APPROVED
Samantha , 09:53:57, 02/15/2022

ZEPANALZ P1530333

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SKEDULERINGSTATUS

SUID-AFRIKA: S5

NAMIBIË: NS3

EIENDOMSNAAM (en doseervorm):
ZEPANALZ 5 mg TABLETS (tablet)
ZEPANALZ 10 mg TABLETS (tablet)

SAMESTELLING:

ZEPANALZ 5 mg TABLETS:
Elke filmbedekte tablet bevat 5 mg donepesielhidrochloried. Bevat suiker: 84 mg laktose.

ZEPANALZ 10 mg TABLETS:
Elke filmbedekte tablet bevat 10 mg donepesielhidrochloried. Bevat suiker: 168 mg laktose.

Die ander bestanddele van **ZEPANALZ TABLETS** is gepregelatiniseerde stysel, mikro-kristallyne sellulose, hidroksipropielsellulose, magnesiumstearaat, hipromellose, poliëtileenglikol, talk en titaandioksied. **ZEPANALZ 10 mg TABLETS** bevat ook ysteroksied geel.

FARMAKOLOGIESE KLASSIFIKASIE:
A 5.3 Cholinomimetika (cholinergiese middels)

FARMAKOLOGIESE WERKING:

Farmakodinamika:
Donepesielhidrochloried is 'n omkeerbare inhibeerder van asetielcholinesterase, die oorheersende cholinesterase in die brein. Donepesielhidrochloried is 'n meer as 1000 keer sterker inhibeerder van hierdie ensiem as butielcholinesterase, 'n ensiem wat hoofsaaklik buite die sentrale senuweestelsel (SSS) voorkom.

In pasiënte met Alzheimer se demensie wat aan kliniese proewe deelgeneem het, het die toediening van enkele daaglikse dosisse van 5 mg of 10 mg donepesiel, platotoestand inhibisie van asetielcholinesteraseaktiwiteit van 63,6 % en 77,3 % onderskeidelik (gemeet in eritrosietmembrane), teweeg gebring nadat dit na dosering gemeet is. Daar is getoon dat die inhibisie van asetielcholinesterase (AChE) deur donepesielhidrochloried in rooibloedselle baie nou verband hou met die effekte in die serebrale korteks. Boonop, is daar 'n beduidende korrelasie tussen die plasmavlakke van donepesielhidrochloried, AChE-inhibisie en verandering in ADAS-cog, 'n sensitiewe en goed gevalideerde skaal wat die kognitiewe optrede – insluitende geheue, oriëntasie, redenasie, taal en prakse ondersoek.

Meganisme van werking:
Huidige teorieë oor die patogenese van die kognitiewe tekens van Alzheimer se siekte, skryf sommige van hierdie tekens toe aan 'n tekort aan cholinergiese neuro-oordrag. Daar word gepostuleer dat donepesielhidrochloried sy terapeutiese effek uitoefen deur die cholinergiese funksie te versterk. Dit word bewerkstellig deur die konsentrasie van asetielcholien deur die omkeerbare inhibisie van sy hidrolise deur asetielcholinesterase te versterk. As hierdie voorgestelde meganisme van werking korrek is, kan die effek van donepesiel afneem namate die siekteproses vorder en minder cholinergiese neurone ongeskonde bly. Daar is geen bewys dat donepesiel die verloop van die onderliggende proses verander nie.

Die ensiem AChE kom ook perifeer in rooibloedselle voor. Daarom kan die bepaling van AChE-aktiwiteit in eritrosietmembrane 'n indeks vir die farmakodinamika van donepesielhidrochloried bied.

Farmakokinetika:
Absorpsie:
Orale toediening van donepesiel lewer voorspelbare plasmakonsentrasies met maksimum vlakke wat ongeveer 3 tot 4 ure na toediening van die dosis bereik word. Plasmakonsentrasies en area onder die kurwe (AOK) neem proporsioneel met die dosis toe. Die eliminasiehalfleeftyd is ongeveer 70 ure. Daarom lei die toediening van veelvuldige enkel daaglikse dosisse tot 'n geleidelike bereiking van platokonsentrasie. Geskatte platokonsentrasie word binne 3 weke na die begin van terapie bereik. Nadat platokonsentrasie bereik is, toon die plasmakonsentrasie van donepesielhidrochloried en sy verwante farmakodinamiese aktiwiteit min veranderlikheid deur die verloop van die dag. Voedsel of tyd van toediening (dosering soggens teenoor saans) het geen effek op die absorpsie van donepesielhidrochloried nie.

Verspreiding:
Die volume van verspreiding teen platokonsentrasie is 12 L/kg. Donepesielhidrochloried word ongeveer 96 % aan menslike plasmaproteïene gebind. Die verspreiding van donepesielhidrochloried in verskillende liggaamsweefsels is nie pertinent bestudeer nie. In 'n massabalansstudie in gesonde manlike vrywilligers, 240 ure na die toediening van 'n enkele 5 mg dosis 14C-gemerkte donepesielhidrochloried, is ongeveer 28 % van die gemerkte middel nie herwin nie. Hieruit wil dit voorkom asof donepesielhidrochloried en/of enige van sy metaboliete vir meer as 10 dae in die liggaam kan bly. Die gemiddelde SSV:plasmaverhouding vir beide dosisse, uitgedruk as persentasie van plasmakonsentrasie, was 15,7 %.

Metabolisme / Uitskeiding:
Donepesiel word in die lewer gemetaboliseer en die oorheersende roete van eliminasie van beide die moederverbinding en sy metaboliete vind deur die niere plaas, aangesien 79 % herwinde dosis in die uriene, met die oorblywende 21 % in die feses gevind is. Boonop is die moederverbinding, donepesiel, die oorheersende eliminasieproduk in die uriene. Die belangrikste metaboliete van donepesiel sluit M1 en M2 (deur O-dealkilering en hidroksilering), M11 en M12 (deur glukuronidasie van M1 en M2, onderskeidelik), M4 (deur hidrolise) en M6 (deur N-oksidasie) in. Daar is geen bewys wat op enterohepatiese hersirkulasie van donepesielhidrochloried en/of sy metaboliete dui nie. Die plasmakonsentrasies van donepesiel neem af met 'n halfleeftyd van ongeveer 70 ure. Geslag, ras en rookgeskiedenis het geen kliniies beduidende invloed op plasmakonsentrasies van donepesielhidrochloried nie.

INDIKASIES:

ZEPANALZ TABLETS word aangedui vir die simptomatiese behandeling van geringe tot matige demensie in Alzheimer se siekte.

KONTRA-INDIKASIES:

ZEPANALZ TABLETS word teenaangedui in pasiënte met 'n bekende hipersensitiwiteit vir donepesielhidrochloried, piperidienderivate of enige van die bestanddele wat in die formulasie gebruik word.

Die veiligheid en doeltreffendheid van **ZEPANALZ TABLETS** is nie in kinders vasgestel nie, daarom word dit nie vir gebruik in kinders aanbeveel nie.

Swangerskap en laktasie (sien **SWANGERSKAP EN LAKTASIE**)

WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS:
Behandeling behoort ingestel te word deur 'n dokter met ondervinding in die behandeling van Alzheimer se demensie. Onderhoudsbehandeling kan voortgesit word vir solank die pasiënt terapeutiese voordeel daaruit put. Daarom moet die kliniese voordeel van **ZEPANALZ TABLETS** op 'n gereelde basis herevalueer word. Wanneer daar nie langer bewys van 'n terapeutiese effek is nie, behoort onttrekking oorweeg te word. Die individuele reaksie tot **ZEPANALZ TABLETS** kan nie voorspel word nie.

