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

APPROVED
Samantha , 2022/12/01 ,11:43:28

DOLIN
P1532540

DOLIN
P1532540

AUROGEN

SKEDULERINGSTATUS

SUID-AFRIKA: S5

NAMIBIË: NS3

EIENDOMSNAAM (en doseervorm):
DOLIN 5 mg (tablet)
DOLIN 10 mg (tablet)
DOLIN 20 mg (tablet)

SAMESTELLING:

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

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

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

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

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

FARMAKOLOGIESE KLASSIFIKASIE:

A 1.2. Psigoanaleptika (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_{maks} is 4 uur na veelvoudige dosering.

Distribusie

Die skynbare volume van distribusie ($V_{d,\beta}$/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 glukuroniede 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_{oraal}) 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 liniêr. Ewewigstoestand plasmavlakke word binne ongeveer 1 week bereik. Die gemiddelde ewewigstoestand konsentrasies van 50 nmol/l (reikwydte 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 VOORSOORGSMAATREËLS").**

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

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 VOORSOORGSMAATREËLS"**). **DOLIN** behoort nie in kombinasie met 'n MAOI gebruik te word nie. **DOLIN** 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 **DOLIN** voordat 'n MAOI begin word.

WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS:

QT-intervalverlenging: Daar is gevind dat **DOLIN** 'n dosisafhanklike verlenging van die QT-interval veroorsaak. Gevalle van QT-intervalverlenging, ventrikulêre verlenging en ventrikulêre disritmieë insluitend torsade de pointes is tydens die nabemarkingperiode 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 **DOLIN** 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 **DOLIN** voorkom, moet die behandeling onttrek word en 'n EKG moet uitgevoer word.

Manie - **DOLIN** behoort onttrek te word in enige pasiënt wat 'n maniese fase binnegaan. **DOLIN** 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 **DOLIN** ondervind. Hierdie paradoksale reaksie bedaar gewoonlik binne twee weke van voortgesette behandeling. 'n Lae aanvangsdosis word aanbeveel om die waarskynlikheid van 'n paradoksale angsiogeniese effek te verminder.

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

Diabetes mellitus - By pasiënte met diabetes mellitus mag behandeling met **DOLIN** 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 - Berigte van bloedingsabnormaliteite van die vel, soos eggimose en purpura het met essitalopram voorgekom. Omsigtigheid word aangeraai by pasiënte wat **DOLIN** 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 bloedingsiektes.

EKT (elektrokonvulsiewe terapie) - Daar is slegs beperkte gepubliseerde kliniese ondervinding van gelyktydige toediening van **DOLIN** 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.

Berigte is ontvang van versterkte effekte toe essitalopram saam met litium of triptofaan gegee is, en dus behoort gelyktydige gebruik van **DOLIN** saam met hierdie medisyne moet omsigtigheid onderneem word.

Effekte op die vermoë om te bestuur en masjiene te gebruik

DOLIN 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 **DOLIN** 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 **DOLIN** saam met medisinale produkte wat die QT-interval verleng, soos Klas IA en III antidisritmiese middels (bv. amiodaroon, kinidien), antipsigotiese middels (bv. fenotiasienderivate, pimosied, haloperidol), trisikliese antidepressante (bv. desimipramien, imipramien), sekere antimikrobiale middels (bv. moksifloksasien, eritromisien IV, pentamidien, antimalariabehandeling veral halofantrien), sekere antihistamiene (bv. misolastien) 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.

Ketokonasool:

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

Simetidien:

Gelyktydige toediening van rasemiese sitalopram saam met simetidien (potente CYP2D6-, 3A4-, en 1A2-inhibeerder), het verhoogde plasmakonsentrasies van die rasemaat veroorsaak (43 % verhoging in AOK, 39 % toename in K_{maks}). Omsigtigheid behoort dus uitgeoefen te word aan die boonste end van die dosisreikwydte van **DOLIN**, 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.

