprednisolone, midazolam, omeprazole, quinidine, sildenafil, simvastatin, tacrolimus, triazolam, vinblastine, phenytoin, and valproate –**KLARIBIN** may therefore be associated with increased levels of these medicines. Serum concentrations of these medicines may require monitoring especially medicines with a narrow safety margin such as theophylline and carbamazepine. Rhabdomyolysis has been reported with concomitant use of **KLARIBIN** and the HMG-CoA reductase inhibitors e.g. simvastatin and lovastatin (See **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"CONTRA-INDICATIONS"**).
- Concurrent use of **KLARIBIN** and medicines causing QT prolongation, cardiac dysrhythmias or torsades de pointes should be used with caution. Quinidine or disopyramide serum levels and ECGs should be monitored during therapy with **KLARIBIN**.
- Concomitant administration of clarithromycin and oral or IV administration of midazolam increases the midazolam AUC 7 and 2,7 fold respectively. Therefore concomitant administration of **KLARIBIN** with oral midazolam should be avoided and with IV midazolam the patient should be closely monitored. The same precautions should apply to other benzodiazepines metabolised by CYP3A4 including alprazolam and triazolam. CNS adverse effects such as somnolence and confusion have occurred.
- Concomitant use of **KLARIBIN** and colchicine especially in the elderly, some of which occurred in patients with renal insufficiency may cause colchicine toxicity. Deaths have been reported in some such patients (see **"CONTRA-INDICATIONS"**).
- Co-administration of clarithromycin and phosphodiesterase type 5 (PDE5) inhibitors may result in increased (PDE5) inhibitor exposure. Reduction of the dosages of sildenafil, tadalafil and vardenafil should be considered when these medicines are co-administered with **KLARIBIN**.
- A reduction in tolterodine dosage may be necessary in the presence of CYP3A4 inhibitors such as **KLARIBIN** in the subset of patients who are devoid of the CYP2D6 enzyme.
- Concomitant administration of omeprazole and **KLARIBIN** led to increases in the mean steady-state concentration and area under the curve of omeprazole. The gastric pH increases. The concentration of clarithromycin (such as in **KLARIBIN**) also increased in gastric tissue and mucus, and to a lesser extent in plasma during the use of omeprazole.
- As increased serum levels have been reported with phenytoin and valproate in combination with CYP3A4 inhibitors including clarithromycin, serum level determinations are recommended for these medicines when administered concomitantly with **KLARIBIN**.
- Hypotension, bradydysrhythmias and lactic acidosis have been observed in patients taking clarithromycin (such as in **KLARIBIN**) and verapamil concomitantly.
- Rifabutin and rifampicin - May decrease serum concentration of **KLARIBIN** by > 50 %. Coadministration has been reported to cause a higher incidence of uveitis compared to rifabutin alone (See **"WARNINGS AND SPECIAL PRECAUTIONS"**).
- Theophylline and carbamazepine - The area under the plasma concentration-time curve is increased with concomitant use with **KLARIBIN**. Monitoring of the serum concentrations of these medicines is recommended (See **"WARNINGS AND SPECIAL PRECAUTIONS"**)
- Anticoagulants such as warfarin - **KLARIBIN** may result in the potentiation of the effects of warfarin. Prothrombin time or INR should be monitored closely.
- Digoxin –**KLARIBIN** has been shown to increase serum digoxin concentrations and lead to digoxin toxicity including fatal dysrhythmias. Monitoring of digoxin serum concentrations is recommended.
- Zidovudine - A decrease in the steady-state concentration of zidovudine may occur. Doses of zidovudine and **KLARIBIN** should be taken at least 4 hours apart.

PREGNANCY AND LACTATION

Safety and efficacy in pregnancy and lactation have not been established. **KLARIBIN** is excreted in the breast milk.

KLARIBIN should not be used during pregnancy as its use has been associated with embryo toxicity in animals.