Die gebruik van **ZEPANALZ TABLETS** in pasiënte met erge demensie, ander tipes demensie of ander tipes geheue-inkorting (bv. ouderdomsverwante kognitiewe afname) is nie vasgestel nie.

Narkose: ZEPANALZ TABLETS, as 'n cholinesterase-inhibeerder, kan waarskynlik die suksinielcholientipe spierverslapping gedurende narkose verhoog.

Kardiovaskulêre Toestande: Weens hul farmakologiese werking, kan **ZEPANALZ TABLETS** vagotoniese effekte op die hart hê (bv. bradikardie). Die potensiaal vir hierdie werking kan veral belangrik wees in pasiënte met "sieksinussindroom" of ander supraventrikulêre hartgeleidingstoestande soos sinoatriale of atrioventrikulêre blok. Sinkopale episodes is in genootskap met die gebruik van donepesiel aangemeld.

Gastroïntestinale Toestande: Maagsuurproduksie kan deur **ZEPANALZ TABLETS** bevorder word. Daarom behoort pasiënte noukeurig vir simptome van aktiewe of verborge gastroïntestinale bloeding gemonitor te word, veral diegene met 'n toename in die risiko vir die ontwikkeling van ulkusse bv. diegene met 'n geskiedenis van ulkussiekte of diegene wat terselfdertyd nie-steroïed anti-inflammatoriese middels (NSAIMs) ontvang. As 'n voorspelbare gevolg van sy farmakologiese eienskappe, is daar bewys dat donepesiel diaree, naarheid en braking veroorsaak. Die effekte, wanneer hulle voorgekom het, het meer dikwels met die 10 mg/dag dosis as met die 5 mg/dag dosis voorgekom. In die meeste gevalle was hierdie effekte matig en van verbygaande aard, wat soms van een tot drie weke geduur het. Hierdie effekte het met die voortgesette gebruik van donepesiel verdwyn.

Genito-urinêr: ZEPANALZ TABLETS kan obstruksie van blaasleidinge veroorsaak.

Neurologiese Toestande: Daar word geglo dat **ZEPANALZ TABLETS** 'n sekere potensiaal besit om algemene konvulsies te veroorsaak. Hierdie stuipaktiwiteit kan egter ook 'n manifestasie van Alzheimer se siekte wees.

Longtoestande: Weens hul cholinomimetiese werking, behoort **ZEPANALZ TABLETS** met sorg aan pasiënte met 'n geskiedenis van asma of obstruktiewe longsiekte voorgeskryf te word. Die toediening van **ZEPANALZ TABLETS** saam met ander inhibeerders van asetielcholinesterase, agoniste of antagoniste van die cholinergiese sisteem behoort vermy te word

Pasiënte wat van blaas- of gastroïntestinale chirurgie herstel: Die gebruik van **ZEPANALZ TABLETS** word nie in pasiënte wat van blaas- of gastroïntestinale chirurgie herstel, aanbeveel nie.

Die gebruik van donepesiel word met gewigsverlies geassosieer. Pasiënte se gewig behoort gedurende die behandeling met **ZEPANALZ TABLETS** gemonitor te word.

Vroulike pasiënte is meer geneig tot naarheid, braking, anoreksie en gewigsverlies.

Belangrike inligting oor sommige van die bestanddele van ZEPANALZ TABLETS:
ZEPANALZ TABLETS bevat laktose en behoort nie aan pasiënte met seldsame oorerflike probleme of 'n geskiedenis van galaktoseonverdraagsaamheid, Lapp-laktasetekort of glukose-galaktose wanabsorpsie gegee te word nie.

Effek op die vermoë om te bestuur en met masjinerie te werk
Demensie kan inkorting van bestuursvermoë veroorsaak of die vermoë om met masjinerie te werk, nadelig beïnvloed. Verder kan **ZEPANALZ TABLETS** moegheid, duiseligheid en spierkrampe veroorsaak, hoofsaaklik wanneer die dosis begin of verhoog word. Die behandelende dokter behoort gereeld die vermoë van pasiënte op **ZEPANALZ TABLETS** se vermoë om te bestuur of met komplekse masjinerie te werk te evalueer.

INTERAKSIES:

Medisyne wat sterk aan plasmaproteïene gebind word:
Medisyneverplasingstudies is *in vitro* tussen hierdie hoogs gebonde medisyne (96 %) en ander medisyne soos furosemied, digoksien en warfarien uitgevoer. **ZEPANALZ TABLETS** teen konsentrasies van 0,3 – 10 µg/mL, beïnvloed nie die binding van furosemied (5 µg/mL), digoksien (2 µg/mL) en warfarien (3 µg/mL) aan menslike albumien nie. So ook word die binding van **ZEPANALZ TABLETS** nie deur furosemied, digoksien en warfarien beïnvloed nie.

Die effek van ZEPANALZ TABLETS op die metabolisme van ander medisyne:
Geen *in vivo* kliniese studies het die effek van **ZEPANALZ TABLETS** op die opruiming van medisyne wat deur CYP3A4 (bv. sisapried) of deur CYP2D6 (bv. imipramien) gemetaboliseer word, bestudeer nie. *In vitro* studies het egter 'n lae graad van binding aan hierdie ensieme (gemiddelde Ki ongeveer 50 – 130 µM) getoon. Teen terapeutiese plasmakonsentrasies van donepesiel (164 nM) wil dit slegs op 'n baie klein waarskynlikheid van inmenging dui. Dit is nie bekend of **ZEPANALZ TABLETS** enige potensiaal vir ensiminduksie besit nie.

Donepesielhidrochloried en/of enige van sy metaboliete inhibeer nie die metabolisme van teofillien, warfarien, simetidien, digoksien, tiodasien, risperidoon en sertralien in mense nie. In 'n studie van pasiënte met Parkinson se siekte op optimale behandeling met L-dopa/karbidopa, het die toediening van donepesiel vir 21 dae geen effek op L-dopa of karbidopa bloedvlakke gehad nie. In hierdie studie is geen effek op motoriese aktiwiteit waargeneem nie.

Effek van ander medisyne op die metabolisme van ZEPANALZ TABLETS:
Ketokonasool en kinidien, inhibeerders van CYP450, 3A4 en 2D6, onderskeidelik, inhibeer die metabolisme van donepesiel *in vitro*. Daarom kan hierdie en ander CYP3A4 inhibeerders, soos itrakonasool en eritromisien en CYP2D6 inhibeerders, soos fluoksetien, die metabolisme van donepesiel inhibeer. Dit is onbekend of daar 'n kliniese effek van hierdie inhibeerders is. In 'n studie in gesonde vrywilligers, het ketokonasool die gemiddelde donepesielkonsentrasie met 30 % verhoog. Hierdie verhoging is kleiner as dié wat deur ketokonasool vir ander middels wat die CYP3A4 baan deel en is waarskynlik nie klinies relevant nie. Die toediening van donepesiel het geen effek op die farmakokinetika van ketokonasool gehad nie. Induseerders van CYP2D6 en CYP3A4 (bv. fenitoïen, karbamasepien, alkohol, deksametasoon, rifampisien en fenobarbital) kan die tempo van eliminasie van **ZEPANALZ TABLETS** versnel.

