PROFESSIONAL INFORMATION

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE
AMDERIP 10 (film-coated tablets)
AMDERIP 25 (film-coated tablets)
AMDERIP 50 (film-coated tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
AMDERIP 10
Each film-coated tablet contains 10 mg amitriptyline hydrochloride
Contains sugar: lactose monohydrate 10 mg.
AMDERIP 25
Each film-coated tablet contains 25 mg amitriptyline hydrochloride
Contains sugar: lactose monohydrate 10 mg.
AMDERIP 50
Each film-coated tablet contains 50 mg amitriptyline hydrochloride
Contains sugar: lactose monohydrate 20 mg.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated tablet.
AMDERIP 10
Round blue colored biconvex tablets debossed AM on one side and 10 on other side.
AMDERIP 25
Round yellow colored biconvex tablets debossed AM on one side and 25 on other side.
AMDERIP 50
Round brown colored biconvex tablets debossed AM on one side and 50 on other side.

4 CLINICAL PARTICULARS
Therapeutic indications
AMDERIP is indicated for the treatment of depression in adults (18 years and older).

Posology and method of administration
Posology
Adults:
Initially 75 mg to 150 mg daily in divided doses.
Maintenance dose is 50 mg to 100 mg daily in divided doses.

Method of administration
Amitriptyline is for oral use.
The tablets should be swallowed with water.

Contraindications
AMDERIP is contraindicated in:
- Patients with hypersensitivity to amitriptyline or to any of the excipients (see section 6.1).
- Concurrent use with monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping treatment with MAOIs (see section 4.5).
- Concurrent use with linezolid.
- Concurrent use with antihypertensive medicines (see section 4.5).
- Recent myocardial infarction, dysrhythmias, particularly heart block to any degree, congestive heart failure, coronary artery insufficiency.
- Pregnancy and lactation (see section 4.6).
- Children under 18 years of age.
- Mania.
- Severe liver disease.

Special warnings and precautions for use
AMDERIP should at all times be kept out of reach of children as even small doses may be fatal to them.
Anticholinergic effects
Peripheral anticholinergic adverse events such as dry mouth, constipation and urinary retention may occur. Patients may also experience pupillary dilatation, blurred vision and changes in visual accommodation. When anticholinergic affects are severe, **AMDERIP** should be discontinued or the dosage should be reduced.
Sedative effects
Drowsiness, excessive sedation, disorientation and agitation may be caused in certain patients. Insomnia and restlessness may also occur. Drowsiness is often experienced at the start of treatment with **AMDERIP**.
Cardiac disease
Special caution should be observed in patients suffering from cardiac disease, as tachycardia, cardiac dysrhythmias, orthostatic hypotension and other unwanted effects on blood pressure may occur. There may also be an increase in conduction disturbances and electrocardiographic abnormalities. Regular cardiological and electrocardiographic examination is advised.
Elderly patients are particularly susceptible to orthostatic hypotension.
There is an increased risk of ventricular dysrhythmias when **AMDERIP** is used with medicines which prolong the QT interval.
Endocrine effects
Endocrine effects include changes in libido, sexual dysfunction, gynaecomastia, breast enlargement and galactorrhoea. Changes in blood sugar concentrations may also occur and less frequently, hyponatraemia which may be due to the inappropriate secretion of antidiuretic hormone (ADH).
Manic depressive psychosis
Caution should be observed with patients suffering from manic depressive psychosis as a shift towards the manic phase may occur. Should the patient enter into a manic phase, amitriptyline should be discontinued.
Suicidal tendencies
Patients with a history of suicide-related events or those experiencing a significant degree of suicidal ideation prior to the start of treatment should receive careful monitoring during treatment, as they are known to be at greater risk of suicidal thoughts or attempts.
Direct acting sympathomimetic and anaesthetics
The pressor effects of the direct-acting sympathomimetic medicines, epinephrine (adrenaline) and norepinephrine (noradrenaline) are potentiated by **AMDERIP**.
Anaesthetics containing these vasoconstrictors should be avoided as hypertensive reactions may occur. When possible, treatment should be discontinued several days before elective surgery. If emergency surgery is unavoidable, the anaesthetist should be informed that the patient is being treated with **AMDERIP**.
Tricyclic antidepressants may counteract the antihypertensive effects of centrally acting antihypertensives.
Porphyria
AMDERIP should be used with caution in patients suffering from acute forms of porphyria.
Cautious use in certain conditions
AMDERIP should be used with caution in patients with a history of epilepsy, impaired liver function, cardiovascular disease, urinary retention, prostatic hypertrophy, hyperthyroidism, constipation, paralytic ileus and narrow angled glaucoma as these conditions may be aggravated by amitriptyline.
Skin conditions
AMDERIP should be withdrawn if allergic skin reactions appear.
Co-administration of certain medicines
AMDERIP may enhance the effects of central nervous system depressants such as alcohol, and barbiturates and anticholinergic medicines. Concomitant use should be avoided.
Electroconvulsive therapy
Unless essential, it is not advisable combine **AMDERIP** and electroconvulsive therapy (ECT).
Hyponatraemia
Hyponatraemia may be due to inappropriate excretion of the antidiuretic hormone.
Elderly patients are particularly susceptible to these adverse events and treatment should be initiated at lower than standard doses.
Lactose warning
AMDERIP contains lactose which may have an effect on the glycaemic control in patients with diabetes mellitus. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

After prolonged administration, abrupt cessation of treatment may produce withdrawal symptoms namely headache, malaise, insomnia or irritability.