Berigte van versterkte effekte is ontvang toe essitalopram saam met litium of triptofaan gegee is en gelyktydige gebruik van **DOLIN** 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 veroorsaak. Omsigtigheid word dus aanbeveel wanneer **DOLIN** 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_{maks} en 'n 52 % verhoging in die AOK van metoprolol veroorsaak. Die kombinasie het egter geen klinies beduidende effekte op bloeddruk en harttempo 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 gemoniteer word by pasiënte op die kombinasie.

SWANGERSKAP EN LAKTASIE:

Die veiligheid van **DOLIN** in swanger en lakterende vrouens is nie vasgestel nie.

DOSIS EN GEBRUIKSAANWYSINGS:

Volwassenes

Major depressiewe episodes:

DOLIN 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 volwassens met hepatiese inkorting is 10 mg daagliks. **DOLIN** word as 'n enkele daaglikse dosis toegedien. **DOLIN** mag sonder inagneming van voedselinname geneem word.

Serotonienonttrekking

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

NEWE EFFEKTE:

Nadelige reaksies wat met **DOLIN** 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 **DOLIN** onttrekkingsreaksies by sommige pasiënte veroorsaak.

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

Metabolisme en voedingversteurings
Frekwent:
Verminderde aptyt
Minder frekwent:
Hiponatremie, gewigsverlies, hiperprolaktienemie

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

Senusisteemversteurings
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, hiperrefleksie, 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

Gastroïntestinale versteurings
Frekwent:
Hardlywigheid, 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, anafilaktoïede 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:

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

DOLIN 10 mg:
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'.

DOLIN 20 mg:
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:

DOLIN 5 mg/ DOLIN 10 mg/ DOLIN 20 mg:

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.

BERGINGSINSTRUKSIES:

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:

SUID-AFRIKA:
DOLIN 5 mg: 44/1.2/0951
DOLIN 10 mg: 44/1.2/0952
DOLIN 20 mg: 44/1.2/0953

NAMIBIË:
DOLIN 5 mg: 20/1.2/0019
DOLIN 10 mg: 20/1.2/0020
DOLIN 20 mg: 20/1.2/0021

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:

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

DATUM VAN PUBLIKASIE VAN DIE PROFESSIONELE INLIGTING:

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

DETACH BEFORE DISPENSING

A/s: 280 x 660 mm Booklet Size: 40 x 60 mm
Colours: Black

AUROBINDO Packaging Development	Product Name	Component	Item Code	Date & Time
	DOLIN	Leaflet	P1532540	01.12.2022 & 01.00 pm
	Customer / Country	Version No.	Reason of Issue	Reviewed / Approved by
	Aurogen-South Africa -U3	01	Commercial	

Team Leader	Kiran K	Dimensions (mm)	Colours:	
Initiator	Bhogi	280 x 660 mm	Black	
Artist	Sree Designers	Pharma Code: 32540	32540	
Additional Information:	Supersede Code: P1524155			Sign & Date

AUROGEN

SCHEDULING STATUS:

SOUTH AFRICA: S5

NAMIBIA: NS3

PROPRIETARY NAME (and dosage form):

DOLIN 5 mg (tablet)
DOLIN 10 mg (tablet)
DOLIN 20 mg (tablet)

COMPOSITION:

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

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

DOLIN 20 mg:
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_1 and D_2 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 ($V_{d,\beta}/F$) 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 been started on a MAOI (see **"INTERACTIONS"**). Some cases presented with features resembling serotonin syndrome (see "**SPECIAL PRECAUTIONS**"). **DOLIN** should not be used in combination with a MAOI. **DOLIN** may be started 14 days after discontinuing treatment with a MAOI. At least 7 days should elapse after discontinuing **DOLIN** treatment before starting a MAOI.

WARNINGS AND SPECIAL PRECAUTIONS:

QT interval prolongation: DOLIN 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 **DOLIN** 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 **DOLIN**, the treatment should be withdrawn and an ECG should be performed.