Formele farmakokinetiese studies het getoon dat die metabolisme van donepesiel nie beduidend deur die medetoediening van digoksien, simetidien, tioridasien, risperidoon of sertralien geaffekteer word nie.

Gebruik saam met anticholinergiese middels:
Weens hul meganisme van werking besit **ZEPANALZ TABLETS** die potensiaal om met die aktiwiteit van anticholinergiese medikasies in te meng.

Die gebruik saam met cholinomimetika en ander cholinesteraseïnhibeerders:
Daar kan 'n sinergistiese effek verwag word wanneer **ZEPANALZ TABLETS** saam met suksinielcholien, soortgelyke neuromuskulêre blokkerende middels of cholinergiese agoniste, soos betanechol of betablokkerende middels wat 'n effek op hartgeleiding het, gegee word. 'n *In vitro* studie het egter getoon dat donepesielhidrochloried minimale effekte op die hidrolise van suksinielcholien gehad het.

SWANGERSKAP EN LAKTASIE:
Die veiligheid van **ZEPANALZ TABLETS** is nie in swangerskap en laktasie vasgestel nie.

DOSIS EN GEBRUIKSAANWYSINGS:

Volwassenes/Bejaardes:
Die aanbevole dosisse vir **ZEPANALZ TABLETS** is 5 mg of 10 mg een keer per dag toegedien. Alhoewel daar geen statisties beduidende bewys is dat 'n groter behandelingseffek met die gebruik van die 10 mg dosis verkry word nie, bestaan daar 'n vermoede dat, gebaseer op ontleding van groepdata, daar sekere bykomende voordele vir sommige pasiënte met die gebruik van die hoër dosis verkry kan word. Behandeling word begin op 5 mg/dag (een keer per dag dosering).

Die 5 mg/dag dosis behoort vir ten minste 4 - 6 weke volgehou te word sodat die vroegste kliniese reaksie op behandeling geëvalueer kan word sodat platokonsentrasies van donepesielhidrochloried bereik kan word. Na die een- maand kliniese evaluasie teen 5 mg/dag, kan die dosis van **ZEPANALZ TABLETS** na 10 mg/dag (een keer per dag dosering) verhoog word. Die maksimum aanbevole daaglikse dosis is 10 mg. Dosisse groter as 10 mg is nie in kliniese proewe bestudeer nie. Met staking van behandeling, word 'n gelydelike afname van die voordelige effek van **ZEPANALZ TABLETS** waargeneem. Na die skielike staking van terapie is daar geen bewys van 'n terugvaleffek nie.

Ingekorte nier- en lewerfunksie:
Aangesien die opruiming van donepesielhidrochloried nie deur nierinkorting of geringe tot matige ingekorte lewerfunksie geaffekteer word nie, kan 'n soortgelyke dosisskedule in pasiënte met hierdie toestande gevolg word.

NEWE EFFEKTE:

Infeksies en infestasies:
Dikwels: Algemene verkoue, griep

Metabolisme- en voedingsafwykings:
Minder dikwels: Dehidrasie, hiponatremie

Psigiatriese afwykings:
Dikwels: Slapeloosheid, abnormale drome, agitasie, delusies, depressie, hallusinasies
Minder dikwels: Abnormale huilery, aggressiewe gedrag, verhoogde libido, geïrriteerdheid, senuweeagtigheid, rusteloosheid, verwardheid

Afwykings van die senuweestelsel:
Dikwels: Duiseligheid, hoofpyn, slaperigheid
Minder dikwels: Afasie, ataksie, parestesie, sinkopee, bewing, stuipaanvalle, ekstrapiramidale simptome

Oogafwykings:
Minder dikwels: Katarakte, oogirritasie, onduidelike sig

Afwykings van die oor en labirint:
Minder dikwels: Vertigo

Hartafwykings:
Minder dikwels: Atrioventrikulêre blok, bradikardie, sinoatriale blok, angina

Vaskulêre afwykings:
Minder dikwels: Warm gloede, hipertensie, hipotensie, vasodilatasie

Respiratoriese, bors- en mediastinale afwykings:
Minder dikwels: Dispnee, seer keel, brongitis

Gastroïntestinale afwykings:
Dikwels: Diaree, naarheid, braking, anoreksie, pankreatitis, fekale inkontinensie, buikafwyking
Minder dikwels: Gastroïntestinale bloeding, epigastriese pyn, opgeblaasdheid, tandpyn, duodenale ulkus, maagulkus

Hepatobileêre afwykings:
Minder dikwels: Hepatitis

Afwykings van die vel en subkutane weefsel:
Minder dikwels: Diaforese, eggimose, pruritus, urtikarie, uitslag

Muskuloskeletale, bindweefsel en beenafwykings:
Dikwels: Spierkrampe, artritis

Nier- en urienafwykings:
Dikwels: Gereelde urinering
Minder dikwels: Nokturie, urien inkontinensie, urienweginfeksie

Algemene afwykings en toestande by die plek van toediening:
Dikwels: Moegheid, pyn
Minder dikwels: Borspyn

Ondersoeke:
Dikwels: Gewigsverlies
Minder dikwels: Klein toenames in die serumkonsentrasies van kreatienkinase, toename in lewertransaminases

Besering en vergiftiging:
Minder dikwels: Ongelukke, beenfraktuur

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Dosisverwante tekens van cholinergiese stimulasie is in diere waargeneem en het 'n afname in spontane beweging, uitgestrekte posisie, waggelende stap, traanvloei, kloniese konvulsies, onderdrukte asemhaling, speekselvloei, miose, fassikulering en verlaagde liggaamsoppervlak temperatuur ingesluit.

Oordosering met **ZEPANALZ TABLETS** kan tot 'n cholinergiese krisis lei wat deur erge naarheid, braking, speekselvloei, sweet, bradikardie, hipotensie, asemhalingsonderdrukking, ineenstorting en stuipaanvalle gekenmerk word.

'n Toename in spierswakheid is 'n moontlikheid en mag tot die dood lei as die asemhalingspiere betrokke is.

Algemene ondersteunende maatreëls behoort toegepas te word. Tersiêre anticholinergiese middels, soos atropien, kan as teenmiddel vir oordosering met **ZEPANALZ TABLETS** gebruik word. Intraveneuse atropiensulfaat wat tot effek getitreer word, word aanbeveel: 'n aanvanklike dosis van 1,0 tot 2,0 mg IV met daaropvolgende dosisse wat op die kliniese reaksie gebaseer word. Atipiese reaksies in die bloeddruk en harttempo is met ander cholinomimetika aangemeld nadat dit met kwaternêre anticholinergiese middels, soos glikopirrolaat, toegedien is. Dit is nie bekend of donepesielhidrochloried en/of sy metaboliete met dialise (hemodialise, peritoneale dialise of hemofiltrasie) verwyder kan word nie.

IDENTIFIKASIE:

ZEPANALZ 5 mg TABLETS:
Wit tot byna-wit, ronde, bikonvekse, filmbedekte tablette met 'X' op die een kant en '11' op die ander kant gedruk.

ZEPANALZ 10 mg TABLETS:
Geel gekleurde, ronde, bikonvekse, filmbedekte tablette met 'X' op die een kant en '12' op die ander kant gedruk.