Interaction with other medicines and other forms of interaction
Simultaneous administration of monoamine oxidase inhibitors (MAOIs) and **AMDERIP** may cause serotonin syndrome (a combination of symptoms such as hyperthermia, convulsions, myoclonus, confusion, agitation). A minimum of 14 days should elapse between discontinuation of a MAOI and starting **AMDERIP**, which should be introduced cautiously and dosage increased gradually (see section 4.3).
AMDERIP may counteract the antihypertensive effects of debrisoquine, bethanidine and clonidine (see section 4.3).
There is an increased risk of hypertension on clonidine withdrawal. All antihypertensive therapy should be reviewed during treatment with **AMDERIP**.
Antibacterials: Concomitant use of **AMDERIP** and linezolid may result in CNS excitation and hypertension (see section 4.3). Plasma concentrations of amitriptyline may be reduced by rifampicin which reduces the antidepressant effect.
Concomitant use **AMDERIP** and reboxetine should be used with caution.
The plasma concentrations of amitriptyline, found in **AMDERIP**, may be increased by selective serotonin reuptake inhibitors (SSRIs). Fluoxetine which is an SSRI, significantly inhibits cytochrome P450 II D6, which is involved in the metabolism of **AMDERIP** and therefore significantly decreases the metabolism of **AMDERIP** which results in increased plasma concentrations. Patients should be monitored for increased antidepressant plasma levels and toxicity when **AMDERIP** is used concurrently with fluoxetine. Dosage adjustments of **AMDERIP** and/or fluoxetine may be required.
Alpha$_2$-adrenocepter stimulants: Concomitant used of apraclonidine and brimonidine with **AMDERIP** should be avoided.
Analgesics: The risk of central nervous system (CNS) toxicity with **AMDERIP** is increased with tramadol. There is a possibility of increased sedation with opioid analgesics.
Anaesthetics: Concomitant therapy with **AMDERIP** and anaesthetics may increase the risk of dysrhythmias and hypotension. If surgery is necessary, the anaesthetist should be informed that the patient is being treated with **AMDERIP.**
Antidysrhythmics: Medicines which prolong the QT interval such as amiodarone, disopyramide, procainamide, propafenone and quinidine may increase the likelihood of ventricular dysrhythmias when taken with tricyclic antidepressants. Concomitant use with **AMDERIP** should be avoided.
AMDERIP should not be given with sympathomimetic medicines such as epinephrine (adrenaline), isoprenaline, norepinephrine (noradrenaline), phenylephrine, and phenylpropanolamine due to hypertension and dysrhythmias.
Methylphenidate may inhibit the metabolism of amitriptyline contained in **AMDERIP** and therefore increase the antidepressant effect of **AMDERIP**.
AMDERIP may enhance the response to alcohol, barbiturates and other CNS depressants.
Concomitant use of disulfiram may inhibit the metabolism of amitriptyline.
Concomitant use of **AMDERIP** and antiepileptics may lead to a lower convulsive threshold and seizures. Dosage adjustments may be necessary.
Barbiturates and carbamazepine may reduce the antidepressant effect of **AMDERIP**.
Antifungals: Fluconazole may increase serum concentrations of amitriptyline found in **AMDERIP**.
Antihistamines: Increased sedative and anticholinergic effects may occur when antihistamines are used concurrently with **AMDERIP**.
Antivirals: The protease inhibiter, ritonavir, may increase the serum levels of amitriptyline, found in **AMDERIP**, whose metabolism is mediated through cytochrome P450 isoenzymes. Careful monitoring of therapeutic and adverse effects is recommended when these medicines are used concomitantly.
Antipsychotics: Concomitant use of amitriptyline, which is found in **AMDERIP**, with pimozide and thioridazine may lead to an increased risk of ventricular dysrhythmias. Avoid concomitant use with pimozide and thioridazine. Concomitant use with antipsychotics may increase the plasma levels of amitriptyline and increase the anticholinergic effects of phenothiazines and possibly clozapine.
Beta-blockers: There is an increased risk of ventricular dysrhythmias when **AMDERIP** is taken with sotalol.
Calcium channel blockers: Verapamil and diltiazem may increase plasma concentrations of amitriptyline found in **AMDERIP**.
Diuretics: There is an increased risk of postural hypotension.
Dopaminergics: Concomitant use of **AMDERIP** and entacapone should be avoided. CNS toxicity has been reported with selegiline.
Muscle relaxants: Concomitant use of baclofen enhances the muscle relaxant effect.
Nitrates: Reduced effect of sublingual nitrates (due to dry mouth).
Estrogens and progestogens: Oral contraceptives antagonise the antidepressant effect of **AMDERIP** but adverse effects may be increased due to increased plasma concentrations of tricyclic antidepressants as per **AMDERIP**.
Excessive anticholinergic effects may occur when **AMDERIP** is combined with anticholinergic medicines. Paralytic ileus, urinary retention or acute glaucoma may be precipitated in elderly patients.
Cimetidine may reduce the hepatic metabolism of **AMDERIP** which may lead to increased plasma levels of amitriptyline.
St. John's Wort may reduce plasma concentrations of amitriptyline which is found in **AMDERIP** thus decreasing the antidepressant effect.
Patients taking thyroid preparations may show an accelerated response to **AMDERIP.** Concomitant use of **AMDERIP** with thyroid hormones may precipitate cardiac dysrhythmias.