DOSAGE AND DIRECTIONS FOR USE

Children:

Safety and efficacy in infants under 6 months of age has not been established. This formulation is not suitable for use in children less than 12 years of age.

Adults and children older than 12 years: 250 mg twice daily. In more severe infections, the dosage may be increased to 500 mg twice daily.

Renal impairment:

Creatinine clearance (<30 ml/min): Reduce dose by half i.e. 250 mg once daily or 250 mg twice daily for severe infections. Limit the duration of treatment to 14 days. **Eradication of *H. pylori***

Adults:

500 mg twice daily, in combination with an appropriate antibiotic and an acid lowering agent, for 7 to 10 days. The safety and efficacy of **KLARIBIN** in combination with proton-pump inhibitors other than omeprazole have not been established.

Concomitant use of ritonavir

The metabolism of **KLARIBIN** is inhibited. No dosage reduction of **KLARIBIN** is needed in patients with normal renal function. Patients with renal function impairment require a reduction in the dosage of **KLARIBIN** as follows:

- Creatinine clearance 30 to 60 ml/min - Reduce dose by 50 %.
- Creatinine clearance of <30 ml/min - Reduce dose by 75 %.

Do not exceed a dose of 1 g/day during concurrent administration of **KLARIBIN** with ritonavir. It has been suggested that other HIV-protease inhibitors and non-nucleoside reverse transcriptase inhibitors may have a similar effect on **KLARIBIN. KLARIBIN** may be taken with or without meals. **SIDE EFFECTS**

Infections and infestations:
Less frequent: Oral candidiasis, gastroenteritis, vaginal infection, pseudomembranous colitis, erysipelas, erythrasma.

Blood and the lymphatic system disorders:
Less frequent: Leucopenia, thrombocytopenia, agranulocytosis.

Immune system disorders:
Less frequent: Allergic reactions, anaphylaxis.

Endocrine disorders:
Less frequent: Hypoglycaemia.

Metabolism and nutrition disorders:
Less frequent: Anorexia, decreased appetite, hypoglycaemia.

Psychiatric disorders:
The following side effects have been reported and frequencies are unknown: Anxiety, insomnia, hallucinations, bad dreams, depersonalisation, psychotic disorder, depression.

Nervous system disorders:
Frequent: Headache *The following side effects have been reported and frequencies are unknown:* Dizziness, vertigo, disorientation, confusion, convulsions, tremor, parosmia, anosmia, disgeusia and ageusia.

Ear and labyrinth disorders:
Less frequent: Hearing loss, vertigo and tinnitus.

Cardiac disorders:
Less frequent: QT prolongation, ventricular tachycardia, torsades de pointes and palpitations.

Respiratory, thoracic and mediastinal disorders:
Less frequent: Epistaxis.

Gastrointestinal disorders:
Frequent: Nausea, vomiting, abdominal pain, abnormal taste, diarrhoea. *Less frequent:* Glossitis, stomatitis, oral candidiasis, tongue discolouration, tooth discolouration, pseudomembranous colitis (abdominal cramps or pain, tenderness, severe, watery diarrhoea which may also be bloody, fever), dyspepsia, gastrointestinal reflux, gastritis, proctalgia, constipation, dry mouth, eructation and acute pancreatitis.

Hepato-biliary disorders:
Less frequent: Increase in liver enzymes, hepatocellular and/or cholestatic hepatitis (with or without jaundice), and hepatic failure.

Skin and subcutaneous tissue disorders:
The following side effects have been reported and frequencies are unknown: Hyperhidrosis, pruritus, mild skin eruptions, acne, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS) and Henoch-Schonlein purpura.

Musculoskeletal, connective tissue and bone disorders:
Less frequent: Myalgia, rhabdomyolysis and myopathy.

Renal and urinary disorders:
The following side effects have been reported and frequencies are unknown: Interstitial nephritis and renal failure.