AANBIEDING:

ZEPANALZ 5 mg and 10 mg TABLETS:

1) **Stolpverpakking:**
Tablette word in 250 µm helder PVC/25 µm PE/90 g/m² PVdc en silwergekleurde, gedrukte 25 µm aluminiumfoelie met 7 g/m² hittegeseëlde lak verpak.
Elke stolpstrokie bevat 10 tablette.
Pakgrootte: 30's – Elke karton bevat 3 stolpstrokies met 10 tablette elk.

2) **HDPE Houer:**
Tablette word in 40 mL wit HDPE houers met 'n wit deksel met induksieseëlprop en 1 x 1 g silikajel sakkie verpak.
Elke houer bevat 30 tablette.
Pakgrootte: 30's – Een HDPE houer bevat 30 tablette.

BERGINGSINSTRUKSIES:
Bewaar teen of benede 25 °C. Beskerm teen lig. Hou die stolpstrokies in die karton tot voor gebruik. Maak die veiligheidshouer deeglik toe na gebruik.

HOU BUITE BEREIK VAN KINDERS

REGISTRASIENOMMERS:
SUID-AFRIKA:
ZEPANALZ 5 mg: 44/5.3/0944
ZEPANALZ 10 mg: 44/5.3/0945

NAMIBIË:
ZEPANALZ 5 mg: 19/5.3/0024
ZEPANALZ 10 mg: 19/5.3/0023

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
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DETACH BEFORE DISPENSING

SUID-AFRIKA: S5
NAMIBIË: NS3
ZEPANALZ 5 mg TABLETS (tablet)
ZEPANALZ 10 mg TABLETS (tablet)
Donepesielhidrochloried

Lees die hele brosjure sorgvuldig voordat u begin om ZEPANALZ TABLETS te neem.
- Hou hierdie bladsy.
- Indien u verdere vrae het, moet u asseblief u dokter of apteker raadpleeg.
- **ZEPANALZ TABLETS** is vir u persoonlik voorgeskryf en u behoort nie u medisyne met ander mense deel nie. Dit mag hulle skade aandoen, ookal het hulle dieselfde simptome as u.

1. WAT ZEPANALZ TABLETS BEVAT

Die aktiewe bestanddeel is donepesielhidrochloried.

ZEPANALZ 5 mg TABLETS:
Elke filmbedekte tablet bevat 5 mg donepesielhidrochloried. Bevat suiker: 84 mg laktose.

ZEPANALZ 10 mg TABLETS:
Elke filmbedekte tablet bevat 10 mg donepesielhidrochloried. Bevat suiker: 168 mg laktose.

Die ander bestanddele in **ZEPANALZ TABLETS** is hipromellose, hidroksipropielsellulose, magnesiumstearaat, mikrokristallyne sellulose, poliëtileenglikol, gepregelatiniseerde stysel, talk en titaandioksied. **ZEPANALZ 10 mg TABLETS** bevat ook ysteroksied geel.

2. WAARVOOR ZEPANALZ TABLETS GEBRUIK WORD

ZEPANALZ TABLETS behoort aan 'n groep medisyne wat asetielcholinesteraseinhibeerders genoem word.

ZEPANALZ TABLETS word gebruik om geringe tot matige demensie ('n breinafwyking wat die vermoë om te onthou, duidelik te dink, te kommunikeer en daaglikse aktiwiteite uit te voer affekteer en wat buie en persoonlikheidsveranderinge mag veroorsaak) wat deur Alzheimer se siekte veroorsaak word, te behandel.

3. VOORDAT U ZEPANALZ TABLETS NEEM

Moenie ZEPANALZ TABLETS neem nie:
- As u hipersensitief (allergies) is vir donepesielhidrochloried, piperidienderivate of enige van die ander bestanddele van **ZEPANALZ TABLETS**.
- **ZEPANALZ TABLETS** behoort nie aan kinders gegee te word nie, aangesien die veiligheid en effektiwiteit van **ZEPANALZ TABLETS** nie in kinders vasgestel is nie.

Neem spesiale sorg met ZEPANALZ TABLETS:
- Die gebruik van **ZEPANALZ TABLETS** in pasiënte met erge demensie, ander tipes demensie of ander tipes geheueprobleme is nie vasgestel nie.

Voordat u ZEPANALZ TABLETS neem, stel u dokter in kennis as u aan die volgende iy of ooit daaraan gely het:
- "Sieksinussindroom" wat teenwoordig kan wees met simptome soos borspyn, kort van asem, duiseligheid, moegheid, naarheid, floute, 'n vinnige hartklop of ander hartsiekte.
- Gastroïntestinale (wat die maag en ingewande affekteer) bloeding, ulkusse, of as u nie-steroïed anti-inflammatoriese middels (NSAIMs) neem.
- Stuipaanvalle of konvulsies.
- Asma of ander obstruktiewe longsiekte.
- Moeite met urinering.
- As u chirurgie moet ondergaan, insluitende tandheelkundige chirurgie, moet u u dokter of tandarts in kennis stel dat u **ZEPANALZ TABLETS** neem.
- As u van onlangse blaas- of gastroïntestinale chirurgie herstel.

Die neem van ZEPANALZ TABLETS met voedsel en drank:
ZEPANALZ TABLETS kan met of sonder voedsel geneem word.

Alkohol kan die effek van **ZEPANALZ TABLETS** verander, aangesien die tempo waarteen **ZEPANALZ TABLETS** uit u sisteem geëlimineer word verhoog word en daardeur verkort dit die tyd wat **ZEPANALZ TABLETS** vir u kan werk.

Swangerskap en borsvoeding:
Die veilige gebruik van **ZEPANALZ TABLETS** gedurende swangerskap en terwyl u u baba borsvoed is nie vasgestel nie.

As u swanger is of u baba borsvoed, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker vir advies nader voordat u **ZEPANALZ TABLETS** neem.

Bestuur en die gebruik van masjinerie:
Demensie mag u vermoë om te bestuur of om met masjinerie te werk affekteer. **ZEPANALZ TABLETS** kan ook moegheid, duiseligheid en spierkrampe veroorsaak, veral nadat u met die dosis begin of wanneer die dosis verhoog word. Moenie bestuur of met masjinerie werk tensy u dokter gesê het dat dit veilig is nie.

Belangrike inligting oor sommige van die bestanddele van ZEPANALZ TABLETS:
ZEPANALZ TABLETS bevat laktose. Daarom moet u u dokter in kennis stel as u laktose overdraagsaam is of het 'n geskiedenis van galaktose-onverdraagsaamheid, Lapp-laktasetekort of aan glukose-galaktosewanabsorsie ly.

Die neem van ander medisyne saam met ZEPANALZ TABLETS:
Voordat u **ZEPANALZ TABLETS** neem, moet u u dokter in kennis stel as u enige van die volgende medisyne gebruik:
- Pynstillers of behandeling vir artritis bv. NSAIMs, soos ibuprofeen of diklofenaknatrium.
- Antibiotika bv. eritromisien, rifampisien.
- Swamwerende medisyne bv. ketokonasool, itrakonasool.
- Antidepressante bv. fluoksetien.
- Antikonvulsiewe middels bv. fenitoïen, karbamasepien, fenobarbitol.
- Medisyne vir 'n harttoestand bv. kinidien.
- Kortikosteroïede bv. deksametasoon.
- Spierverslappers bv. suksinielcholien.
- Algemene narkose - as u 'n operasie moet ondergaan wat algemene narkose vereis, behoort u u dokter of narkotiseur in kennis te stel dat u **ZEPANALZ TABLETS** neem.