Fertility, pregnancy and lactation
Pregnancy
Safety and efficacy of **AMDERIP** during pregnancy has not been established (see section 4.3).
Only limited data are available regarding exposed pregnancies. Animal studies have shown reproductive toxicity.
Breastfeeding
Safety and efficacy of **AMDERIP** during lactation has not been established (see section 4.3).
Mothers on **AMDERIP** should not breastfeed their babies (see section 4.3).
Fertility
Amitriptyline reduced the pregnancy rate in rats.
No data on the effects of amitriptyline on human fertility are available.

Effects on ability to drive and use machines
At the time of initiation of therapy, patients should be advised not to drive a motor vehicle, climb dangerous heights or operate dangerous machinery for at least several days. In these situations, impaired decision making could lead to accidents.
Since adverse reactions such as drowsiness, dizziness and blurred vision have been reported in patients receiving **AMDERIP**, patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that **AMDERIP** does not adversely affect their ability to do so (see section 4.8).

Undesirable effects
a. Summary of the safety profile
AMDERIP may induce adverse events similar to other tricyclic antidepressants. Some of the below mentioned adverse events e.g. headache, tremor, disturbance in attention, constipation and decreased libido may also be symptoms of depression and usually attenuate when the depressive state improves.

b. Tabulated summary of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Less frequent	Bone marrow depression including agranulocytosis, eosinophilia, leucopoenia, thrombocytopenia and purpura
Immune system disorders	Less frequent	Hypersensitivity reactions including skin rash, urticaria, photosensitization, oedema of face and tongue, angioedema
Endocrine disorders	Less frequent	Syndrome of inappropriate ADH secretion (SIADH), hyperglycaemia, hypoglycaemia, hyponatraemia
Metabolism and nutrition disorders	Less frequent	Increased appetite, weight gain, weight loss, anorexia
Psychiatric disorders	Less frequent	Confusional state, disorientation, agitation, insomnia, nightmares, delusions, hallucinations, mania or hypomania, excitement, anxiety, restlessness, disturbed concentration, behavioural changes, suicidal thoughts or behaviour
Nervous system disorders	Frequent	Drowsiness or excessive sedation
	Less frequent	Dizziness, headache, peripheral neuropathy, numbness, paraesthesia, ataxia, tremors, coma, convulsions, altered EEG, extrapyramidal disorder including dysarthria (speech disorder), tardive dyskinesia and abnormal involuntary movements
Eye disorders	Frequent	Accommodation disorder, blurred vision, increased intra-ocular pressure
	Less frequent	Mydriasis
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Less frequent	Tachycardia, palpitations, myocardial infarction, heart block, dysrhythmias, changes in atrioventricular conduction, nonspecific ECG changes
Vascular disorders	Less frequent	Hypotension, hypertension, postural hypotension, syncope, stroke
Gastrointestinal disorders	Frequent	Dry mouth, constipation
	Less frequent	Diarrhoea, vomiting, nausea, paralytic ileus, epigastric distress, dysgeusia, metallic taste, stomatitis, parotid swelling, black tongue
Hepato-biliary disorders	Less frequent	Hepatitis (including hepatic impairment and cholestatic jaundice)
Skin and subcutaneous tissue disorders	Less frequent	Rash, alopecia
Musculoskeletal and connective tissue disorders	Less frequent	Increased risk of bone fractures
Renal and urinary disorders	Frequent	Urinary retention
	Less frequent	Urinary frequency, urinary tract dilation
Reproductive system and breast disorders	Less frequent	Gynaecomastia, breast enlargement, galactorrhoea, testicular swelling, changes in libido, impotence, sexual dysfunction
General disorders and administration site conditions	Frequent	Hyperthermia
	Less frequent	Fatigue, weakness, increased perspiration

AMDERIP should be used with caution in patients with a history of epilepsy, impaired liver function, urinary retention, prostatic hypertrophy, hyperthyroidism and narrow angled glaucoma as these conditions may be aggravated by **AMDERIP**.

Peripheral anticholinergic adverse events notably dry mouth, constipation, urinary retention and pupillary dilatation with blurred vision and changes in visual accommodation, have been reported. When anticholinergic affects are severe, **AMDERIP** should be discontinued or reduced.

Simultaneous administration of monoamine oxidase inhibitors (MAOIs) and **AMDERIP** may cause serotonin syndrome (a combination of symptoms such as hyperthermia, convulsions, myoclonus, confusion, agitation). A minimum of 14 days should elapse between discontinuation of a MAOI and starting **AMDERIP**, which should be introduced cautiously and dosage increased gradually (see section 4.3).

