Pharmacode position may change as per the supplier's m/c requirement

APPROVED
Samantha , 2023/02/17 ,07:48:20

ZYESCITO TABLETS
P1533005

ZYESCITO TABLETS
P1533005

16/02/2023

PROFESSIONELE INLIGTING VIR MEDISYNE VIR MENSLIKE GEBRUIK

SKEDULERINGSTATUS

S5

EIENDOMSNAAM (en dosisvorm):

ZYESCITO 5 mg TABLETS (tablet)
ZYESCITO 10 mg TABLETS (tablet)
ZYESCITO 20 mg TABLETS (tablet)

SAMESTELLING:

ZYESCITO 5 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 5 mg essitalopram. Suikervry.

ZYESCITO 10 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 10 mg essitalopram. Suikervry.

ZYESCITO 20 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 20 mg essitalopram. Suikervry.

Die ander mengmiddels in die formulering is: gesilliseerde mikrokristalliene sellulose, natriumkroskarmellose, butielhidroksitolueen, butielhidroksi-anisool, mikrokristalliyne sellulose, kolloïdale watervrye silika, talk, magnesiumstearaat.

Bedekkingsmateriaal: hipromellose, makrogol 400, titaandioksied (Kl. nr. 77891).

FARMAKOLOGIESE KLASSIFIKASIE:

A1.2: Psigonaalaktiku (antidepressante)

FARMAKOLOGIESE WERKINGS:

Farmakodinamika:

Essitalopram is 'n potente en selektiewe inhibeerder van serotonien(5-HT)-opname.

Essitalopram het 'n minimale effek op die opname van noradrenalien (NA), dopamien (DA) en gamma-aminobottersuur (GABA). Essitalopram het geen of 'n baie lae affiniteit vir 'n reeks reseptore insluitend 5-HT$_{1A}$, 5-HT$_2$-, DA, D_1 en D_2-reseptore, α_1-, α_2-, β-adrenoseptore, histamien H$_1$-, muskarieniese, bensodiasepien- en opioïede reseptore.

Farmakokinetika:

Absorpsie

Absorpsie is onafhanklik van voedselinname; gemiddelde t_{max} is 4 uur na veelvoudige dosering.

Distribusie

Die skynbare volume van distribusie (V_{d}/F) na orale toediening is ongeveer 12 tot 26 l/kg. Die plasmaproteïenbinding van essitalopram is ongeveer 55 %.

Biotransformasie

Essitalopram word gemetaboliseer in die lewer tot demetileerde en didemetileerde metaboliete. As alternatief mag die stikstof geoksideer word om 'n N-oksied-metaboliet te vorm. Beide die stamverbinding en die metaboliete word gedeeltelik as glukuronide uitgeskei. Onveranderde essitalopram is die oorheersende verbinding in plasma. Na veelvoudige dosering is die gemiddelde konsentrasies van die demetiel- en die didemetiel-metaboliete gewoonlik onderskeidelik 28-31 % en < 5 % van die essitalopramkonsentrasie. Biotransformasie van essitalopram na die gedemetileerde metaboliet word deur 'n kombinasie van CYP2C19, CYP3A4 en CYP2D6, bemiddel.

Eliminasie

Die eliminasie halfleeftyd na veelvoudige dosering is ongeveer 30 uur en die plasmaopruiming na orale toediening (Cl_{oral}) is ongeveer 0,6 l/min. Dit word aanvaar dat essitalopram en die hoofmetaboliete beide deur die hepatiese (metaboliese) en die renale roetes geëlimineer word en dat die grootste deel van die dosis as metaboliete in die urine uitgeskei word.

Hepatiese opruiming vind hoofsaaklik deur die P450-ensiemsisteem plaas. CYP2C19 is die primêre isoënsiem wat by die demetilering van essitalopram betrokke is, gevolg deur CYP3A4 en CYP2D6. Die farmakokinetika is lineêr. Ewewigstoestand plasmavlakke word binne ongeveer 1 week bereik. Die gemiddelde ewewigstoestand konsentrasies van 50 nmol/l (ooreenkomstig met 20 tot 125 nmol/l) word teen 'n daaglikse dosis van 10 mg bereik.

Bejaarde pasiënte (> 65-jarige ouderdom)

'n Langer halfleeftyd (ongeveer 50 %) en verminderde opruimingswaardes as gevolg van 'n verlaagde tempo van metabolisme is by bejaardes gedemonstreer.

Verminderde hepatiese funksie

Essitalopram word stadiger in pasiënte met verminderde hepatiese funksie uitgeskei. Die halfleeftyd van essitalopram is twee keer so lank by pasiënte met hepatiese inkorting en ewewigstoestand essitalopramkonsentrasies teen 'n gegewe dosis sal ongeveer twee keer hoër wees as by pasiënte met normale lewerfunksie.

Verminderde renale funksie

Essitalopram word stadiger by pasiënte met ligte tot matige vermindering van renale funksie uitgeskei sonder dat dit 'n groot impak op die essitalopramkonsentrasies in serum het. Tans is geen inligting vir die behandeling van pasiënte met ernstig verminderde renale funksie (kreatinienopruiming < 30 ml/min), beskikbaar nie.

Polimorfisme

Gegrond op *in vitro* resultate met essitalopram is genetiese polimorfisme met betrekking tot CYP2D6 nie bekend nie; met betrekking tot CYP2C19 mag dit klinies relevant wees soos in 'n beperkte aantal pasiënte al aangedui kon word.

INDIKASIES:

Behandeling van major depressiewe episodes.

KONTRA-INDIKASIES:

Hipersensitiwiteit teen essitalopram of enigeen van die mengmiddels.

Kinders onder die ouderdom van 18 jaar, omdat veiligheid en doeltreffendheid nie in hierdie bevolking vasgestel is nie.

Pasiënte met bekende QT-intervalverlenging of aangebore lang-QT-sindroom (sien **"WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS").**

Medisinale produkte wat bekend is daarvoor dat dit die QT-interval verleng (sien **"WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS")**.

Monoamienoksidase-inhibeerders: Gevalle van ernstige reaksies is aangemeld by pasiënte wat 'n selektiewe serotonienheropname-inhibeerder (SSHI) in kombinasie met 'n monoamienoksidase-inhibeerder (MAOI) ontvang het, en by pasiënte wat onlangs 'n SSHI gestaak het en op 'n MAOI begin is (sien **"INTERAKSIES").** Sommige gevalle het gepresenteer met eienskappe wat lyk soos serotoniensindroom (sien **"SPESIALE VOORSORGSMAATREËLS").**

ZYESCITO TABLETS behoort nie in kombinasie met 'n MAOI gebruik te word nie. **ZYESCITO TABLETS** mag 14 dae na staking van behandeling met 'n MAOI begin word. Ten minste 7 dae behoort verby te gaan na staking van behandeling met **ZYESCITO TABLETS** voordat 'n MAOI begin word.

WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS:

QT-intervalverlenging: Daar is gevind dat **ZYESCITO TABLETS** 'n dosisafhanklike verlenging van die QT-interval veroorsaak. Gevalle van QT-intervalverlenging, ventrikulêre verlenging en ventrikulêre disritmieë insluitend torsade de pointes is tydens die nabemarkkingsperiode aangemeld, hoofsaaklik by pasiënte van vroulike geslag, met hipokalemie, of met voorafbestaande QT-intervalverlenging of ander hartsiektes.

Omsigtigheid word aanbeveel by pasiënte met beduidende bradikardie; of by pasiënte met onlangse akute miokardiale infarksie of ongekompenseerde hartversaking.

Elektrolietversteurings soos hipokalemie en hipomagnesemie verhoog die risiko van maligne disritmie en behoort gekorrigeer te word voordat behandeling met **ZYESCITO TABLETS** begin word.

Indien pasiënte met stabiele hartsiekte behandel word, behoort 'n EKG-ondersoek oorweeg te word voordat behandeling begin word.

Indien tekens van kardiale disritmie gedurende behandeling met **ZYESCITO TABLETS** voorkom, moet die behandeling onttrek word en 'n EKG moet uitgevoer word.