Mania – DOLIN should be discontinued in any patient entering a manic phase. **DOLIN** 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 **DOLIN**. 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 - **DOLIN** should be discontinued in any patient who develops seizures. **DOLIN** should be avoided in patients with unstable epilepsy and patients with controlled epilepsy should be carefully monitored. **DOLIN** should be discontinued if there is an increase in seizure frequency.

Diabetes mellitus- In patients with diabetes mellitus treatment with **DOLIN** 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 **DOLIN**, 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 **DOLIN** 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 **DOLIN** with these medicines should be undertaken with caution.

Effects on ability to drive and use machines
DOLIN 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 **DOLIN** 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 **DOLIN** 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 **DOLIN**.

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 **DOLIN** 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 **DOLIN** 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 **DOLIN** 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 **DOLIN** in pregnant and lactating women has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Adults

Major depressive episodes:

DOLIN 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. **DOLIN** is administered as a single daily dose. **DOLIN** may be taken without regard to food intake.

Serotonin withdrawal

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

SIDE EFFECTS

Adverse reactions observed with **DOLIN** 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 **DOLIN** 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:

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

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

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

PRESENTATION:

DOLIN 5 mg/ DOLIN 10 mg / DOLIN 20 mg:

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:

SOUTH AFRICA:
DOLIN 5 mg: 44/1.2/0951
DOLIN 10 mg: 44/1.2/0952
DOLIN 20 mg: 44/1.2/0953

NAMIBIA:
DOLIN 5 mg: 20/1.2/0019
DOLIN 10 mg: 20/1.2/0020
DOLIN 20 mg: 20/1.2/0021

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

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

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:

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Date of revision:
15 November 2022

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↑ DETACH BEFORE DISPENSING

SOUTH AFRICA: S5

NAMIBIA: NS3

DOLIN 5 mg (tablet)
DOLIN 10 mg (tablet)
DOLIN 20 mg (tablet)
Escitalopram oxalate

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

The active substance is escitalopram oxalate.

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

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

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

The other ingredients of **DOLIN** are butylhydroxyanisole, butylhydroxytoluene, cellulose microcrystalline, croscarmellose sodium, hypromellose, macrogol 400, magnesium stearate, silica colloidal anhydrous, silicified microcrystalline cellulose, talc and titanium dioxide (C.I. No. 77891).

2. WHAT DOLIN IS USED FOR

DOLIN belongs to a group of antidepressants called selective serotonin reuptake inhibitors (SSRIs). **DOLIN** is used to treat depression (major depressive episodes).

3. BEFORE YOU TAKE DOLIN

Do not take DOLIN:
- If you are hypersensitive (allergic) to escitalopram, or any of the other ingredients of **DOLIN**.
- If you are under 18 years of age – Because the safety and effectiveness of **DOLIN** have not been determined in children.
- If you take other medicines which belongs to a group called monoamine oxidase inhibitors (MAOIs). If you have taken any of these medicines you will need to wait 14 days before you start taking **DOLIN**. After stopping **DOLIN**, you must allow 7 days before taking any of these medicines.

Take special care with DOLIN:
Before taking **DOLIN**, tell 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 have epilepsy. Treatment with **DOLIN** should be stopped if seizures occur or if there is an increase in seizure frequency.
- If you have diabetes. Insulin and/or oral medication dosage may need to be adjusted.
- If you are receiving electroconvulsive treatment.
- If you have liver disease. Your doctor may need to adjust your dosage.
- If you have kidney disease.
- If you have or have ever had bleeding problems.
- If you are an elderly patient.
- **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. Since **DOLIN** may take time 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 **DOLIN**. These anxiety symptoms usually decrease within two weeks of continued treatment.

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

Pregnancy and Breast-feeding:
- The safe use of **DOLIN** during pregnancy and breastfeeding has not been determined.

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care professional for advice before taking this medicine.