Caution should be observed with patients suffering from manic depressive psychosis as a shift towards the manic phase may occur. Should the patient enter into a manic phase, amitriptyline should be discontinued.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

Overdose
Overdosage and poisoning may be characterised by central nervous system depression or excitation, severe anticholinergic effects and cardiotoxicity. The signs and symptoms of an overdosage include: drowsiness, restlessness, ataxia, coma, stupor, cardiac dysrhythmias, pyrexia, palpitations, hypotension, tachycardia, convulsions and respiratory depression. Mixed poisoning with other central nervous system depressants is not uncommon.
Treatment for overdosage is symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Category and Class: A 1.2 Psychoanaleptics (antidepressants).
Pharmacotherapeutic group: Antidepressants - Non-selective monoamine reuptake inhibitor (tricyclic antidepressant)
ATC code: N06AA09

Amitriptyline is a tricyclic antidepressant. It has marked anticholinergic and sedative properties. It prevents the re-uptake, and hence the inactivation of noradrenaline and serotonin at nerve terminals. Re-uptake prevention of these monoamine neurotransmitters potentiate their action in the brain. This appears to be associated with the antidepressant activity.

Pharmacokinetic properties
Absorption
Amitriptyline is absorbed after oral administration, reaching its maximum plasma concentration approximately 6 hours after administration.
Distribution
Amitriptyline and nortriptyline are widely distributed throughout the body with a high binding to plasma proteins and tissues. An elimination half-life ranging from 9 - 25 hours has been estimated.
Amitriptyline and nortriptyline pass across the placental barrier. In nursing mothers, amitriptyline and nortriptyline, are excreted in the breast milk.
Biotransformation
Amitriptyline is extensively demethylated in the liver to its primary active metabolite, nortriptyline. The metabolism pathway includes N-oxidation and conjugation with glucuronic acid.
Elimination
Amitriptyline is excreted as glucuronide or conjugate sulfate metabolites and little medicine appears unchanged in the urine.

6 PHARMACEUTICAL PARTICULARS
List of excipients
Tablet core:
Colloidal silicon dioxide
Corn maize starch
Croscarmellose sodium
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose
Talc

Tablet coating AMDERIP 10:
Hypromellose
Macrogol 6000
Macrogol (E1521)
Polyvinyl alcohol (E1203)
Talc (E553b)
Titanium dioxide (E171)
FD&C Blue #1/Brilliant Blue FCF Aluminum Lake (E133)

Tablet coating AMDERIP 25:
Hypromellose
Iron oxide yellow (E172)
Macrogol 6000
Macrogol (E1521)
Polyvinyl alcohol (E1203)
Talc (E553b)
Titanium dioxide (E171)

Tablet coating AMDERIP 50:
Hypromellose
Iron oxide yellow (E172)
Iron oxide red (E172)
Macrogol 6000
Macrogol (E1521)
Polyvinyl alcohol (E1203)
Talc (E553b)
Titanium dioxide (E171)

Incompatibilities
Not applicable.

Shelf life
2 years. Store at or below 25 °C.

Special precautions for storage
No special precautions for storage exist for **AMDERIP**.

Nature and contents of container
AMDERIP 10 are packed in PVC/PVdC/Aluminium blisters containing 30 film-coated tablets. The blister strips are packed in a printed carton.

AMDERIP 25 are packed in PVC/PVdC/Aluminium blisters containing 30 or 60 film-coated tablets. The blister strips are packed in a printed carton.

AMDERIP 50 are packed in PVC/PVdC/Aluminium blisters containing 30 film-coated tablets. The blister strips are packed in a printed carton.

Not all pack sizes may be marketed.

Special precautions for disposal <and other handling>
No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION
Strides Pharma SA (Pty) Ltd
106 16th Road
Building 2
Midrand

8 REGISTRATION NUMBER(S)
AMDERIP 10: 54/1.2/0684.681
AMDERIP 25 54/1.2/0684.682
AMDERIP 50: 54/1.2/0684.683

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
29 March 2022

10 DATE OF REVISION OF THE TEXT
N.A

PROFESSIONELE INLIGTING

SKEDULERINGSTATUS

S5

1 NAAM VAN DIE GENEESMIDDEL
AMDERIP 10 (filmbedekte tablette)
AMDERIP 25 (filmbedekte tablette)
AMDERIP 50 (filmbedekte tablette)

2 KWALITATIEWE EN KWANTITATIEWE KOMPOSISIE
AMDERIP 10
Elke filmbedekte tablet bevat 10 mg amitriptilien hidrochloried
Bevat suiker: laktosemonohidraat 10 mg.
AMDERIP 25
Elke filmbedekte tablet bevat 25 mg amitriptilien hidrochloried
Bevat suiker: laktosemonohidraat 10 mg.
AMDERIP 50
Elke filmbedekte tablet bevat 50 mg amitriptilien hidrochloried
Bevat suiker: laktosemonohidraat 10 mg.

Sien afdeling 6.1 vir 'n volledige lys van hulpstowwe.