Manie - ZYESCITO TABLETS behoort onttrek te word in enige pasiënt wat 'n maniese fase binnegaan. **ZYESCITO TABLETS** behoort met versigtigheid gebruik te word by pasiënte met 'n geskiedenis van manie/hipomanie.

Paradoksale angs - Sommige pasiënte met paniekversteuring mag 'n toename in simptome van angs aan die begin van behandeling met **ZYESCITO TABLETS** ondervind. Hierdie paradoksale reaksie bedaar gewoonlik binne twee weke van voortgesette behandeling. 'n Lae aanvangsdosis word aanbeveel om die waarskynlikheid van 'n paradoksale angsgeïnsteerde effek te verminder.

Aanvalle - ZYESCITO TABLETS moet gestaak word by enige pasiënt wat aanvalle ontwikkel. **ZYESCITO TABLETS** behoort vermy te word by pasiënte met onstabiele epilepsie en pasiënte met behoerde epilepsie behoort versigtig gemoniteer te word. **ZYESCITO TABLETS** moet gestaak word indien daar 'n toename in die frekwensie van aanvalle voorkom.

Diabetes mellitus - By pasiënte met diabetes mellitus mag behandeling met **ZYESCITO TABLETS** glisemiese beheer verander, moontlik as gevolg van verbetering van depressiewe simptome. Die dosisse insulien en/of orale hipoglisemiese medikasies sal moontlik aangepas moet word.

Selfmoord - Omdat 'n verbetering nie tydens die eerste paar weke of meer van behandeling mag voorkom nie, moet pasiënte versigtig gemoniteer word vir die risiko van selfmoord.

Bloeding - Bevatte van bloedingsabnormaliteite van die vel, soos eggimoses en purpura het met essitalopram voorgekom. Omsigtigheid word aangeraai by pasiënte wat **ZYESCITO TABLETS** neem, veral tydens gelyktydige gebruik saam met medisyne waar dit bekend is dat dit plaatjiefunksie affekteer (bv. atipiese antipsigotiese middels en fenotiasiene, die meerderheid van trisikliese antidepressante, aspirien en nie-steroïedale anti-inflammatoriese medisyne (NSAIMs)), asook by pasiënte met 'n geskiedenis van bloedsiektes.

EKT (elektrokonvulsiewe terapie) - Daar is slegs beperkte gepubliseerde kliniese ondervinding van gelyktydige toediening van **ZYESCITO TABLETS** en EKT beskikbaar, omsigtigheid word dus aanbeveel.

Risiko van Serotoniensindroom

Gelyktydige toediening saam met MAOIs mag serotoniensindroom veroorsaak.

Gelyktydige toediening saam met ander serotonergiese medisyne (bv. tramadol, sumatriptan), asook ander antidepressante met serotonergiese eienskappe mag lei tot 'n versterking van serotonien-geassosieerde effekte, bv. die serotoniensindroom.

Bereging is ontvang van versterkte effekte toe essitalopram saam met litium of triptofaan gegee is, en dus behoort gelyktydige gebruik van **ZYESCITO TABLETS** saam met hierdie medisyne moet omsigtigheid ondersteen word.

Effekte op die vermoë om te bestuur en masjiene te gebruik

ZYESCITO TABLETS benadeel nie die intellektuele funksie of psigomotoriese prestasie nie.

Pasiënte wat depressief is en behandeling benodig, mag ingekorte vermoëns hê om te bestuur of masjiene te hanteer. Hulle behoort oor hierdie moontlikheid gewaarsku te word en aangeraai word om sulke take te vermy indien hulle so geaffekteer word.

INTERAKSIES:

Essitalopram het 'n lae potensiaal vir klinies beduidende medisyne-interaksies. *In vitro* studies het aangedui dat die biotransformasie van essitalopram na sy gedemetileerde metaboliete afhanklik is van drie parallelle bane (sitochroom P450 (CYP) 2C19, 3A4 en 2D6). Essitalopram is 'n swak inhibeerder van isoënsiem CYP1A2, 2C9, 2C19, 2E1, en 3A en 'n swak inhibeerder van 2D6.

QT-intervalverlenging

Farmakokinetiese en farmakodinamiese studies van **ZYESCITO TABLETS** gekombineer met ander medisinale produkte wat die QT-interval verleng, is nie uitgevoer nie. 'n Additiewe effek van essitalopram en hierdie medisinale produkte kan nie uitgesluit word nie. Gelyktydige toediening van **ZYESCITO TABLETS** saam met medisinale produkte wat die QT-interval verleng, soos Klas IA en III antidistritmiese middels (bv. amiodaron, kinidien), antipsigotiese middels (bv. fenotiasiendervate, pimosied, haloperidol), trisikliese antidepressante (bv. desimipramien, imipramien), sekere antimikrobiale middels (bv. moksifloksasien, eritromisien IV, pentamidien, antimalariaalbehandeling veral halofantrien), sekere antihistamiene (bv. misolasien) en antiretrovirale middels (bv. ritonavir, sakinavir, lopinavir), is dus teenaangedui.

Ritonavir:

Die farmakokinetika van enkeldosisse van essitalopram is nie deur gelyktydige toediening met 'n enkele dosis ritonavir (CYP3A4-inhibeerder), verander nie.

Ketokonazool:

Gelyktydige toediening saam met ketokonazool (potente CYP3A4-inhibeerder) het geen effek op die farmakokinetika van **ZYESCITO TABLETS** nie.

Simetidien:

Gelyktydige toediening van rasemiese sitalopram saam met simetidien (potente CYP2D6-, 3A4-, en 1A2-inhibeerder), het verhoogde plasmakonsentrasies van die rasemaat verooraak (43 % verhoging in AOK, 39 % toename in K_{max}). Omsigtigheid behoort dus uitgeoefen te word aan die boonste end van die dosisreikwydte van **ZYESCITO TABLETS**, wanneer dit saam met hoë dosisse simetidien gebruik word.

Monoamienoksidase-inhibeerders MAOIs, Sumatriptan & Tramadol;

Gelyktydige toediening saam met MAO-inhibeerders mag serotoniensindroom veroorsaak (Sien **"KONTRA-INDIKASIES"**).

Gelyktydige toediening saam met ander serotonergiese medisyne (bv. tramadol, sumatriptan), asook ander antidepressante met serotonergiese eienskappe mag lei tot 'n versterking van serotonien-geassosieerde effekte, bv. serotoniensindroom.

Bereging van versterkte effekte is ontvang toe essitalopram saam met litium of triptofaan gegee is en gelyktydige gebruik van **ZYESCITO TABLETS** saam met hierdie medisyne behoort dus met omsigtigheid onderneem te word (sien **"WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS"**).

Desipramien:

Gelyktydige toediening saam met 'n enkele dosis desipramien ('n CYP2D6-substraat) het 'n tweevoudige verhoging in die plasmavlakke van desipramien verooraak. Omsigtigheid word dus aanbeveel wanneer **ZYESCITO TABLETS** en desipramien saam toegedien word. 'n Soortgelyke toename in plasmavlakke van desipramien na toediening van imipramien is waargeneem toe dit saam met rasemiese sitalopram toegedien is.

Metoprolol:

Gelyktydige toediening met 'n enkele dosis metoprolol 100 mg ('n CYP2D6-substraat) het 'n tweevoudige verhoging in die K_{max} en in 52 % verhoging in die AOK van metoprolol verooraak. Die kombinasie het egter geen klinies beduidende effekte op bloeddruk en hartfrempo gehad nie.

Selegilien:

Rasemiese sitalopram het die AOK van selegilien met 29 % verhoog.

Ander:

Farmakokinetiese interaksiestudies met rasemiese sitalopram het geen klinies belangrike interaksies met karbamasepien (CYP3A4-substraat), triasolam (CYP3A4-substraat), teofillien (CYP1A2-substraat) (enkele dosis), warfarien (CYP3A4- en CYP2C9-substraat), levomepromasien (CYP2D6-inhibeerder), litium en digoksien gedemonstreer nie.

Protrombientyd was egter effens verhoog na 'n enkele dosis van 25 mg warfarien. Die Internasionale Genormaliseerde Verhouding (INR) moet versigtig gemonitoer word by pasiënte op die kombinasie.