General disorders and administration site conditions:
Less frequent: Asthenia.

Investigations:
The following side effects have been reported and frequencies are unknown: Increased INR and prolonged prothrombin time, abnormal globulin ratio.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT See **"SIDE EFFECTS AND SPECIAL PRECAUTIONS"**

Symptoms of overdose

Ingestion of large amounts of **KLARIBIN** can be expected to produce gastrointestinal symptoms. Adverse reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed medicine and supportive measures. Altered mental status, paranoid behaviour, hypokalaemia and hypoxaemia may occur.

Treatment of overdose

Treatment is symptomatic and supportive. **KLARIBIN** is not expected to be appreciably affected by haemodialysis or dialysis.

IDENTIFICATION

KLARIBIN TABLETS 250 mg: Light yellow coloured, oval shaped, biconvex film-coated tablets, with 'D' debossed on one side and '62' on the other side.

KLARIBIN TABLETS 500 mg: Light yellow coloured, oval shaped, biconvex film-coated tablets, with 'D' debossed on one side and '63' on the other side.

PRESENTATION

KLARIBIN TABLETS 250 mg:

1. PVC / PVdC Blister Pack:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC and printed aluminium foil with 6-8 gsm heat seal lacquer.

Pack size: 10's – Each carton contains 1 blister of 10 tablets. 14's - Each carton contains 1 blister of 14 tablets.

2. HDPE Container Pack:

Tablets are packed in 100 ml white HDPE container of 38 mm neck finish (OFC 113 ml) with 38mm-400RS white closure with induction seal wad.

Pack size: 100's- One HDPE container of 100 tablets.

KLARIBIN TABLETS 500 mg:

1) PVC / PVdC Blister Pack:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC and printed aluminium foil with 6-8 gsm heat seal lacquer.

Pack size: 10's – Each carton contains 1 blister of 10 tablets. 14's - Each carton contains 1 blister of 14 tablets.

2) HDPE Container Pack:

Tablets are packed in 120 ml white HDPE container of 38 mm neck finish (OFC 138 ml) with 38mm-400RS white closure with induction seal wad.

Pack size: 100's- One HDPE container of 100 tablets.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from moisture.

Keep HDPE containers tightly closed.

Keep the blisters in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

KLARIBIN TABLETS 250 mg: 42/20.1.1/0852
KLARIBIN TABLETS 500 mg: 42/20.1.1/0853

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, Johannesburg,
South Africa, 1448

DATE OF PUBLICATION OF THE PACKAGE INSERT

Date of registration:
01 July 2014

Date of revision:
01 January 2023

P1533504

DETACH BEFORE DISPENSING

- Decreased appetite
- Anxiety
- Insomnia
- Hallucinations
- Bad dreams
- Depersonalisation
- Depression
- Dizziness
- Vertigo
- Confusion
- Tremor
- Hearing loss
- Vertigo
- Tinnitus (ringing in your ears)
- Nausea,
- Vomiting
- Muscle pain

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

6. STORING AND DISPOSING OF KLARIBIN

Store all medicines out of reach of children.

Store at or below 25 °C.

Protect from moisture.

Keep HDPE containers tightly closed.

Keep the blisters in the carton until required for use.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF KLARIBIN

KLARIBIN TABLETS 250 mg:

1. PVC / PVdC Blister Pack:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC and printed aluminium foil with 6-8 gsm heat seal lacquer.

Pack size: 10's - Each carton contains 1 blister of 10 tablets. 14's - Each carton contains 1 blister of 14 tablets.

2. HDPE Container Pack:

Tablets are packed in 100 ml white HDPE container of 38 mm neck finish (OFC 113 ml) with 38mm-400RS white closure with induction seal wad.

Pack size: 100's- One HDPE container of 100 tablets.

KLARIBIN TABLETS 500 mg:

1. PVC / PVdC Blister Pack:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC and printed aluminium foil with 6-8 gsm heat seal lacquer.