1 FARMASEUTIESE VORM
Filmbedekte tablette.
AMDERIP 10
Blougekleurde, ronde, bikonvekse tablette met AM gebosseleer aan die een kant en 10 aan die ander kant
AMDERIP 25
Geelgekleurde, ronde, bikonvekse tablette met AM gebosseleer aan die een kant en 25 aan die ander kant.
AMDERIP 50
Bruingekleurde, ronde, bikonvekse tablette met AM gebosseleer aan die een kant en 50 aan die ander kant.

3 KLINIESE BESONDERHEDE
Terapeutiese indikasies
AMDERIP word aangedui vir die behandeling van depressie in volwassenes (18 jaar en ouer).

Posologie en metode van toediening
Posologie
Volwassenes:
Aanvanklik 75 mg tot 150 mg daagliks in verdeelde dosisse.
Instandhoudingsdosis is 50 mg tot 100 mg daagliks in verdeelde dosisse.

Metode van toediening
Amitriptilien is vir orale gebruik.
Die tablette moet met water geneem word.

Kontraindikasies
AMDERIP word teenaangedui in:
- Pasiënte met hipersensitiwiteit vir amitriptilien of vir enige van die hulpstowwe (sien afdeling 6.1).
- Gelyktydige gebruik met monoamienoksidase-inhibeerders (MAOIs) of binne 14 dae nadat behandeling met MAOIs gestaak is (sien afdeling 4.5).
- Gelyktydige gebruik met linesolied.
- Gelyktydige gebruik met antihipertensiewe medisyne (sien afdeling 4.5).
- Onlangse miokardiale infarksie, disritmieë, veral hartblok tot enige graad, kongestiewe hartversaking, koronêre arterie ontoereikendheid.
- Swangerskap en laktasie (sien afdeling 4.6).
- Kinders onder die ouderdom van 18 jaar oud.
- Manie.
- Ernstige lewersiekte.

Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
AMDERIP moet ten alle tye buite bereik van kinders gehou word, aangesien selfs klein dosisse noodlottig vir hulle kan wees.
Anticholinergiese effekte
Perifere anticholinergiese newe-effekte soos droë mond, hardlywigheid en urienretensie kan voorkom. Pasiënte kan ook pupillêre dilatasie, versteurde visie en veranderinge in visuele akkommodasie ervaar. Wanneer anticholinergiese effekte ernstig is, moet **AMDERIP** gestaak word of die dosis moet verminder word.
Kalmerende effekte
Lomerigheid, oormatige sedasie, disoriëntasie en agitasie kan by sekere pasiënte veroorsaak word. Slapeloosheid en rusteloosheid kan ook voorkom. Lomerigheid word dikwels ervaar aan die begin van behandeling met **AMDERIP**.
Hartsiekte
Spesiale sorg moet geneem word by pasiënte wat aan hartsiekte ly, aangesien tagikardie, hartdisritmieë, ortostatiese hipotensie en ander ongewenste effekte op bloeddruk kan voorkom. Daar kan ook 'n toename in geleidingsversteurings en elektrokardiografiese abnormaliteite wees. Gereelde kardiologiese en elektrokardiografiese ondersoek word aanbeveel.
Bejaarde pasiënte is veral vatbaar vir ortostatiese hipotensie.
Daar is 'n verhoogde risiko van ventrikulêre disritmieë wanneer **AMDERIP** gebruik word saam met medisyne wat die QT-interval verleng.
Endokriene effekte
Endokriene effekte sluit in veranderinge in libido, seksuele disfunksie, ginekomastie, borsvergroting en galaktoree.
Veranderinge in bloedsuikerkonsentrasies kan ook voorkom en minder gereeld, hiponatremie wat kan as gevolg van die onvanpaste afskeiding van antidiuretiese hormoon (ADH) wees.
Maniese-depressiewe psigose
Pasiënte wat aan maniese-depressiewe psigose ly, moet versigtig wees, aangesien 'n verskuiwing na die maniese fase kan voorkom. Indien die pasiënt 'n maniese fase betree, moet amitriptilien gestaak word.
Selfmoord neigings
Pasiënte met 'n geskiedenis van selfmoordverwante gebeure of diegene wat 'n beduidende mate van selfmoordgedagtes ervaar voor die aanvang van behandeling moet noukeurige monitering tydens behandeling ontvang, aangesien dit bekend is dat hulle 'n groter risiko loop vir selfmoordgedagtes of -pogings.
Direkwerkende simpatomimetika en verdowingsmiddels
Die pressor-effekte van die direkwerkende simpatomimetiese medisyne, epinefrien (adrenalien) en norepinefrien (noradrenalien) word versterk deur **AMDERIP**.
Verdowingsmiddels wat hierdie vasokonstriktors bevat moet vermy word aangesien hipertensiewe reaksies kan voorkom. Indien moontlik, moet behandeling 'n paar dae voor elektiewe chirurgie gestaak word. Indien noodchirurgie onvermydelik is, moet die narkotiseur in kennis gestel word dat die pasiënt behandel word **AMDERIP**.
Trisikliese antidepressante kan die antihipertensiewe effekte van sentraalwerkende antihipertensiewe middels teenwerk.
Porfirie
AMDERIP moet met omsigtigheid gebruik word by pasiënte wat aan akute vorme van porfirie ly.
Versigtige gebruik in sekere toestande
AMDERIP moet met omsigtigheid gebruik word by pasiënte met 'n geskiedenis van epilepsie, verswakte lewerfunksie, kardiovaskulêre siekte, urienretensie, prostaathipertrofie, hipertiroïedisme, hardlywigheid, paralitiese ileus en nouhoek-gloukoom aangesien hierdie toestande deur amitriptilien vererger kan word.
Veltoestande
AMDERIP moet gestaak word indien allergiese velreaksies voorkom.
Gelyktydige toediening van sekere medisyne
AMDERIP kan die effekte van sentrale senuweestelsel-depressante soos alkohol, en barbiturate en anticholinergiese medisyne versterk. Gelyktydige gebruik moet vermy word.
Elektrokonvulsiewe terapie
Tensy dit noodsaaklik is, is dit nie raadsaam om **AMDERIP** en elektrokonvulsiewe terapie (EKT) te kombineer nie.
Hiponatremie
Hiponatremie kan as gevolg van onvanpaste uitskeiding van die antidiuretiese hormoon wees.
Bejaarde pasiënte is veral vatbaar vir hierdie nadelige gebeurtenisse en behandeling moet teen laer as standaard dosisse begin word.
Laktose waarskuwing
AMDERIP bevat laktose wat 'n effek kan hê op die glukemiese beheer by pasiënte met diabetes mellitus. Pasiënte met seldsame oorerflike probleme van galaktose-intoleransie, totale laktase-tekort of glukose-galaktose-wanabsorpsie moet nie hierdie medisyne gebruik nie.