SWANGERSKAP EN LAKTASIE:

Die veiligheid van **ZYESCITO TABLETS** in swangeer en lakterende vrouens is nie vasgestel nie.

DOSIS EN GEBRUIKSAANWYSINGS:

Volwassenes

Major depressiewe episodes:

ZYESCITO TABLETS behoort as 'n enkele orale dosis van 10 mg daagliks in andersins gesonde volwassenes toegedien te word. Afhangende van die individuele pasiënt se reaksie, mag die dosis verhoog word tot 'n maksimum van 20 mg daagliks.

Gewoonlik is 2-4 weke nodig vir 'n antidepressante reaksie.

Bejaarde pasiënte (>65-jarige ouderdom)

'n Langer halfleeftyd en 'n verminderde opruiming is by bejaardes gedemonstreer. Die maksimum aanbevole dosis vir bejaarde pasiënte is 10 mg daagliks.

Verminderde renale funksie

Dosisaanpassing is nie by pasiënte met ligte tot matige renale inkorting nodig nie.

Geen inligting is beskikbaar oor die behandeling van pasiënte met ernstige ingekorte renale funksie (kreatinienopruiming <30 ml/min).

Verminderde hepatiese funksie

Dosisse behoort gehalveer te word tot die laer end van die dosisreikwydte by pasiënte met hepatiese ontoereikendheid. Die maksimum aanbevole dosis vir volwasses met hepatiese inkorting is 10 mg daagliks. **ZYESCITO TABLETS** word as 'n enkele daaglikse dosis toegedien. **ZYESCITO** mag sonder ingneming van voedselinname geneem word.

Serotonienontrekking

Wanneer terapie met **ZYESCITO TABLETS** gestaak word, behoort geleidelike dosisvermindering oorweeg te word.

NEWE EFFEKTE:

Nadelige reaksies wat met **ZYESCITO TABLETS** waargeneem is, is meer frekwent tydens die eerste een of twee weke van behandeling en mag in intensiteit en frekwensie met voorgesette behandeling afneem.

Na langdurige toediening, mag skielike staking van **ZYESCITO TABLETS** onttrekkingsreaksies by sommige pasiënte veroorsaak.

Endokriene versteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Omvanpaste ADH-sekresie

Metaboliese en voedingsversteurings
Frekwent:
Verminderde aptyt
Minder frekwent:
Hiponatremie, gewigsverlies, hiperprolaktinemie

Psigiatriese versteurings
Frekwent:
Verminderde libido, selfmoordgedagtes, slaaploosheid
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Hallusinasies, manie, verwarring, agitasie, angs, depersonalisasie, paniekaanvalle, senuagtigheid

Senusisteenversteurings
Frekwent:
Duiseligheid, lomerigheid
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Slaapversteuring, aanvalle, tremor, bewegingsversteurings, lomerigheid, smaakversteuring, serotoniensindroom (tipies gekenmerk deur 'n vinnige aanvang van veranderings in geestestoestand, met verwarring, manie, agitasie, hiperaktiwiteit, bewerasies, koors, tremor, okulêre bewegings, mioklonus, hiperreflekse, en inkoördinasie)

Kardiovaskulêre versteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Elektrokardiogram QT-verlenging, ventrikulêre disritmie insluitend torsade de pointes

Oogversteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Abnormale visie

Vaskulêre versteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Posturale hipotensie

Respiratoriese, torakale en mediastinale versteurings
Frekwent:
Sinusitis, gaap

Gastrointestinale versteurings
Frekwent:
Hardblywigheid, diarree, droë mond, naarheid
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Braking, anoreksie, dispepsie

Hepatobiliêre versteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Abnormale lewerfunksietoetse

Vel- en onderhuidse weefselversteurings
Frekwent:
Toename in sweet
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Veluitslag, eggimoses, pruritus, alopesie, fotosensitiwiteit, urtikarie, pireksie

Immuunsisteemversteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Angio-edeem, anafilaktiese reaksies

Muskuloskeletale, bindweefsel- en beenversteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Artralgie, mialgie

Renale en urinêre versteurings
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Urinêre retensie

Voortplantingsisteem- en borsversteurings
Frekwent:
Ejakulasieversteuring, impotensie, abnormale orgasme (vroulik)
Minder frekwent:
Anorgasmie
Die volgende newe effekte is aangemeld en die frekwensies is onbekend:
Galaktoree

Algemene versteurings & toestande by die toedieningsplek
Frekwent:
Moegheid

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:

Behandeling

Daar is geen spesifieke teenmiddel nie. Behandeling is ondersteunend en simptomaties. Maagspoeling behoort so gou as moontlik na orale inname uitgevoer te word. Monitering van kardiale en vitale tekens word saam met algemene simptomatiese ondersteunende maatreëls aanbeveel.

IDENTIFIKASIE:

ZYESCITO 5 mg TABLETS:
Wit tot naaswit gekleurde, rondevormige, filmbedekte, bikonvekse tablette, gebosseleer met 'F' aan die een kant en '53' aan die ander kant.

ZYESCITO 10 mg TABLETS:
Wit tot naaswit gekleurde, ovaalvormige, filmbedekte, bikonvekse tablette, gebosseleer met 'F' aan die een kant en '54' aan die ander kant met 'n diep keeplyn tussen die '5' en die '4'.

ZYESCITO 20 mg TABLETS:
Wit tot naaswit gekleurde, ovaalvormige, filmbedekte, bikonvekse tablette, gebosseleer met 'F' aan die een kant en '56' aan die ander kant met 'n diep keeplyn tussen die '5' en die '6'.

AANBIEDING:

ZYESCITO TABLETS:

1) Stolpverpakking:
Tablette word verpak in helder PVC-film en bedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.

Verpakkingsgrootte: 30s - Elke karton bevat 3 stolpverpakkings van 10 tablette elk.

BEREIDINGSINSTRUKSIES:

Bewaar by of benede 25 °C.

Moenie die stolpverpakkings uit die karton verwyder nie tot dit vir gebruik benodig word.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:

ZYESCITO 5 mg TABLETS: 44/1.2/0948
ZYESCITO 10 mg TABLETS: 44/1.2/0949
ZYESCITO 20 mg TABLETS: 44/1.2/0950

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Bemark deur:

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DATUM VAN PUBLIKASIE VAN DIE PROFESSIONELE INLIGTING:

Datum van registrasie:
5 Desember 2013
Datum van hersiening:
15 November 2022

PASIËNTINLIGTINGSBLAD

S5

ZYESCITO 5 mg TABLETS (tablet)
ZYESCITO 10 mg TABLETS (tablet)
ZYESCITO 20 mg TABLETS (tablet)

Lees die hele teksin voordat jy voortdan begin om ZYESCITO TABLETS te neem.
- Hou hierdie bladsyl. Jy mag dit moontlik weer wil lees.
- Indien jy enige verdere vrae het, vra jou apteker of dokter of spreker raadpleeg.
- **ZYESCITO TABLETS** is vir jou persoonlik voorgeskryf en u behoort nie u medisyne met ander mense te deel nie. Dit mag hulle benadeel, selfs al het hulle dieselfde simptome as u.

1. WAT ZYESCITO TABLETS IS EN WAT DIE GEBRUIK DAARVAN IS VIR:

Die aktiewe bestanddeel is essitalopramoksalaat.

ZYESCITO 5 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 5 mg essitalopram. Suikervry.

ZYESCITO 10 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 10 mg essitalopram. Suikervry.

ZYESCITO 20 mg TABLETS:
Elke filmbedekte tablet bevat essitalopramoksalaat ekwivalent aan 20 mg essitalopram. Suikervry.

Die ander bestandele van **ZYESCITO TABLETS** is butielhidroksitolueen, butielhidroksianisool, mikrokristalliyne sellulose, kroskarmellosenatrium, ligromeliese, mannitol, makrogol 400, magnesiumstearaat.

ZYESCITO TABLETS behoort as deel van 'n behandelingsprogram vir major depressiewe episodes (MDE) gebruik te word.

2. WAARVOOR ZYESCITO TABLETS GEBRUIK WORD

ZYESCITO TABLETS behoort aan 'n groep antidepressante wat selektiewe serotonienheropname-inhibeerders (SSHI's) genoem word, behoort gebruik te word vir die behandeling van depressie (emotiele depressiewe episodes) behandel.