Pack size: 10's - Each carton contains 1 blister of 10 tablets. 14's - Each carton contains 1 blister of 14 tablets.

2) HDPE Container Pack:

Tablets are packed in 120 ml white HDPE container of 38 mm neck finish (OFC 138 ml) with 38mm-400RS white closure with induction seal wad.

Pack size: 100's- One HDPE container of 100 tablets.

8. IDENTIFICATION OF KLARIBIN

KLARIBIN TABLETS 250 mg: Light yellow coloured, oval shaped, biconvex filmcoated tablets, with 'D' debossed on one side and '62' on the other side.
KLARIBIN TABLETS 500 mg: Light yellow coloured, oval shaped, biconvex filmcoated tablets, with 'D' debossed on one side and '63' on the other side.

9. REGISTRATION NUMBER/REFERENCE NUMBER

KLARIBIN TABLETS 250 mg: 42/20.1.1/0852
KLARIBIN TABLETS 500 mg: 42/20.1.1/0853

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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

11. DATE OF PUBLICATION

Date of registration:
01 July 2014

Date of revision:
01 January 2023

S4
KLARIBIN TABLETS 250 mg (Tablet)
KLARIBIN TABLETS 500 mg (Tablet)
Clarithromycin

Read all of this leaflet carefully before you start taking KLARIBIN.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **KLARIBIN** 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.

1. WHAT KLARIBIN CONTAINS

The active substance is clarithromycin.

KLARIBIN TABLETS 250 mg: Each film-coated tablet contains 250 mg clarithromycin. Sugar free.
KLARIBIN TABLETS 500 mg: Each film-coated tablet contains 500 mg clarithromycin. Sugar free.

The other ingredients are cellulose microcrystalline, croscarmellose sodium, magnesium stearate, Opadry yellow (hypromellose, propylene glycol, titanium dioxide, hydroxypropyl cellulose, vanillin, sorbic acid and iron oxide yellow), povidone and silica colloidal anhydrous.

2. WHAT KLARIBIN IS USED FOR

KLARIBIN is indicated for the symptomatic treatment of:

- Chest infections such as bronchitis and pneumonia.
- Throat and sinus infections such as pharyngitis and sinusitis.
- Mild to moderately severe acute otitis media (infection of your middle ear).
- Skin and soft tissue infections.
- Eradication of *Helicobacter pylori* (the bacteria responsible for causing gastric or duodenal ulcers) when used in combination with a proton pump inhibitor and another antibiotic to decrease recurrence of duodenal ulcers.

3. BEFORE YOU TAKE KLARIBIN

Do not take KLARIBIN:

- If you have a hypersensitivity to clarithromycin or any macrolide antibiotics or to any component of the formulation.
- If you are taking astemizole, cisapride or pimozide.
- If you suffer from porphyria.
- If you are pregnant.
- If you are taking ergotamine or dihydroergotamine commonly used to treat migraine as the combination with **KLARIBIN** may cause constriction of blood vessels resulting in a decrease of oxygen supply to the brain and hands and feet ultimately causing tissue damage.
- If you are taking statins e.g. simvastatin and lovastatin, medicines used to treat high cholesterol, as it may increase the risk of rhabdomyolysis which is the breakdown of damaged muscle.
- If you are taking colchicine, a medicine used to treat gout.