Na langdurige toediening kan skielike staking van behandeling onttrekkingsimptome veroorsaak, naamlik hoofpyn, algemene ongemak, slapeloosheid of prikkelbaarheid.

1.2 Interaksie met ander medisyne en ander vorme van interaksie
Gelyktydige toediening van monoamienoksidase-inhibeerders (MAOI's) en **AMDERIP** kan serotoniensindroom veroorsaak ('n kombinasie van simptome soos hipertermie, stuiptrekkings, mioklonus, verwarring, agitasie). 'n Minimum van 14 dae behoort te verloop tussen die staking van 'n MAOI en die aanvang van **AMDERIP**, wat versigtig bekendgestel moet word en die dosis geleidelik verhoog moet word (sien afdeling 4.3).
AMDERIP kan die antihipertensiewe effekte van debrisokien, betanidien en klonidien teenwerk (sien afdeling 4.3).
Daar is 'n verhoogde risiko van hipertensie by klonidienonttrekking. Alle antihipertensiewe terapie moet hersien word tydens behandeling met **AMDERIP**.
Antibakteriese medisyne: Gelyktydige gebruik van **AMDERIP** en linesolied kan lei tot SSS-eksitasie en hipertensie (sien afdeling 4.3). Plasmakonsentrasies van amitriptilien kan verminder word deur rifampisien wat die antidepressante effek verminder.
Gelyktydige gebruik van **AMDERIP** en reboksetien moet met omsigtigheid gebruik word.
Die plasmakonsentrasies van amitriptilien, gevind in **AMDERIP**, kan verhoog word deur selektiewe serotonienheropname inhibeerders (SSHIs). Fluoksetien wat 'n SSHI is, inhibeer sitochroom P450 II D6 beduidend, wat betrokke is by die metabolisme van **AMDERIP** en verminder dus die metabolisme van **AMDERIP** aansienlik, wat lei tot verhoogde plasmakonsentrasies. Pasiënte moet gemonitor word vir verhoogde antidepressante plasmavlakke en toksisiteit wanneer **AMDERIP** gelyktydig met fluoksetien gebruik word. Dosisaanpassings van **AMDERIP** en/of fluoksetien mag nodig wees.
Alfa$_2$-adrenosepter stimulante: Die gelyktydige gebruik van apraklonidien en brimonidien met **AMDERIP** moet vermy word.
Analgetika: Die risiko van sentrale senuweestelsel (SSS) toksisiteit met **AMDERIP** word verhoog met tramadol. Daar is 'n moontlikheid van verhoogde sedasie met opioïed-pynstillers.
Narkose: Gelyktydige terapie met **AMDERIP** en narkosemiddels kan die risiko van disritmieë en hipotensie verhoog. Indien chirurgie nodig is, moet die narkotiseur in kennis gestel word dat die pasiënt met **AMDERIP** behandel word.
Antidisritmiese medisyne: Medisyne wat die QT-interval verleng, soos amiodaroon, disopiramied, prokaïenamied, propafenoon en kinidien kan die waarskynlikheid van ventrikulêre disritmie verhoog wanneer dit saam met trisikliese antidepressante geneem word. Gelyktydige gebruik met **AMDERIP** moet vermy word.
AMDERIP moet nie saam met simpatomimetiese medisyne soos epinefrien (adrenalien), isoprenalien, norepinefrien (noradrenalien), fenielefrien en fenielpropanolamien gegee word nie as gevolg van hipertensie en disritmieë.
Metielfenidaat kan die metabolisme van amitriptilien, vervat in **AMDERIP**, inhibeer en dus die antidepressante effek van **AMDERIP** verhoog.
AMDERIP kan die reaksie op alkohol, barbiturate en ander SSS-depressante versterk.
Gelyktydige gebruik van disulfiram kan die metabolisme van amitriptilien inhibeer.
Gelyktydige gebruik van **AMDERIP** en anti-epileptika kan tot 'n laer konvulsie drempel en aanvalle lei. Dosisaanpassings mag nodig wees.
Barbiturate en karbamasepien kan die antidepressante effek van **AMDERIP** verminder.
Antiswam medisyne: Flukonasool kan die serumkonsentrasies van amitriptilien wat in **AMDERIP** voorkom verhoog.
Antihistamiene: Verhoogde kalmerende en anticholinergiese effekte kan voorkom wanneer antihistamiene gelyktydig met **AMDERIP** toegedien word.
Antivirale medisyne: Die protease-inhibeerder, ritonavir, kan die serumvlakke van amitriptilien, gevind in **AMDERIP**, verhoog, wat se metabolisme deur sitochroom P450 isoensieme bemiddel word. Noukeurige monitering van terapeutiese en nadelige effekte word aanbeveel wanneer hierdie medisyne gelyktydig gebruik word.
Antipsigotika: Gelyktydige gebruik van amitriptilien, wat in **AMDERIP** voorkom, met pimosied en tioridasien kan lei tot 'n verhoogde risiko van ventrikulêre disritmieë. Vermy gelyktydige gebruik met pimosied en tioridasien. Gelyktydige gebruik met antipsigotika kan die plasmavlakke van amitriptilien verhoog en die anticholinergiese effekte van fenotiasien, en moontlik klosapien, verhoog.
Betablokkers: Daar is 'n verhoogde risiko van ventrikulêre disritmieë wanneer **AMDERIP** saam met sotalol geneem word.
Kalsiumkanaalblokkers: Verapamiel en diltiasem kan die plasmakonsentrasies van amitriptilien wat in **AMDERIP** voorkom, verhoog.
Diuretika: Daar is 'n verhoogde risiko van posturale hipotensie.
Dopaminergiese medisyne: Gelyktydige gebruik van **AMDERIP** en entakapoon moet vermy word. SSS-toksisiteit is aangemeld met selegilien.
Spierverslappers: Gelyktydige gebruik van baklofeen verhoog die spierverslappende effek.
Nitrate: Verminderde effek van sublinguale nitrate (as gevolg van droë mond).
Estrogeen en progestogene: Orale voorbehoedmiddels antagoniseer die antidepressante effek van **AMDERIP**, maar nadelige effekte kan verhoog word as gevolg van verhoogde plasmakonsentrasies van trisikliese antidepressante soos per **AMDERIP**.
Oormatige anticholinergiese effekte kan voorkom wanneer **AMDERIP** gekombineer word met anticholinergiese medisyne. Paralitiese ileus, urienretensie of akute gloukoom kan by bejaarde pasiënte presipiteer word.
Simetidien kan die lewermetabolisme van **AMDERIP** verminder wat kan lei tot verhoogde plasmavlakke van amitriptilien.
Johanneskruid kan die plasmakonsentrasies van amitriptilien, wat in **AMDERIP** voorkom, verminder en sodoende die antidepressante effek verminder.
Pasiënte wat skildklierpreparate neem, kan 'n versnelde reaksie op **AMDERIP** vertoon. Gelyktydige gebruik van **AMDERIP** met tiroïedhormone kan kardiale disritmieë presipiteer.