3. VOORDAT U ZYESCITO NEEM

Moenie ZYESCITO TABLETS neem nie:
- As u allergies (oorgevoelig) bent vir essitalopram of enige van die ander bestandele van **ZYESCITO TABLETS** is nie.
- As u jonger as 18 jaar oud is nie – aangesien die veiligheid en effektiwiteit van **ZYESCITO TABLETS** nog nie bewys is nie.
- As u ander medisyne neem wat aan 'n groep wat monoamienoksidaseinhibeerders MAOIs genoem word, behoort te behoort (insluitend selegilien wat gebruik word vir die behandeling van Parkinson se siekte). Moenie **ZYESCITO TABLETS** neem indien u nie 14 dae verby gegaan het nadat u gestaak het om 'n MAOI te neem nie. Ten minste 7 dae moet verby gegaan het voordat u begin om 'n MAOI te neem nadat u gestaak het om **ZYESCITO TABLETS** te neem. Moet voorgaande behandeling vermyn hierdie periodes nie.

Dit neem van ZYESCITO TABLETS met voedsel:
ZYESCITO kan met of sonder voedsel geneem word.

Swangerskap en borsvoeding:
- As u swanger is of is dalta bonvoed, moet u asseblief u dokter, spreker of ander professionele gesondheidsorgverskaffer raadpleeg voordat u **ZYESCITO TABLETS** drink.

Ethe op die vermoë om te bestuur of om met masjinerie te werk:
- Moenie 'n motor bestuur of met masjinerie werk voordat u nie weet hoe u geaffekteer word nie.

Dit neem van ander medisyne saam met ZYESCITO TABLETS:
- Monoamienoksidaseinhibeerders (MAOIs) bv. moklobemied, tranielsipromien of linesiien. **ZYESCITO TABLETS** behoort nie saam met 'n MAOI gebruik te word nie. As u enige van hierdie medisyne saam met **ZYESCITO TABLETS** neem, mag dit newe effekte veroorsaak. Moet **ZYESCITO TABLETS** gestaak het, moet u vir 7 dae wag voordat u enige van hierdie medisyne begin.
- Ander medisyne wat serotonien verhoog bv. sumatriptan (gebruik om migraine te behandel), tramadol (wat vir enige pyn gebruik word), litium (gebruik vir die behandeling van manie-depressiewe siekte), triptofaan, fluoksetien, fenfluramien, fenelsien en tranielsipromien. Dit kan die kanse verhoog dat newe effekte voorkom, insluitend braking, duiseligheid, lomerigheid en floute.
- Aspirien en ander anti-inflammatoriese middels (middels wat gebruik word om pyn te verlig).
- Warfarien (wat vir maagbloeie gebruik word). Dit kan die kanse verhoog dat maagbloeie voorkom.
- Middels antidepressante (gebruik om depressie te behandel).
- Middels antipsigotiese middels (gebruik om psigose te behandel).
- Middels antidepressante (gebruik om depressie te behandel).
- Lithium (gebruik vir die behandeling van manie-depressiewe siekte).
- Amfetamien (wat vir aandagafleibaarheidsindroom gebruik word).
- Middels wat die bloedstolproses beïnvloed (insluitend nie-steroïdale anti-inflammatoriese middels (middels wat gebruik word om pyn te verlig) en maagbloeie gebruik word).

A/s: 280 x 660 mm
Black

AUROBINDO Packaging Development	Product Name	Component	Item Code	Date & Time
	ZYESCITO tablets	Leaflet	P1533005	15.02.2023 & 10.30 am
	Customer / Country	Version No.	Reason Of Issue	Reviewed / Approved by
	South Africa - Zydus	01	Submission	
Team Leader: Kiran Kumar	Dimensions	No. of Colours : 01		
Initiator: Bhogi	280 x 660 mm			
Artist: SCD	Pharmacode 33305	33305		
Additional Information : Supersede Code: P1525116				Sign / Date

Volwassenes:
- Die normale aanbevole dosis vir **ZYESCITO** is 10 mg, geneem as 1 daaglikse dosis.
- Dit kan tot 4 weke neem voordat u begin voel of **ZYESCITO** vir u werk.
- Dit mag 2 tot 4 weke neem voordat u begin voel hoe goed **ZYESCITO** te neem, selfs al neem u dit reeds.
- U dokter sal u laer begin- en maksimumdosis oorweeg.
- Dit is gewoonlik nie nodig om die dosis te verhoog tot meer as 20 mg per dag nie.

Bejaarde pasiënte:
- Die dosis behoort gehalveer te word.

Pasiënte met leversiekte:
- Die dosis behoort gehalveer te word.

As u nie seker is oor hoe om ZYESCITO TABLETS te neem:
- Raadpleeg dokter, spreker of ander professionele gesondheidsorgverskaffer.

As u vergeet het om ZYESCITO TABLETS te neem:
- Moenie 'n dubbele dosis neem om 'n vergete dosis te vervang nie. As dit egter byna tyd vir die volgende dosis is, slaan die dosis oor en hervat die oorspronklike dosisskedulering. Moenie die dosis verdubbel om vir 'n vergete dosis te vervang nie.

As u ophou om ZYESCITO TABLETS te neem:
- Moenie ophou om **ZYESCITO TABLETS** te neem sonder om eerste met u dokter te praat nie. Indien u **ZYESCITO TABLETS** tot meer effekte kry.
- Indien u dit wil staak, moet u dokter u help om dit geleidelik te doen (oor 'n periode van ongeveer 'n week of langer) voordat u **ZYESCITO TABLETS** heeltemal staak. Dit kan voorkom dat u newe effekte kry, soos duiseligheid, veranderde slaappatroon (insomnia of slaperigheid), senuagtigheid, angs, pankskaamte, senuweeagtigheid, duiselighied, onvermoë om te slaap, sweet, hoofpyn, naarheid, braking, prikkelbaarheid, veranderde persoonlikheid, verwarring, depressie, tinnitus, bewerigheid, spierpyn, veranderde sigbeelding en floute. Indien u enige van hierdie effekte kry, of enige ander effekte onderneem hoe u **ZYESCITO TABLETS** moet staak, raadpleeg u dokter, spreker of ander professionele gesondheidsorgverskaffer om advies raadpleeg.

6. OPBERGING EN WEDGEVEN VAN ZYESCITO TABLETS

Die houer moet digte gehou word.

Die houer moet buite bereik van kinders gehou word.

Bêre jou medisyne buite die sig en bereik van kinders.

Neem alle ongebruikte medisyne na u apteker toe.

Gebruik nie **ZYESCITO TABLETS** na die vervaldatum wat op die houer/omhulsel/etiket (na 'Uitdien' aangegee) nie.

7. AANBIEDING VAN ZYESCITO TABLETS

ZYESCITO TABLETS:

1) Stolpverpakking:
Tablette word in helder PVC film en gedrukte aluminiumfoelie verpak. Elke stolpverpakking bevat 10 tablette.

Verpakkingsgroottes: 30s - Elke karton bevat 3 stroke van 10 tablette elk.

2) HDPE fles:
Tablette word verpak in 40 ml HDPE houers met polipropileendoppies wat 'n indoksie seëlkrop verpak. Elke houer bevat 50 tablette.

Verpakkingsgroottes: 50s - Elke houer bevat 1 stolpverpakking.

8. IDENTITEITSAKE VAN ZYESCITO TABLETS

ZYESCITO TABLETS:
Wit tot naaswit gekleurde, rondevormige, filmbedekte, bikonvekse tablette met 'F' op die een kant en '53' op die ander kant gedruk.

ZYESCITO 10 mg TABLETS:
Wit tot naaswit gekleurde, ovaalvormige, filmbedekte, bikonvekse tablette met 'F' op die een kant en '54' op die ander kant gedruk met 'n diep keeplyn tussen die '5' en die '4'.

ZYESCITO 20 mg TABLETS:
Wit tot naaswit gekleurde, ovaalvormige, filmbedekte, bikonvekse tablette, gebosseleer met 'F' op die een kant en '56' op die ander kant gedruk met 'n diep keeplyn tussen die '5' en die '6'.