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

Taking other medicines with DOLIN:
Before taking **DOLIN**, tell your doctor if you are using any of the following medicines:
- Monoamine oxidase inhibitors (MAOIs) e.g. moclobemide, tranylcypromine, phenelzine. **DOLIN** should not be used together with a MAOI. If you have taken any of these medicines you will need to wait 14 days before you start taking **DOLIN**. After stopping **DOLIN**, you must allow 7 days before taking any of these medicines.
- 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 disorder) and tryptophan (an amino acid found in dietary supplements that may be used for depression and insomnia).
- Cimetidine (used to treat stomach ulcers). These may cause increased blood levels of **DOLIN**.
- Desipramine (used to treat depression).
- Metoprolol (used in heart diseases).
- Other antidepressants (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).

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

If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **DOLIN** with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional, for advice.

4. HOW TO TAKE DOLIN

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

Adults:
Depression:
- The normal recommended dose of **DOLIN** is 10 mg taken as one 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 **DOLIN** even if it takes some time before you feel an improvement in your condition.

Elderly patients (above 65 years of age):
- Your doctor may consider a lower starting dose and maximum dose.

Patients with kidney disease:
- It is usually not necessary to adjust the dosage in mild or moderate kidney impairment.

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

If you stop taking DOLIN: When you have completed your course of treatment, it is generally advised that the dose of **DOLIN** should be gradually reduced.
If you take more DOLIN than you should:

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

If you forget to take DOLIN:
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.

5. POSSIBLE SIDE EFFECTS

DOLIN 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, sudden swelling of skin or mucosa (angioedema).

Call your doctor at once if you have any of these serious side effects:
- **DOLIN** may cause a very serious condition called serotonin syndrome. Symptoms of serotonin syndrome include: confusion, mania, agitation, hyperactivity (excessively increased activity), shivering, high fever, tremor (shake), eye movements, twitchy muscles, loss of coordination.
- Seizures (fits) or convulsions.
- Hallucinations (seeing things or hearing voices that do not exist) or mania (unusual excitement).
- Difficulties urinating.

Other side effects include: increase in the amount of urine excreted; low level of sodium in the blood; sexual disturbances (ejaculation problems, loss of male sexual ability, decreased sexual drive and women may experience difficulties achieving orgasm); confusion; agitation; anxiety; panic attacks; nervousness; dizziness; inability to sleep; sleepiness; tremor (shake); movement disorders (involuntary movements of the muscles); problems with vision; dizziness when you stand up due to low blood pressure (postural hypotension); blocked or runny nose (sinusitis); yawning; taste disturbances; diarrhoea (frequent or loose watery stools); constipation; dry mouth; nausea; vomiting; lack of appetite; abnormal liver function tests (increased amounts of liver enzymes in the blood); increased sweating; bruise, bleeding into the skin; itching; joint pain; muscle pain; flow of milk in women that are not nursing; fatigue; inability to sleep; dizziness; drowsiness; fever.

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 **DOLIN**.

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

6. STORING AND DISPOSING OF DOLIN

Store at or below 25 °C (room temperature).
The containers must be tightly closed.
Do not remove blisters from carton until required for use.

Store all medicines out of the 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 DOLIN

DOLIN 5 mg / DOLIN 10 mg / DOLIN 20 mg:
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 40 ml HDPE containers with polypropylene closures with induction sealing wad. Each container contains 30 tablets.
Pack size:30's - One HDPE container contains 30 tablets.

8. IDENTIFICATION OF DOLIN

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

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

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

9. REGISTRATION NUMBER/REFERENCE NUMBER
SOUTH AFRICA:
DOLIN 5 mg: 44/1.2/0951
DOLIN 10 mg: 44/1.2/0952
DOLIN 20 mg: 44/1.2/0953

NAMIBIA:
DOLIN 5 mg: 20/1.2/0019
DOLIN 10 mg: 20/1.2/0020
DOLIN 20 mg: 20/1.2/0021

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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

11. DATE OF PUBLICATION

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Date of revision:
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