Vrugbaarheid, swangerskap en laktasie
Swangerskap
Die veiligheid en effektiwiteit van **AMDERIP** tydens swangerskap is nie vasgestel nie (sien afdeling 4.3).
Slegs beperkte data is beskikbaar oor blootgestelde swangerskappe. Dierestudies het reproduktiewe toksisiteit getoon.
Laktasie
Die veiligheid en effektiwiteit van **AMDERIP** tydens laktasie is nie vasgestel nie (sien afdeling 4.3).
Moeders op **AMDERIP** moet nie hul babas borsvoed nie (sien afdeling 4.3).
Vrugbaarheid
Amitriptilien het die dragtigheidsyfer by rotte verminder.
Geen data oor die uitwerking van amitriptilien op menslike vrugbaarheid is beskikbaar nie.

Effekte op die vermoë om te bestuur en masjiene te gebruik
Tydens die aanvang van terapie, moet pasiënte aangeraai word om nie 'n motorvoertuig te bestuur, gevaarlike hoogtes te klim of gevaarlike masjinerie vir ten minste 'n paar dae te gebruik nie. In hierdie situasies kan verswakte besluitneming tot ongelukke lei.
Aangesien nadelige reaksies soos lomerigheid, duiseligheid en versteurde visie aangemeld is by pasiënte wat **AMDERIP** ontvang, moet pasiënte nie bestuur, masjinerie gebruik of enige take verrig wat konsentrasie vereis nie, totdat hulle seker is dat **AMDERIP** nie hul vermoë om dit te doen nadelig beïnvloed nie (sien afdeling 4.8).