Take special care with KLARIBIN:

- If you suffer from liver problems. If you experience yellowing of skin and white of the eyes, abdominal pain and tenderness, dark urine and severe itchy skin you should stop taking **KLARIBIN** immediately.
- If you suffer from kidney problems - the elimination of **KLARIBIN** is reduced in patients with renal function impairment, especially those with a creatinine clearance of <30 ml/min.
- If you are taking rifabutin and/or rifampicin as the combination will cause a decrease of **KLARIBIN** in your blood. Co-administration has been reported to cause a higher incidence of uveitis, an inflammation of part of the eye compared to when rifabutin is taken alone.
- If you are taking theophylline, a medicine used to open your airways to help you breath better.
- If you experience severe diarrhoea, you may be suffering from pseudomembranous colitis due to **KLARIBIN**.
- If you are taking benzodiazepines e.g. midazolam, triazolam or triazolam, medicines used as muscle relaxants and to treat anxiety.
- If you are taking blood glucose lowering medicines such as insulin as it maycause hypoglycaemia, where your glucose level drops too much.

Taking KLARIBIN with food and drink:

You may take **KLARIBIN** with or without food.

Pregnancy and Breast-feeding:

If you are pregnant or breast-feeding, you should not take **KLARIBIN** as safety and efficacy in pregnancy and breast-feeding have not been established. **KLARIBIN** is excreted in the breast milk.

If you are pregnant or breast-feeding, please consult your doctor, pharmacist or other health care professional for advice before taking **KLARIBIN**.

Driving and operating machines:

Do not drive or operate machines before you know how **KLARIBIN** will affect you.

Taking other medicines with KLARIBIN:

- You should not take **KLARIBIN** with colchicine (gout medicines), statins (high cholesterol medicines) or migraine medications.
- Taking **KLARIBIN** with astemizole, cisapride or pimozide may cause irregular heart rhythms and can be fatal.
- Medicines such as rifampicin, phenytoin, carbamazepine, phenobarbital, efavirenz, etravirine and St John's Wort may increase the metabolism of **KLARIBIN** and therefore reduce its efficacy.
- Antifungals such as fluconazole and itraconzole and antiretrovirals such as atazanavir and saquinavir may increase the blood concentration of **KLARIBIN**.
- Other medicines which may be affected by **KLARIBIN** include ciclosporin, disopyramide, carbamazepine, methylprednisolone, omeprazole, quinidine, sildenafil, tacrolimus, triazolam, vinblastine, digoxin, zidovudine, phenytoin, and valproate.
- If you are taking warfarin or any other blood thinning medicines.
- If you are immunocompromised and treated with higher doses of **KLARIBIN** for a long period you may experience the following: nausea, vomiting, taste perversion, abdominal pain, diarrhoea, rash, flatulence, headache, and hearing disturbance.

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

4. HOW TO TAKE KLARIBIN

Always take **KLARIBIN** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. If you have the impression that the effect of **KLARIBIN** is too strong or too weak, talk to your doctor or pharmacist.

Children

Safety and efficacy in infants under 6 months of age has not been established. **KLARIBIN** is not suitable for use in children under the age of 12 years. **Adults and children older than 12 years:** 250 mg twice daily.

In more severe infections, the dosage may be increased to 500 mg twice daily. **KLARIBIN** may be taken with or without food. Your doctor will prescribe an appropriate dose according to your condition.

If you take more KLARIBIN than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control center.

If you forget to take KLARIBIN:

Do not take a double dose to make up for forgotten individual doses.

5. POSSIBLE SIDE EFFECTS

KLARIBIN can have side effects.

If you experience any of the following, stop taking **KLARIBIN** and tell your doctor immediately:

- An allergic reaction where you have difficulty breathing
- Dizziness, blurred vision or fainting as you may have low blood glucose levels.
- Irregular heartbeats for example too fast or too slow.
- A severe peeling rash which may spread to your mouth or eyes.
- Yellowing of your skin and white of the eyes, dark urine or a painful, tender abdomen as you may have jaundice.

If you experience any of the following symptoms, tell your doctor as soon as possible:

- Abdominal cramps or pain, tenderness, severe, watery diarrhoea which may also be blood
- Fever
- Convulsions
- Disorientation
- Muscle pain

These are all serious side effects. You may need urgent medical attention. Tell your doctor if you notice any of the following:

- Oral thrush, or a vaginal infection