9. NAAM EN ADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

AUROGEN SOUTH AFRICA (EDMS.) BPK.
Woodhill Kantoorpark, Gebou Nr. 1, Eerste Vloer
Phillip Engelbrechtlaan 53,
Meyerstad, Uitbr. 12, Johannesburg,
1448, Suid-Afrika

Bemark deur:

ZYDUS HEALTHCARE SA (EDMS.) BPK.
Southdowns Gebou
22 Karee Straat
Centurion, 0157
Suid Afrika

11. DATUM VAN PUBLIKASIE:

Datum van registrasie:
5 Desember 2013
Datum van hersiening:
23 November 2022

10. DATUM WANNEER DIE TEKS VAN HIERDIE PASIËNTINLIGTINGSBLAD LAAS HERSIEN IS

Neem **ZYESCITO TABLETS** altyd presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. As u ook iemand is dat die effek van **ZYESCITO** is dink of te swak is, moet u dokter of apteker inlig.

PATIENT INFORMATION LEAFLET

[S5]

ZYESCITO 5 mg TABLETS: (tablet)
ZYESCITO 10 mg TABLETS: (tablet)
ZYESCITO 20 mg TABLETS: (tablet)

Read all of this leaflet carefully before you start taking ZYESCITO TABLETS.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **ZYESCITO TABLETS** has been prescribed for you personally, and you should not share your medicine with others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

1. WHAT ZYESCITO TABLETS CONTAIN

ZYESCITO 5 mg:
Each film-coated tablet contains escitalopram oxalate equivalent to 5 mg escitalopram. Sugar free.

ZYESCITO 10 mg:
Each film-coated tablet contains escitalopram oxalate equivalent to 10 mg escitalopram. Sugar free.

ZYESCITO 20 mg:
Each film-coated tablet contains escitalopram oxalate equivalent to 20 mg escitalopram. Sugar free.

The other ingredients of **ZYESCITO TABLETS** are butylhydroxytoluene, butylhydroxyanisole, cellulose anhydrous, silicified microcrystalline cellulose, croscarmellose sodium, butylhydroxytoluene, butylhydroxyanisole, cellulose microcrystalline, colloidal anhydrous silica, talc, magnesium stearate.

Coating material: hypromellose, macrogol 400, titanium dioxide (C.I. No. 77891).

2. WHAT ZYESCITO TABLETS ARE USED FOR

ZYESCITO TABLETS contain escitalopram, which belongs to a group called selective serotonin reuptake inhibitors (SSRIs). **ZYESCITO TABLETS** is used to treat depression (major depressive episodes).

3. BEFORE YOU TAKE ZYESCITO TABLETS

Do not take ZYESCITO TABLETS:
- If you are hypersensitive (allergic) to escitalopram, or any of the other ingredients of **ZYESCITO TABLETS** (see section 6).
- If you have taken any of these medicines you will need to wait 14 days before you start taking **ZYESCITO TABLETS**. After stopping **ZYESCITO TABLETS**, you must allow 7 days before taking any of these medicines.
  - Irreversible, non-selective monoamine oxidase inhibitors (MAOIs) (also see "**MAOIs**" below).
  - Reversible MAOIs linezolid (an antibiotic) and methylene blue (also see "**MAOIs**" below).
  - Other medicines that increase serotonin e.g. sumatriptan (used to treat migraine), tramadol (used against severe pain), lithium (used in the treatment of manic-depressive disorders) and tryptophan.
  - Non-selective reversible monoamine oxidase inhibitors (MAOIs) such as linezolid, intravenous methylene blue, moclobemide (used to treat depression) or buspirone (used to treat anxiety).
  - Cimetidine (used to treat stomach ulcers). These may cause increased blood levels of **ZYESCITO TABLETS**.
  - Warfarin (used to treat thrombosis), dipyridamole (used to prevent blood clots).
  - Metoprolol (used in heart diseases).
  - Mirtazapine (used to treat depression).
  - Selegiline (used to treat Parkinson's disease, depression and senile dementia).
  - Aspirin and non-steroidal anti-inflammatory drugs (medicines used for pain relief or to thin the blood).
  - Warfarin (medicine used to thin the blood).
  - Pimozide (an antipsychotic), fluoxetine (a medicine used to treat depression) or intravenous sodium thiopental (a medicine used to produce anesthesia) as the risk of certain side effects may be increased.
  - Mefloquine (used to prevent and treat malaria), bupropion (used to help you stop smoking), tramadol (a pain killer), ondansetron (used to prevent and treat nausea and vomiting) as the risk of seizures may be increased.
  - Flecainide, propafenone (used to treat irregular heartbeat), metoprolol (used to treat heart diseases, hypertension or chest pain) as the risk of certain side effects may be increased.
  - Tricyclic antidepressants (used to treat depression), mianserin (used to treat depression), haloperidol (an antipsychotic) as the risk of certain side effects may be increased.
  - Medicines that lower the seizure threshold such as tricyclic antidepressants, SSRIs, phenothiazines, butyrophenones (antipsychotics), mefloquine (antimalarial), bupropion, tramadol.
  - Medicines that cause electrolyte imbalance, as the risk of these side effects may be increased.
  - Medicines that affect the heart rhythm, including medicines that cause electrolyte imbalance, as the risk of these side effects may be increased.
  - Medicines that affect the blood clotting process (including atypical antipsychotics, tricyclic antidepressants, most phenothiazines, SSRIs and SNRIs), as the risk of bleeding may be increased.
  - Medicines that lower the seizure threshold such as tricyclic antidepressants, SSRIs, phenothiazines, butyrophenones (antipsychotics), mefloquine (antimalarial), bupropion, tramadol.

Take special care with ZYESCITO TABLETS:
- If you have epilepsy, you should be under regular supervision by your doctor.
- If you have or have had mania. Some patients with a history of mania/hypomania may enter a manic phase. If you experience this, contact your doctor.
- If you experience restlessness or difficulty sitting still during the first few weeks of treatment, **ZYESCITO TABLETS** should be stopped if seizures occur or if there is an increase in seizure frequency.
- If you have diabetes, treatment with **ZYESCITO TABLETS** may need to be adjusted.
- If you have liver disease. Your doctor may need to adjust your dose.
- If you have or have ever had bleeding problems.
- If you are pregnant or breast-feeding.
- **If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.** If you are depressed you can sometimes have thoughts of harming or killing yourself. It may take two weeks or more before you start to feel better, as it takes time for the medicine to work. An improvement may not occur during the first few weeks or more of treatment.
- Some patients with panic disorder may experience increased anxiety symptoms when they start to take medicines like **ZYESCITO TABLETS**. These symptoms usually decrease within two weeks of continued treatment.

Taking other medicines with ZYESCITO TABLETS and drink:
Do not take **ZYESCITO TABLETS** with alcohol.

Pregnancy and Breast-feeding:
If you are pregnant or breastfeeding, think you may become pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. You should not take **ZYESCITO TABLETS** if you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional before **ZYESCITO TABLETS**.

Driving and using machines:
Do not drive a car or operate machinery until you know how **ZYESCITO TABLETS** affects you.

Important information about some of the ingredients of ZYESCITO TABLETS:
Before taking **ZYESCITO TABLETS**, tell your doctor if you are taking any of the following medicines:

4. HOW TO TAKE ZYESCITO TABLETS

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

Adults:
Depression:
- The usual recommended dose of **ZYESCITO TABLETS** is 10 mg tablet once daily dose.
- The dose may be increased by your doctor to a maximum of 20 mg per day.
- It may take 2 to 4 weeks before you start to feel better. Continue to take **ZYESCITO TABLETS** even if it takes time before you start to feel better.

Elderly patients (above 65 years of age):
- The usual dose is half the dose. Your doctor will increase the dose if necessary.

Patients with kidney disease:
- Use usually not necessary to adjust the dose in mild or moderate kidney impairment.

Patients with liver disease:
- Your doctor should consider a lower dose.

If you stop taking ZYESCITO TABLETS: When you have completed your course of treatment, it is best to stop taking **ZYESCITO TABLETS** gradually over a period of several weeks.