As u enige van die bogenoemde medisyne gebruik, mag dit moontlik wees dat u nie **ZEPANALZ TABLETS** kan gebruik nie, of u kan moontlik 'n dosisaanpassing benodig of u dokter moet u moontlik noukeurig vir newe effekte monitor.

Stel altyd u professionele gesondheidswerker in kennis as u enige ander medisyne gebruik. (Dit sluit komplementêre en tradisionele medisyne in.)

4. HOE OM ZEPANALZ TABLETS TE NEEM

Neem **ZEPANALZ TABLETS** altyd presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. As u van mening is dat die effek van **ZEPANALZ TABLETS** te sterk of te swak is, moet u u dokter of apteker raadpleeg.

Volwassenes en bejaardes:
- Die gewone begindosis is 5 mg een keer per dag.
- Na een maand kan u dokter die dosis na 10 mg een keer per dag verhoog.
- Die maksimum aanbeode dosis is 10 mg een keer per dag.
- Die dosis is soortgelyk vir pasiënte met niersiekte of geringe tot matige lewersiekte.

As u te veel ZEPANALZ TABLETS geneem het:
Simptome van oordosering kan naarheid en braking, kwyl, sweet, stadige hartklop, lae bloeddruk, asemhalingsprobleme, bewussynverlies en stuipaanvalle insluit.

As u vergeet het om ZEPANALZ TABLETS te neem:
Neem die oorgeslaande sodra u daarvan onthou. As dit egter byna tyd vir die volgende dosis is, slaan die gemiste dosis oor en neem die medisyne weer op die volgende geskeduleerde tyd. Moenie die dosis verdubbel om vir die oorgeslaande individuele dosis op te maak nie.

A/s: 360 x 480 mm ■ Black

AUROBINDO Packaging Development		Product Name	Component	Item Code	Date & Time
		ZEPANALZ	Leaflet	P1530333	11.02.2022 & 03.00 pm
		Country	Version No.	Reason of Issue	Reviewed / Approved by
		South Africa - APL	00	Commercial	
Team Leader	Kiran K	Dimensions (mm)	Colours: 01		
Initiator	Bhogi	A/s : 360 x 480 mm	30333		
Artist	Sree Designers	Pharma Code: 30333			
Additional Information: Supersede Code: P1512130 sai charan					

SCHEDULING STATUS

SOUTH AFRICA: S5
NAMIBIA: NS3

PROPRIETARY NAME (and dosage form):

ZEPANALZ 5 mg TABLETS (tablet)
ZEPANALZ 10 mg TABLETS (tablet)

COMPOSITION:
ZEPANALZ 5 mg TABLETS:
Each film-coated tablet contains donepezil hydrochloride 5 mg. Contains sugar: 84 mg lactose.

ZEPANALZ 10 mg TABLETS:
Each film-coated tablet contains donepezil hydrochloride 10 mg. Contains sugar: 168 mg lactose.

The other excipients in the formulations are pregelatinised starch, microcrystalline cellulose, hydroxypropylcellulose, magnesium stearate, hypromellose, polyethylene glycol, talc and titanium dioxide. **ZEPANALZ 10 mg TABLETS** also contains iron oxide yellow.

PHARMACOLOGICAL CLASSIFICATION:
A 5.3 Cholinomimetics (cholinergics)

PHARMACOLOGICAL ACTION:

Pharmacodynamics:
Donepezil hydrochloride is a reversible inhibitor of acetylcholinesterase, the predominant cholinesterase in the brain. Donepezil hydrochloride is over 1000 times more potent an inhibitor of this enzyme than of butylcholinesterase, an enzyme which is present mainly outside the central nervous system (CNS).

In patients with Alzheimer's dementia participating in clinical trials, administration of single daily doses of 5 mg or 10 mg of donepezil produced steady-state inhibition of acetylcholinesterase activity (measured in erythrocyte membranes) of 63,6 % and 77,3 %, respectively when measured post dose. The inhibition of acetylcholinesterase (AChE) in red blood cells by donepezil hydrochloride has been shown to correspond closely to the effects in the cerebral cortex. In addition, significant correlation was demonstrated between plasma levels of donepezil hydrochloride, AChE inhibition and change in ADAS-cog, a sensitive and well-validated scale which examines cognitive performance - including memory, orientation, attention, reason, language and praxis.

Mechanism of action:
Current theories on the pathogenesis of the cognitive signs and symptoms of Alzheimer's disease attribute some of them to a deficiency of cholinergic neurotransmission. Donepezil hydrochloride is postulated to exert its therapeutic effect by enhancing cholinergic function. This is accomplished by increasing the concentration of acetylcholine through reversible inhibition of its hydrolysis by acetylcholinesterase. If this proposed mechanism of action is correct, donepezil's effect may lessen as the disease process advances and fewer cholinergic neurons remain intact. There is no evidence that donepezil alters the course of the underlying process.

The enzyme AChE also occurs peripherally in red blood cells, therefore, measurement of AChE activity in erythrocyte membranes provides an index for donepezil hydrochloride pharmacodynamics.

Pharmacokinetics:
Absorption:
Oral administration of donepezil produces predictable plasma concentrations with maximal values achieved approximately 3 to 4 hours after dose administration. Plasma concentrations and area under the curve (AUC) rise in proportion to the dose. The elimination half-life is approximately 70 hours, thus, administration of multiple single-daily doses results in gradual approach to steady-state. Approximate steady-state is achieved within 3 weeks after the initiation of therapy. Once at steady-state, plasma donepezil hydrochloride concentrations and the related pharmacodynamic activity show little variability over the course of the day. Neither food nor time of administration (morning versus evening dose) affect the absorption of donepezil hydrochloride.

Distribution:
The steady-state volume of distribution is 12 L/kg. Donepezil hydrochloride is approximately 96 % bound to human plasma proteins. The distribution of donepezil hydrochloride in various body tissues has not been definitively studied. However, in a mass balance study conducted in healthy male volunteers, 240 hours after the administration of a single 5 mg dose of 14C-labelled donepezil hydrochloride, approximately 28 % of the labelled substance remained unrecovered. This suggests that donepezil hydrochloride and/or any of its metabolites may persist in the body for more than 10 days. The average CSF:plasma ratio for both doses, expressed as a percentage of the concentration in plasma was 15,7 %.

Metabolism / Excretion:
Donepezil is hepatically metabolised and the predominant route for the elimination of both the parent compound and its metabolites is renal, as 79 % of the recovered dose was found in the urine with the remaining 21 % in the faeces. Moreover, the parent compound, donepezil, is the predominant elimination product in urine. The major metabolites of donepezil include M1 and M2 (via O-dealkylation and hydroxylation), M11 and M12 (via glucuronidation of M1 and M2 respectively), M4 (via hydrolysis) and M6 (via N-oxidation). There is no evidence to suggest enterohepatic recirculation of donepezil hydrochloride and/or any of its metabolites. Plasma donepezil concentrations decline with a half-life of approximately 70 hours. Sex, race and smoking history have no clinically significant influence on plasma concentrations of donepezil hydrochloride.

INDICATIONS:
ZEPANALZ TABLETS are indicated for the symptomatic treatment of mild or moderate dementia in Alzheimer's disease.