If you take more ZYESCITO TABLETS than you should:

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital emergency department.

If you forget to take ZYESCITO TABLETS:
- If you forget a dose, take it 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.

5. WHAT ARE THE SIDE EFFECTS

Get emergency medical help if you have any of these **signs of an allergic reaction:**
- Swelling of your face, tongue, or throat, difficulty swallowing, swelling of your face, lips, tongue, or throat, sudden swelling of skin or mucosal (eyelashes).

Call your doctor if you have any of these serious side effects:
- Serotonin syndrome. Symptoms of serotonin syndrome include: restlessness, hallucinations, loss of coordination, fast heartbeat, increased body temperature, fast changes in blood pressure, increased reflexes, diarrhea, coma, nausea, vomiting.
- Withdrawal symptoms when treatment is stopped (see "**WARNINGS AND SPECIAL PRECAUTIONS**").
- Seizures (fits).
- Abnormal bleeding, including bleeding of the skin (such as easy bruising).
- Hyponatremia (low blood sodium levels). Symptoms include: feeling sick, weakness, confusion, memory problems, loss of balance, falls.
- Mania.
- Hallucinations (seeing things or hearing voices that do not exist) or mania (unusual excitement).
- Difficulties urinating.
- Swelling of your skin.
- Increase in the amount of cortisol secreted, low level of sodium in the blood, sexual disfunctions (ejaculation problems, loss of male sexual ability, decreased sexual drive and women may experience inability to have sexual intercourse), weight loss, nausea, vomiting, dizziness, increased risk of bleeding disorders (including gastrointestinal bleeding), gastrointestinal disorders, pancreatitis, movements of the muscles, problems with vision, dizziness when you stand up due to low blood pressure (postural hypotension), fast heartbeat, irregular heartbeat, fainting, liver problems (including hepatitis and yellowing of the skin, kidney problems, urinary problems, menstrual problems, sexual problems (disorders of ejaculation, orgasm and erection), pregnancy, worsening of existing psychiatric disorders, panic attacks, nervousness, hallucinations, confusion, drowsiness, sudden reactions, ringing in the ears, shivering, joint pain, muscle pain, flow of milk in women that are not nursing, fatigue, inability to sleep, increased sweating, rash, hair loss.

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

Other side effects that may occur are listed below. If you get any of the side effects listed, you should tell your doctor as soon as possible. Do not stop taking **ZYESCITO TABLETS** unless you discuss it with your doctor first. Some of these side effects may be serious but most are not long lasting.

Very common (affects more than 1 user in 10):
- Nausea.

Common (affects 1 to 10 users in 100):
- Increased appetite.
- Anxiety, feeling nervous, difficulty sleeping, abnormal dreams, decreased sex drive, difficulty reaching orgasm, sleepiness.
- Dizziness, pins and needles sensation, tremor, migraine.
- Yawning.
- Diarrhea, constipation, vomiting, dry mouth.
- Sweating (including night sweats).
- Muscle pain, joint pain.
- Difficulty getting an erection, ejaculation disorder (including delayed ejaculation), decreased libido, menstrual disorders including irregular menstruation, heavy menstruation, painful menstruation and absence of menstruation, breast pain.
- Feeling tired, feeling irritable, feeling weak, chest pain.
- Weight loss, weight gain.

Uncommon (affects 1 to 10 users in 1,000):
- Allergic reactions.
- Increased appetite.
- Depersonalization, agitation, panic attacks, confusion, decreased libido, grinding teeth.
- Fainting, restless legs syndrome, involuntary movements, disturbance in attention, memory impairment, abnormal coordination, balance disorder, taste disturbance.
- Dilation of the pupils, visual disturbance such as double vision.
- Ringing in the ears.
- Slow heart rate.
- Nosebleed.
- Vomiting, indigestion, stomach discomfort, abdominal pain, gastrointestinal inflammation, dry mouth.
- Hair loss, rash, itching, hives, sensitivity to sunlight.
- Muscle stiffness, muscle twitching, joint stiffness.
- Inability to urinate, frequent urination, urinary tract infection.
- Menstrual irregularities including irregular menstruation, heavy menstruation, painful menstruation and absence of menstruation, breast pain, vaginal discharge, erectile dysfunction, delayed ejaculation.
- Swelling of the face, swelling, fever, difficulty walking, feeling unsteady, feeling of chest pain, feeling irritable, feeling abnormal, decreased weight, increased weight.

Rare (affects 1 to 10 users in 10,000):
- Hyponatremia (low blood sodium levels).
- Inappropriate secretion of antidiuretic hormone.
- Bruising.
- Blood in urine.
- Menstrual disorder including metrorrhagia (uterine bleeding) and menorrhagia (heavy menstrual bleeding).
- Swelling of the limbs.

Not known (frequency cannot be estimated from the available data):
- Suicidal thoughts, suicidal behavior.
- Abnormal liver function tests.
- Inflammation of the liver (hepatitis).
- Skin rashes, hives, sensitivity to sunlight, purple spots on the skin, inflammation of the blood vessels.
- Breaking down of muscle tissue.
- Urinary retention.
- Abnormal milk production.
- Prolonged painful erection of the penis.
- Abnormal vaginal bleeding.
- Increased tendency to bleed.
- Withdrawal symptoms when treatment is stopped.

6. STORAGE AND DISPOSAL OF ZYESCITO TABLETS

Store at or below 25 °C room temperature.
The containers must be tightly closed.
Store in the original package until dispensed for use.
Do not use **ZYESCITO TABLETS** after the expiry date which is stated on the carton and blister strip.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

7. PRESENTATION OF ZYESCITO TABLETS

ZYESCITO TABLETS:
1) Blister Pack:
Tablets are packed in clear PVC film and printed aluminium foil. 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 clear HDPE containers with polypropylene closures with induction sealing seal.
Each container contains 30 tablets.
Pack size: Each carton contains 30 tablets.

8. MANUFACTURATION OF ZYESCITO TABLETS

ZYESCITO 5 mg TABLETS:
White to off–white coloured, round shaped, film-coated, biconvex tablets debossed with 'I' on one side and '5' on the other side.

ZYESCITO 10 mg TABLETS:
White to off–white coloured, oval shaped, film-coated, biconvex tablets debossed with 'I' on one side and '10' on the other side with a deep scoreline between '5' and '4'.

ZYESCITO 20 mg TABLETS:
White to off–white coloured, oval shaped, film-coated, biconvex tablets debossed with 'I' on one side and '20' on the other side with a deep scoreline between '5' and '6'.

9. REGISTRATION NUMBER/REFERENCE NUMBER

ZYESCITO 5 mg TABLETS: 44/1.2/0948
ZYESCITO 10 mg TABLETS: 44/1.2/0949
ZYESCITO 20 mg TABLETS: 44/1.2/0950

10. NAME AND ADDRESS OF REGISTRATION HOLDER

AUROGEN SOUTH AFRICA (PTY) LTD
Woodhill Office Park, Building 1 First Floor
53 Phillip Engelbrecht Avenue
Meyerstal Ext 12, 1448
Johannesburg, South Africa

Marketed by:
ZYOUS HEALTHCARE SA (PTY) LTD
Southdowns Office Park
22 Karee Street
Centurion, 0157
South Africa

11. DATE OF REVISION OF THE PACKAGE INSERT

Date of publication:
5 December 2013
23 November 2022

P1533305

PROFESSIONAL INFORMATION FOR HUMAN USE

SCHEDULING STATUS:

[S5]

PROPRIETARY NAME (and dosage form) :

ZYESCITO 5 mg TABLETS (tablet)
ZYESCITO 10 mg TABLETS (tablet)
ZYESCITO 20 mg TABLETS (tablet)

COMPOSITION:

ZYESCITO 5 mg TABLETS:
Each film-coated tablet contains escitalopram oxalate equivalent to 5 mg escitalopram. Sugar free.

ZYESCITO 10 mg TABLETS:
Each film-coated tablet contains escitalopram oxalate equivalent to 10 mg escitalopram. Sugar free.

ZYESCITO 20 mg TABLETS:
Each film-coated tablet contains escitalopram oxalate equivalent to 20 mg escitalopram. Sugar free.

The other excipients in the formulation are: silicified microcrystalline cellulose, croscarmellose sodium, butylhydroxytoluene, butylhydroxyanisole, cellulose microcrystalline, colloidal anhydrous silica, talc, magnesium stearate.

Coating material: hypromellose, macrogol 400, titanium dioxide (C.I. No. 77891).

PHARMACOLOGICAL CLASSIFICATION:

A 1.2 Psychoanaleptics (antidepressants)

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Escitalopram is a potent and selective inhibitor of serotonin (5-HT)-uptake.

Escitalopram has minimal effect on noradrenaline (NA), dopamine (DA) and gamma aminobutyric acid (GABA) uptake. Escitalopram has no or very low affinity for a series of receptors including 5-HT$_{1A}$, 5-HT$_2$, DA, D_2 and D_3 receptors, α_1-, α_2-, β-adrenoceptors, histamine H_1, muscarinic, benzodiazepine and opioid receptors.

Pharmacokinetics:

Absorption
Absorption is independent of food intake; mean t_{max} is 4 hours after multiple dosing.

Distribution
The apparent volume of distribution (V_{d}/F) after oral administration is about 12 to 26 l/kg. The plasma protein binding of escitalopram is approximately 55 %.

Biotransformation
Escitalopram is metabolised in the liver to demethylated and didemethylated metabolites. Alternatively, the nitrogen may be oxidised to form a N-oxide metabolite. Both parent compound and metabolites are partly excreted as glucuronides. Unchanged escitalopram is the predominant compound in plasma. After multiple dosing the mean concentrations of the demethyl and didemethyl metabolites are usually 28-31 % and < 5 % of the escitalopram concentration, respectively. Biotransformation of escitalopram to the demethylated metabolite is mediated by a combination of CYP2C19, CYP3A4 and CYP2D6.

Elimination
The elimination half-life after multiple dosing is about 30 hours and the plasma clearance after oral administration (Cl_{oral}) is about 0.6 l/min. Escitalopram and major metabolites are assumed to be eliminated both by the hepatic (metabolic) and the renal routes with the major part of the dose excreted as metabolites in urine.

Hepatic clearance is mainly by the P450 enzyme system. CYP2C19 is the primary isoenzyme involved in the demethylation of escitalopram, followed by CYP3A4 and CYP2D6. There is linear pharmacokinetics. Steady state plasma levels are achieved in about 1 week. Average steady state concentrations of 50 nmol/l (range 20 to 125 nmol/l) are achieved at a daily dose of 10 mg.

Elderly patients (> 65 years of age)
A longer half-life (about 50 %) and decreased clearance values, due to a reduced rate of metabolism, have been demonstrated in the elderly.

Reduced hepatic function
Escitalopram is eliminated more slowly in patients with reduced hepatic function. The half-life of escitalopram is twice as long in patients with hepatic impairment and steady state escitalopram concentrations at a given dose will be approximately twice as high as in patients with normal liver function.

Reduced renal function
Escitalopram is eliminated more slowly in patients with mild to moderate reduction of renal function with no major impact on the escitalopram concentrations in serum. At present no information is available for the treatment of patients with severely reduced renal function (creatinine clearance < 30 ml/min).

Polymorphism
Based on *in vitro* results with escitalopram, genetic polymorphism with respect to CYP2D6 is not known; with respect to CYP2C19, it may be of clinical relevance, as shown in limited number of patients.

INDICATIONS:
Treatment of major depressive episodes.

CONTRA-INDICATIONS:
Hypersensitivity to escitalopram or to any of the excipients.

Children under 18 years of age; as safety and efficacy have not been established in this population.

Patients with known QT interval prolongation or congenital long QT syndrome (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

Medicinal products that are known to prolong QT interval (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

Monoamine Oxidase Inhibitors: Cases of serious reactions have been reported in patients receiving a serotonin selective reuptake inhibitor (SSRI) in combination with a monoamine oxidase inhibitor (MAOI), and in patients who have recently discontinued an SSRI and have started on a MAOI (see **"INTERACTIONS"**). Some cases presented with features resembling serotonin syndrome (see **"SPECIAL PRECAUTIONS"**). **ZYESCITO TABLETS** should not be used in combination with a MAOI. **ZYESCITO TABLETS** may be started 14 days after discontinuing treatment with a MAOI. At least 7 days should elapse after discontinuing **ZYESCITO TABLETS** treatment before starting a MAOI.

WARNINGS AND SPECIAL PRECAUTIONS:

QT interval prolongation: ZYESCITO TABLETS has been found to cause a dose-dependent prolongation of the QT interval. Cases of QT interval prolongation, ventricular prolongation and ventricular dysrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT interval prolongation or other cardiac diseases.

Caution is advised in patients with significant bradycardia; or in patients with recent acute myocardial infarction or uncompensated heart failure.

Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk of malignant dysrhythmia and should be corrected before treatment with **ZYESCITO TABLETS** is started.

If patients with stable cardiac disease are treated, an ECG review should be considered before treatment is started.

If signs of cardiac dysrhythmia occur during treatment with **ZYESCITO TABLETS**, the treatment should be withdrawn and an ECG should be performed.

Mania – ZYESCITO TABLETS should be discontinued in any patient entering a manic phase. **ZYESCITO TABLETS** should be used with caution in patients with a history of mania/hypomania.

Paradoxical anxiety - Some patients with panic disorder may experience increased anxiety symptoms at the start of treatment with **ZYESCITO TABLETS**. This paradoxical reaction usually subsides within two weeks of continued treatment. A low starting dose is advised to reduce the likelihood of a paradoxical anxiogenic effect.

Seizures - **ZYESCITO TABLETS** should be discontinued in any patient who develops seizures. **ZYESCITO TABLETS** should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. **ZYESCITO TABLETS** should be discontinued if there is an increase in seizure frequency.

Diabetes mellitus- In patients with diabetes mellitus treatment with **ZYESCITO TABLETS** may alter glycaemic control, possibly due to improvement of depressive symptoms. The doses of insulin and/or oral hypoglycaemic medications may need to be adjusted.

Suicide- As an improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored for the risk of suicide.

Haemorrhage - There have been reports of cutaneous bleeding abnormalities, such as ecchymoses and purpura, with escitalopram. Caution is advised in patients taking **ZYESCITO TABLETS**, particularly in concomitant use with medicines known to affect platelet function (e.g. atypical antipsychotics and phenothiazines, most tricyclic antidepressants, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs)), as well as in patients with a history of bleeding disorders.

ECT (electroconvulsive therapy) - There is limited published clinical experience of concurrent administration of **ZYESCITO TABLETS** and ECT, therefore caution is advisable.

Risk of Serotonin syndrome

Co-administration with MAOIs may cause serotonin syndrome.

Co-administration with other serotonergic medicines (e.g. tramadol, sumatriptan) as well as other antidepressants with serotonergic properties may lead to an enhancement of serotonin associated effects, e.g. the serotonin syndrome.

There have been reports of enhanced effects when escitalopram has been given with lithium or tryptophan and therefore concomitant use of **ZYESCITO TABLETS** with these medicines should be undertaken with caution.

Effects on ability to drive and use machines

ZYESCITO TABLETS does not impair intellectual function or psychomotor performance.

Patients who are depressed and require treatment may have an impaired ability to drive or operate machinery. They should be warned of this possibility and advised to avoid such tasks if so affected.

INTERACTIONS:

Escitalopram has a low potential for clinically significant medicine interactions. *In vitro* studies have shown that the biotransformation of escitalopram to its demethylated metabolites depends on three parallel pathways (cytochrome P450 (CYP) 2C19, 3A4 and 2D6). Escitalopram is a weak inhibitor of isoenzyme CYP1A2, 2C9, 2C19, 2E1, and 3A, and weak inhibitor of 2D6.

QT interval prolongation

Pharmacokinetic and pharmacodynamic studies of **ZYESCITO TABLETS** combined with other medicinal products that prolong the QT interval have not been performed. An additive effect of escitalopram and these medicinal products cannot be excluded. Therefore, co-administration of **ZYESCITO TABLETS** with medicinal products that prolong the QT interval, such as Class IA and III antidysrhythmics (e.g. amiodarone, quinidine), antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants (e.g. desimipramine, imipramine), certain antimicrobial agents (e.g. moxifloxacin, erythromycin IV, pentamidine, anti-malarial treatment particularly halofantrine), certain antihistamines (e.g. mizolastine) and anti-retrovirals (e.g. ritonavir, saquanivir, lopinavir), is contra-indicated.