CONTRA-INDICATIONS:
ZEPANALZ TABLETS is contra-indicated in patients with a known hypersensitivity to donepezil hydrochloride, piperidine derivatives or to any other ingredients used in the formulation.

The safety and efficacy of **ZEPANALZ TABLETS** has not been established in children; therefore it is not recommended for use in children.

Pregnancy and lactation (see **PREGNANCY AND LACTATION**).

WARNINGS AND SPECIAL PRECAUTIONS:
Treatment should be initiated by a doctor experienced in the treatment of Alzheimer's dementia. Maintenance treatment can be continued for as long as a therapeutic benefit for the patient exists. Therefore, the clinical benefit of **ZEPANALZ TABLETS** should be reassessed on a regular basis. When evidence of a therapeutic effect is no longer present, discontinuation should be considered. Individual response to **ZEPANALZ TABLETS** cannot be predicted.

The use of **ZEPANALZ TABLETS** in patients with severe dementia, other types of dementia or other types of memory impairment (e.g. age related cognitive decline), has not been established.

Anaesthesia: ZEPANALZ TABLETS, as a cholinesterase inhibitor, is likely to exaggerate succinylcholine type muscle relaxation during anaesthesia.

Cardiovascular Conditions: Due to their pharmacological action, **ZEPANALZ TABLETS** may have vagotonic effects on heart rate (e.g. bradycardia). The potential for this action may be particularly important to patients with "sick sinus syndrome" or other supraventricular cardiac conduction conditions such as sinoatrial or atrioventricular block. Syncopal episodes have been reported in association with the use of donepezil.

Gastrointestinal Conditions: Gastric acid production may be promoted by **ZEPANALZ TABLETS**. Therefore patients should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those at increased risk of developing ulcers e.g. those with a history of ulcer disease or those receiving concurrent non-steroidal anti-inflammatory drugs (NSAIDs). Donepezil, as a predictable consequence of its pharmacological properties, has been shown to produce diarrhoea, nausea and vomiting. These effects, when they occur, appeared more frequently with the 10 mg/day dose than with the 5 mg/day dose. In most cases, these effects have been mild and transient, sometimes lasting one to three weeks, and have resolved during continued use of donepezil.

Genitourinary: ZEPANALZ TABLETS may cause bladder outflow obstruction.

Neurological Conditions: ZEPANALZ TABLETS are believed to have some potential to cause generalised convulsions. However, seizure activity may also be a manifestation of Alzheimer's disease.

Pulmonary Conditions: Due to their cholinomimetic actions, **ZEPANALZ TABLETS** should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease. The administration of **ZEPANALZ TABLETS** concomitantly with other inhibitors of acetylcholinesterase, agonists or antagonists of the cholinergic system should be avoided.

Patients recovering from bladder or gastrointestinal surgery: ZEPANALZ TABLETS use is not recommended in patients recovering from bladder or gastrointestinal surgery.

The use of donepezil is associated with weight loss. Patients' weight should be monitored during treatment with **ZEPANALZ TABLETS**.

Female patients are more susceptible to nausea, vomiting, anorexia and weight loss.

Important information about some of the ingredients of ZEPANALZ TABLETS:
ZEPANALZ TABLETS contains lactose and should not be given to patients with rare hereditary problems, or a history of galactose intolerance, Lapp-lactose defciency or glucose-galactose malabsorption.

Effects on the ability to drive and use machines
Dementia may cause impairment of driving performance or compromise the ability to use machinery. Furthermore, **ZEPANALZ TABLETS** can induce fatigue, dizziness and muscle cramps, mainly when initiating or increasing the dose. The treating doctor should routinely evaluate the ability of patients on **ZEPANALZ TABLETS** to continue driving or operating complex machines.

INTERACTIONS:

Medicines highly bound to plasma proteins:
Medicine displacement studies have been performed *in vitro* between this highly bound medicine (96 %) and other medicines such as furosemide, digoxin and warfarin. **ZEPANALZ TABLETS** at concentrations of 0,3 - 10 µg/mL does not affect the binding of furosemide (5 µg/mL), digoxin (2 µg/mL), and warfarin (3 µg/mL) to human albumin. Similarly, the binding of **ZEPANALZ TABLETS** to human albumin is not affected by furosemide, digoxin and warfarin.

Effect of ZEPANALZ TABLETS on the metabolism of other medicines:
No *in vivo* clinical trials have investigated the effect of **ZEPANALZ TABLETS** on the clearance of medicines metabolised by CYP3A4 (e.g. cisapride) or by CYP2D6 (e.g. imipramine). However, *in vitro* studies show a low rate of binding to these enzymes (mean Ki about 50 - 130 µM), that, given the therapeutic plasma concentrations of donepezil (164 nM), indicates little likelihood of interference. Whether **ZEPANALZ TABLETS** has any potential for enzyme induction is not known.

Donepezil hydrochloride and/or any of its metabolites do not inhibit the metabolism of theophyline, warfarin, cimetidine, digoxin, thioridazine, risperidone and sertraline in humans. In a study of Parkinson's disease patients on optimal treatment with L-dopa/carbidopa, administration of donepezil for 21 days had no effects on L-dopa or carbidopa blood levels. In this study, no effects on motor activity were observed.

Effects of other medicines on the metabolism of ZEPANALZ TABLETS:
Ketoconazole and quinidine, inhibitors of CYP450, 3A4 and 2D6, respectively, inhibit donepezil metabolism *in vitro*. Therefore these and other CYP3A4 inhibitors, such as itraconazole and erythromycin, and CYP2D6 inhibitors, such as fluoxetine could inhibit the metabolism of donepezil. Whether there is a clinical effect of these inhibitors is not known. In a study in healthy volunteers, ketoconazole increased mean donepezil concentrations by 30 %. These increases are smaller than those produced by ketoconazole for other agents sharing the CYP-3A4 pathway and are not likely to be clinically relevant. Administration of donepezil had no effect on the pharmacokinetics of ketoconazole. Inducers of CYP2D6 and CYP3A4 (e.g. phenytoin, carbamazepine, alcohol, dexamethasone, rifampicin and phenobarbital) could increase the rate of elimination of **ZEPANALZ TABLETS**.

Formal pharmacokinetic studies demonstrated that the metabolism of donepezil is not significantly affected by concurrent administration of digoxin, cimetidine, thioridazine, risperidone or sertraline.

Use with anticholinergics:
ZEPANALZ TABLETS have the potential to interfere with the activity of anticholinergic medications, because of their mechanism of action.

Use with cholinomimetics and other cholinesterase inhibitors:
A synergistic effect may be expected when **ZEPANALZ TABLETS** are given concurrently with succinylcholine, similar neuromuscular blocking agents or cholinergic agonists such as bethanechol or beta blocking agents which have an effect on cardiac conduction, but an *in vitro* study showed that donepezil hydrochloride had minimal effects on hydrolysis of succinylcholine.

PREGNANCY AND LACTATION:
The safety of **ZEPANALZ TABLETS** in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Adults/Elderly:
The recommended dosages of **ZEPANALZ TABLETS** are 5 mg or 10 mg administered once daily. Although there is no statistically significant evidence that a greater treatment effect is obtained from the use of the 10 mg dose, there is a suggestion, based on analysis of group data that some additional benefits may accrue to some patients from the use of the higher dose. Treatment is initiated at 5 mg/day (once-a-day dosing).