Ritonavir:

The pharmacokinetics of single doses of escitalopram was not changed by co-administration with a single dose of ritonavir (CYP3A4 inhibitor).

Ketoconazole:

Co-administration with ketoconazole (potent CYP3A4 inhibitor) has no effect on pharmacokinetics of **ZYESCITO TABLETS**.

Cimetidine:

Co-administration of racemic citalopram with cimetidine (potent CYP2D6, 3A4 and 1A2 inhibitor) resulted in increased plasma concentrations of the racemate (43 % increase in AUC, 39 % increase in C_{max}). Thus, caution should be exercised at the upper end of the dose range of **ZYESCITO TABLETS** when used concomitantly with high doses of cimetidine.

Monoamine Oxidase inhibitors (MAOIs), Sumatriptan and Tramadol:

Co-administration with MAO inhibitors may cause serotonin syndrome (See "**CONTRA-INDICATIONS**").

Co-administration with other-serotonergic medicines (e.g. tramadol, sumatriptan) as well as other antidepressants with serotonergic properties may lead to an enhancement of serotonin associated effects, e.g. the serotonin syndrome.

There have been reports of enhanced effects when escitalopram has been given with lithium or tryptophan and therefore concomitant use of **ZYESCITO TABLETS** with these medicines should be undertaken with caution (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

Desipramine:

Co-administration with a single dose of desipramine (a CYP2D6 substrate) resulted in a twofold increase in plasma levels of desipramine. Therefore, caution is advised when **ZYESCITO TABLETS** and desipramine are co-administered. A similar increase in plasma levels of desipramine, after administration of imipramine, was seen when given together with racemic citalopram.

Metoprolol:

Co-administration with a single dose of metoprolol 100 mg (a CYP2D6 substrate) resulted in a twofold increase in the C_{max} and a 52 % increase of the AUC of metoprolol. However, the combination had no clinically significant effects on blood pressure and heart rate.

Selegiline:

Racemic citalopram increased the AUC of selegiline by 29 %.

Other:

Pharmacokinetic interaction studies with racemic citalopram have demonstrated no clinically important interactions with carbamazepine (CYP3A4 substrate), triazolam (CYP3A4 substrate), theophylline (CYP1A2 substrate) (single dose), warfarin (CYP3A4 and CYP2C9 substrate), levomepromazine (CYP2D6 inhibitor), lithium and digoxin.

However, prothrombin time was slightly increased after a single dose of 25 mg warfarin. The International Normalised Ratio (INR) needs to be carefully monitored in patients on the combination.

PREGNANCY AND LACTATION:

The safety of **ZYESCITO TABLETS** in pregnant and lactating women has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Adults

Major depressive episodes:

ZYESCITO TABLETS should be administered as a single oral dose of 10 mg daily in otherwise healthy adults. Depending on individual patient response, the dose may be increased to a maximum of 20 mg daily.

Usually 2 - 4 weeks are necessary for an antidepressant response.

Elderly patients (> 65 years of age)

A longer half-life and a decreased clearance have been demonstrated in the elderly. The maximum recommended dose for elderly patients is 10 mg daily.

Reduced renal function

Dosage adjustment is not necessary in patients with mild or moderate renal impairment.

No information is available on the treatment of patients with severely reduced renal function (creatinine clearance < 30 ml/min).

Reduced hepatic function

Dosages should be halved to the lower end of the dose range in patients with hepatic insufficiency. The maximum recommended dose for adult patients with hepatic impairment is 10 mg daily. **ZYESCITO TABLETS** is administered as a single daily dose. **ZYESCITO TABLETS** may be taken without regard to food intake.

Serotonin withdrawal

When stopping **ZYESCITO TABLETS** therapy, gradual dose reduction should be considered.

SIDE EFFECTS

Adverse reactions observed with **ZYESCITO TABLETS** are most frequent during the first one or two weeks of treatment and may decrease in intensity and frequency with continued treatment.

After prolonged administration abrupt cessation of **ZYESCITO TABLETS** may produce withdrawal reactions in some patients.

Endocrine disorders
The following side effects have been reported and frequencies are unknown:
Inappropriate ADH secretion

Metabolism and nutrition disorders
Frequent:
Decreased appetite
Less frequent:
Hyponatraemia, weight loss, hyperprolactinaemia

Psychiatric disorders
Frequent:
Decreased libido, suicidal ideation, insomnia
The following side effects have been reported and frequencies are unknown:
Hallucinations, mania, confusion, agitation, anxiety, depersonalisation, panic attacks, nervousness

Nervous system disorders
Frequent:
Dizziness, somnolence
The following side effects have been reported and frequencies are unknown:
Sleep disorder, seizures, tremor, movement disorders, drowsiness, taste disturbance, serotonin syndrome (typically characterised by a rapid onset of changes in mental state, with confusion, mania, agitation, hyperactivity, shivering, fever, tremor, ocular movements, myoclonus, hyperreflexia, and incoordination)

Cardiovascular disorders
Frequency unknown:
Electrocardiogram QT prolongation, ventricular dysrhythmia including torsade de pointes

Eye disorders
The following side effects have been reported and frequencies are unknown:
Abnormal vision

Vascular disorders
The following side effects have been reported and frequencies are unknown:
Postural hypotension

Respiratory, thoracic and mediastinal disorders
Frequent:
Sinusitis, yawning

Gastrointestinal disorders
Frequent:
Constipation, diarrhoea, dry mouth, nausea
The following side effects have been reported and frequencies are unknown:
Vomiting, anorexia, dyspepsia

Hepato-biliary disorders
The following side effects have been reported and frequencies are unknown:
Abnormal liver function tests

Skin and subcutaneous tissue disorders
Frequent:
Increased sweating
The following side effects have been reported and frequencies are unknown:
Rash, ecchymoses, pruritus, angioedema, alopecia, photosensitivity, urticaria, pyrexia

Immune system disorders
The following side effects have been reported and frequencies are unknown:
Angioedema, anaphylactoid reactions

Musculoskeletal, connective tissue and bone disorders
The following side effects have been reported and frequencies are unknown:
Arthralgia, myalgia

Renal and urinary disorders
The following side effects have been reported and frequencies are unknown:
Urinary retention

Reproductive system and breast disorders
Frequent:
Ejaculation disorder, impotence, abnormal orgasm (female)
Less frequent:
Anorgasmia
The following side effects have been reported and frequencies are unknown:
Galactorrhoea

General disorders and administrative site conditions
Frequent:
Fatigue

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Treatment

There is no specific antidote. Treatment is supportive and symptomatic. Gastric lavage should be carried out as soon as possible after oral ingestion. Cardiac and vital signs monitoring are recommended along with general symptomatic supportive measures.

IDENTIFICATION:

ZYESCITO 5 mg TABLETS:
White to off–white coloured, round shaped, film-coated, biconvex tablets debossed with 'I' on one side and '53' on the other side.

ZYESCITO 10 mg TABLETS:
White to off–white coloured, oval shaped, film-coated, biconvex tablets debossed with 'I' on one side and '54' on the other side with a deep scoreline between '5' and '4'.

ZYESCITO 20 mg TABLETS:
White to off–white coloured, oval shaped, film-coated, biconvex tablets debossed with 'I' on one side and '56' on the other side with a deep scoreline between '5' and '6'.

PRESENTATION:

ZYESCITO TABLETS:
Tablets are packed in clear PVC film and printed aluminium foil. Each blister contains 10 tablets.
Pack size: 30's –Each carton contains 3 blisters of 10 tablets each.

STORAGE INSTRUCTIONS:
Store at or below 25 °C.
Do not remove blisters from carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:
ZYESCITO 5 mg TABLETS: 44/1.2/0948
ZYESCITO 10 mg TABLETS: 44/1.2/0949
ZYESCITO 20 mg TABLETS: 44/1.2/0950

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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