The 5 mg/day dose should be maintained for at least 4 – 6 weeks in order to allow the earliest clinical responses to treatment to be assessed and to allow steady-state concentrations of donepezil hydrochloride to be achieved. Following a one-month clinical assessment of treatment at 5 mg/day, the dose of **ZEPANALZ TABLETS** can be increased to 10 mg/day (once-a-day dosing). The maximum recommended daily dose is 10 mg. Doses greater than 10 mg/day have not been studied in clinical trials. Upon discontinuation of treatment, a gradual abatement of the beneficial effects of **ZEPANALZ TABLETS** is seen. After abrupt discontinuation of therapy, there is no evidence of a rebound effect.

Renal and Hepatic Impairment:
A similar dose schedule can be followed for patients with renal or mild to moderate hepatic impairment as clearance of donepezil hydrochloride is not affected by these conditions.

SIDE EFFECTS:

Infections and infestations:
Frequent: Common cold, influenza

Metabolism and nutrition disorders:
Less frequent: Dehydration, hyponatraemia

Psychiatric disorders:
Frequent: Insomnia, abnormal dreams, agitation, delusions, depression, hallucinations
Less frequent: Abnormal crying, aggressive behaviour, increased libido, irritability, nervousness, restlessness, confusion

Nervous system disorders:
Frequent: Dizziness, headache, somnolence
Less frequent: Aphasia, ataxia, paraesthaesia, syncope, tremor, seizure, extrapyramidal symptoms

Eye disorders:
Less frequent: Cataract, eye irritation, blurred vision

Ear and labyrinth disorders:
Less frequent: Vertigo

Cardiac disorders:
Less frequent: Atrioventricular block, bradycardia, sinoatrial block, angina

Vascular disorders:
Less frequent: Hot flushes, hypertension, hypotension, vasodilation

Respiratory, thoracic and mediastinal disorders:
Less frequent: Dyspnoea, sore throat, bronchitis

Gastrointestinal disorders:
Frequent: Diarrhoea, nausea, vomiting, anorexia, pancreatitis, faecal incontinence, abdominal disturbance
Less frequent: Gastrointestinal haemorrhage, epigastric pain, bloating, toothache, duodenal ulcer, gastric ulcer

Hepato-biliary disorders:
Less frequent: Hepatitis

Skin and subcutaneous tissue disorders:
Less frequent: Diaphoresis, ecchymosis, pruritus, urticaria, rash

Musculoskeletal, connective tissue and bone disorders:
Frequent: Muscle cramps, arthritis

Renal and urinary disorders:
Frequent: Frequent urination
Less frequent: Nocturia, urinary incontinence, urinary tract infection

General disorders and administrative site conditions:
Frequent: Fatigue, pain
Less frequent: Chest pain

Investigations:
Frequent: Weight decrease
Less frequent: Minor increases in serum concentrations of creatine kinase, increased liver transaminases

Injury and poisoning:
Less frequent: Accidents, bone fracture

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Dose-related signs of cholinergic stimulation were observed in animals and included reduced spontaneous movement, prone position, staggering gait, lacrimation, clonic convulsions, depressed respiration, salivation, miosis, fasciculation and lower body surface temperature. Overdosage with **ZEPANALZ TABLETS** can result in cholinergic crisis characterised by severe nausea, vomiting, salivation, sweating, bradycardia, hypotension, respiratory depression, collapse and convulsions.

Increasing muscle weakness is a possibility and may result in death if respiratory muscles are involved.

General supportive measures should be utilised. Tertiary anticholinergics such as atropine may be used as an antidote for **ZEPANALZ TABLETS** overdosage. Intravenous atropine sulphate titrated to effect is recommended: an initial dose of 1,0 to 2,0 mg IV with subsequent doses based upon clinical response. Atypical responses in blood pressure and heart rate have been reported with other cholinomimetics when co-administered with quaternary anticholinergics such as glycopyrrolate. It is not known whether donepezil hydrochloride and/or its metabolites can be removed by dialysis (hemodialysis, peritoneal dialysis, or hemofiltration).

IDENTIFICATION:

ZEPANALZ 5 mg TABLETS:
White to off-white, circular, biconvex, film-coated tablets debossed with 'X' on one side and '11' on the other side.

ZEPANALZ 10 mg TABLETS:
Yellow coloured, circular, biconvex, film-coated tablets debossed with 'X' on one side and '12' on the other side.

PRESENTATION:

ZEPANALZ 5 5 mg and 10 mg TABLETS:
1) **Blister Pack:**
Tablets are packed in 250 µm clear PVC/25 µm PE/90 g/m² PVdc and silver coloured printed 25 µm aluminium foil with 7 g/m² heat seal lacquer.
Each blister contains 10 tablets.
Pack size: 30's –Each carton contains 3 blisters of 10 tablets each.

2) **HDPE Container Pack:**
Tablets are packed in 40 mL HDPE white containers with white closure with induction sealing wad containing 1 x 1 g silica gel sachet.
Each container contains 30 tablets.
Pack size: 30's - One HDPE container contains 30 tablets.

STORAGE INSTRUCTIONS:
Store at or below 25 °C. Protect from light. Do not remove blisters from carton until required for use. Keep securitainer well-closed after use.

KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBERS:

SOUTH AFRICA:
ZEPANALZ 5 mg: 44/5.3/0944
ZEPANALZ 10 mg: 44/5.3/0945

NAMBIA:
ZEPANALZ 5 mg: 19/5.3/0924
ZEPANALZ 10 mg: 19/5.3/0923

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

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:
Date of registration:
20 June 2013

Date of revision:
18 September 2021

P15300333

DETACH BEFORE DISPENSING

5. POSSIBLE SIDE EFFECTS
ZEPANALZ TABLETS can have side effects.
Get emergency medical help if you have any of these signs of an allergic reaction:
- Hives; difficulty breathing, swelling of your face, lips, tongue or throat.

Call your doctor at once if you have any of these serious side effects:
- Seizures (fits) or convulsions
- Slow heartbeat
- Fainting
- Black, bloody, or tarry stools
- Coughing up blood or vomit that looks like blood or coffee grounds
- Chest pain
- Hepatitis (inflammation of the liver). The symptoms of hepatitis are nausea or vomiting, loss of appetite; feeling generally unwell; fever; itching; yellowing of the skin and eyes and dark coloured urine.

Other side effects include: the common cold; flu; excessive loss of body water; inability to sleep; abnormal dreams; being agitated; depression; abnormal crying; aggressive behaviour; increased sexual desire; nervousness; restlessness; hallucinations (seeing or hearing things that are not really there); dizziness; headache; sleepiness; language disorder; loss of muscle co-ordination; numbness, tingling, pins and needles; tremor (shake); decrease in vision due to clouding of the lens of the eye; eye irritation; blurred vision; hot flushes; high blood pressure; low blood pressure; shortness of breath; sore throat; diarrhoea (frequent or loose watery stools); lack of appetite; stomach pain; abnormal swelling due to a collection of gas or fluid in your abdomen; toothache; stomach ulcer; duodenal ulcer (ulcer in the duodenum); increased sweating; itching; muscle cramps; passing urine frequently; inability to control urination; infection of the urinary tract; extreme tiredness; pain; loss of weight; accidents; bone fractures.

Tell your doctor if any of the above side effects are severe, bothersome, do not go away or about any other concerns you have while taking **ZEPANALZ TABLETS.**

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

6. STORING AND DISPOSING OF ZEPANALZ TABLETS
Store at or below 25 °C. Protect from light. Do not remove blisters from carton until required for use. Keep securitainer well-closed after use.

Store all medicines out of reach of children.

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

7. PRESENTATION OF ZEPANALZ TABLETS
ZEPANALZ 5 mg and 10 mg TABLETS:
1) **Blister Pack:**
Tablets are packed in 250 µm clear PVC/25 µm PE/90 g/m² PVdc and silver coloured printed 25 µm aluminium foil with 7 g/m² heat seal lacquer.
Each blister contains 10 tablets.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.

2) **HDPE Container Pack:**
Tablets are packed in 40 mL HDPE white containers with white closure with induction sealing wad containing 1 x 1 g silica gel sachet.
Each container contains 30 tablets.
Pack size: 30's - One HDPE container contains 30 tablets.

8. IDENTIFICATION OF ZEPANALZ TABLETS
ZEPANALZ 5 mg TABLETS:
White to off-white, circular, biconvex, film-coated tablets debossed with 'X' on one side and '11' on the other side.
ZEPANALZ 10 mg TABLETS:
Yellow coloured, circular, biconvex, film-coated tablets debossed with 'X' on one side and '12' on the other side.

9. REGISTRATION NUMBERS
SOUTH AFRICA:
ZEPANALZ 5 mg: 44/5.3/0944
ZEPANALZ 10 mg: 44/5.3/0945
NAMBIA:
ZEPANALZ 5 mg: 19/5.3/0924
ZEPANALZ 10 mg: 19/5.3/0923

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, 1448
Johannesburg
South Africa

11. DATE OF PUBLICATION
Date of registration:
20 June 2013
Date of revision:
18 September 2021

SOUTH AFRICA: S5
NAMIBIA: NS3

ZEPANALZ 5 mg TABLETS (tablet)
ZEPANALZ 10 mg TABLETS (tablet)
Donepezil hydrochloride

Read all of this leaflet carefully before you start taking ZEPANALZ TABLETS.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **ZEPANALZ 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.

1. WHAT ZEPANALZ TABLETS CONTAIN
The active ingredient is donepezil hydrochloride.

ZEPANALZ 5 mg TABLETS:
Each film-coated tablet contains donepezil hydrochloride 5 mg. Contains sugar: 84 mg lactose.

ZEPANALZ 10 mg TABLETS:
Each film-coated tablet contains donepezil hydrochloride 10 mg. Contains sugar: 168 mg lactose.

The other ingredients of **ZEPANALZ TABLETS** are hypromellose, hydroxypropyl cellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, pregelatinised starch, talc and titanium dioxide. **ZEPANALZ 10 mg TABLETS** also contains iron oxide yellow.

2. WHAT ZEPANALZ TABLETS ARE USED FOR
ZEPANALZ TABLETS belongs to a group of medicines called acetylcholinesterase inhibitors.

ZEPANALZ TABLETS are used to treat mild to moderate dementia (a brain disorder that affects the ability to remember, think clearly, communicate, and perform daily activities and may cause changes in mood and personality) caused by Alzheimer's disease.

3. BEFORE YOU TAKE ZEPANALZ TABLETS
Do not take ZEPANALZ TABLETS:
- If you are hypersensitive (allergic) to donepezil hydrochloride, piperidine derivatives or any of the other ingredients of **ZEPANALZ TABLETS**.
- **ZEPANALZ TABLETS** should not be given to children as the safety and effectiveness of **ZEPANALZ TABLETS** has not been established in children.

Take special care with ZEPANALZ TABLETS:
- The use of **ZEPANALZ TABLETS** in patients with severe dementia, other types of dementia or other types of memory problems has not been determined.

Before taking ZEPANALZ TABLETS, tell your doctor if you have or have had:
- "Sick sinus syndrome" which may present with symptoms such as chest pain, shortness of breath, dizziness, fatigue, nausea, fainting or a fast heartbeat, or other heart disease.
- Gastrointestinal (affecting the stomach and intestines) bleeding, ulcers, or if you are taking non-steroidal anti-inflammatory drugs (NSAIDs).
- Seizures (fits) or convulsions.
- Asthma or other obstructive lung disease.
- Difficulty passing urine.
- If you are having surgery, including dental surgery, tell the doctor or dentist that you are taking **ZEPANALZ TABLETS**.
- If you are recovering from recent bladder or gastrointestinal surgery.

Taking ZEPANALZ TABLETS with food and drink:
ZEPANALZ TABLETS can be taken with or without food.

Alcohol may change the effect of **ZEPANALZ TABLETS**, as the rate that **ZEPANALZ TABLETS** is eliminated from your system is increased therefore decreasing the duration that **ZEPANALZ TABLETS** may work for you.

Pregnancy and breastfeeding:
The safe use of **ZEPANALZ TABLETS** during pregnancy and while breastfeeding your baby has not been established.

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

Driving and using machinery:
Dementia may impair your ability to drive or operate machinery. Also, **ZEPANALZ TABLETS** can cause tiredness, dizziness and muscle cramps, especially when starting or increasing the dose. You must not drive or operate machinery unless your doctor tells you that it is safe to do so.

Important information about some of the ingredients of ZEPANALZ TABLETS:
ZEPANALZ TABLETS contain lactose, therefore you should tell your doctor if you are lactose intolerant or have a history of galactose intolerance, Lapp-lactose deficiency or glucose-galactose malabsorption.

Taking other medicines with ZEPANALZ TABLETS:
Before taking **ZEPANALZ TABLETS**, tell your doctor if you are using any of the following medicines:
- Pain killers or treatment for arthritis e.g. NSAIDs such as ibuprofen or diclofenac sodium.
- Antibiotics e.g. erythromycin, rifampicin.
- Anti-fungal medicines e.g. ketoconazole, itraconazole.
- Anti-depressants e.g. fluoxetine.
- Anticonvulsants e.g. phenytoin, carbamazepine, phenobarbital.
- Medication for a heart condition e.g. quinidine.
- Corticosteroids e.g. dexamethasone.
- Muscle relaxants e.g. succinylcholine.
- General anaesthetic – If you are going to have an operation that requires you to have a general anaesthetic, you should tell your doctor or anaesthetist that you are taking **ZEPANALZ TABLETS**.

If you are using any of the above medicines, you may not be able to take **ZEPANALZ TABLETS**, or you may need dosage adjustments or your doctor may need to monitor you carefully for side effects.

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

4. HOW TO TAKE ZEPANALZ TABLETS

Always take **ZEPANALZ TABLETS** 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 **ZEPANALZ TABLETS** is too strong or too weak, talk to your doctor or pharmacist.

Adults and the elderly:
- The usual starting dose is 5 mg once a day.
- After one month, your doctor may increase your dose to 10 mg once a day.
- The maximum recommended dose is 10 mg once a day.
- The dose is similar for patients with kidney disease or mild to moderate liver disease.

If you take more ZEPANALZ TABLETS than you should:
Symptoms of overdose may include nausea and vomiting, drooling, sweating, slow heart rate, low blood pressure, breathing problems, losing consciousness and seizures (fits).

If you forget to take ZEPANALZ TABLETS:
Take the missed dose as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at your next regularly scheduled time. Do not take a double dose to make up for forgotten individual doses.

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