Ongewenste effekte
a. Opsomming van die veiligheidsprofiel
AMDERIP kan newe-effekte veroorsaak wat soortgelyk is aan ander trisikliese antidepressante. Sommige van die onderstaande nadelige gebeurtenisse bv. hoofpyn, bewing, versteuring in aandag, hardlywigheid en verminderde libido kan ook simptome van depressie wees en gewoonlik verswak wanneer die depressiewe toestand verbeter.

b. Getabelleerde opsomming van nadelige reaksies

MedDRA-stelsel orgaanklas	Frekwensie	Nadelige reaksies
Bloed- en limfatiese sisteemafwykings	Minder dikwels	Beenmurgonderdrukking insluitend agranulositose, eosinofilie, leukopenie, trombositopenie en purpura
Immuunstelselafwykings	Minder dikwels	Hipersensitiwiteitsreaksies insluitend veluitslag, urtikaria, fotosensibilisering, edeem van die gesig en tong, angio-edeem
Endokriene afwykings	Minder dikwels	Sindroom van onvanpaste ADH-afskeiding (SIADH), hiperglisemie, hipoglusemie, hiponatremie
Metabolisme en voedingsafwykings	Minder dikwels	Verhoogde eetlus, gewigstoename, gewigsverlies, anoreksie
Psigiatriese afwykings	Minder dikwels	Verwarringstoestand, disoriëntasie, agitasie, slapeloosheid, nagmerries, delusies, hallusinasies, manie of hipomanie, opgewondenheid, angs, rusteloosheid, versteurde konsentrasie, gedragsveranderinge, selfmoordgedagtes of gedrag
Senustelsel afwykings	Dikwels	Lomerigheid of oormatige sedasie
	Minder dikwels	Duiseligheid, hoofpyn, perifere neuropatie, gevoelloosheid, parestesie, ataksie, bewing, koma, stuiptrekkings, veranderde EEG, ekstrapiramidale versteuring insluitend disartrie (spraakversteuring), tardiewe diskinesie en abnormale onwillekeurige bewegings
Oog afwykings	Dikwels	Akkommodasieversteuring, versteurde visie, verhoogde intra-okulêre druk
	Minder dikwels	Midriasis
Oor- en labirintafwykings	Minder dikwels	Tinnitus
Kardiale afwykings	Minder dikwels	Tagikardie, hartkloppings, miokardiale infarksie, hartblok, disritmieë, veranderinge in atrioventrikulêre geleiding, nie-spesifieke EKG veranderinge
Vaskulêre afwykings	Minder dikwels	Hipotensie, hipertensie, posturale hipotensie, sinkopee, beroerte
Gastro-intestinale afwykings	Dikwels	Droë mond, hardlywigheid
	Minder dikwels	Diarree, braking, naarheid, paralitiese ileus, epigastriese nood, disgeusie, metaalsmaak, stomatitis, parotis swelling, swart tong
Hepatiese-biliêre afwykings	Minder dikwels	Hepatitis (insluitend lewerversaking en cholestatiese geelsug)
Vel, velaanhangsel en subkutane weefsel afwykings	Minder dikwels	Vel uitslag en alopesie
Muskuloskeletale en bindweefselafwykings	Minder dikwels	Verhoogde risiko van beenfrakture
Renale en urinêre afwykings	Dikwels	Urienretensie
	Minder dikwels	Verhoogde urinering, urienwegdilatasie
Voortplantingstelsel en borsafwykings	Minder dikwels	Ginekomastie, borsvergroting, galaktoree, testikulêre swelling, veranderinge in libido, impotensie, seksuele disfunksie
Algemene afwykings en toedieningsplek kondisies	Dikwels	Hipertermie
	Minder dikwels	Moegheid, swakheid, verhoogde sweet

AMDERIP moet met omsigtigheid gebruik word by pasiënte met 'n geskiedenis van epilepsie, verswakte lewerfunksie, urienretensie, prostaathipertrofie, hipertiroïedisme en nouhoek-gloukoom aangesien hierdie toestande vererger kan word deur **AMDERIP**.

Perifere anticholinergiese newe-effekte, veral droë mond, hardlywigheid, urienretensie en pupillêre dilatasie met versteurde visie en veranderinge in visuele akkommodasie, is aangemeld. Wanneer anticholinergiese effekte ernstig is, moet **AMDERIP** gestaak of verminder word.

Gelyktydige toediening van monoamienoksidase-inhibeerders (MAOI's) en **AMDERIP** kan serotoniensindroom veroorsaak ('n kombinasie van simptome soos hipertermie, stuiptrekkings, mioklonus, verwarring, agitasie). 'n Minimum van 14 dae behoort te verloop tussen die staking van 'n MAO-inhibeerder en die aanvang van **AMDERIP**, wat versigtig bekendgestel moet word en die dosis geleidelik verhoog moet word (sien afdeling 4.3).

Omsigtigheid moet in ag geneem word met pasiënte wat aan manies-depressiewe psigose ly, aangesien 'n verskuiwing na die maniese fase kan voorkom. Indien die pasiënt 'n maniese fase betree, moet amitriptilien gestaak word.

Aanmelding van vermoedelike nadelige reaksies
Dit is belangrik om newe-effekte wat vermoed word na die medisyne gemagtig is, te rapporteer. Dit laat die voortgesette monitering van die voordeel/risiko-balans van die medisyne toe. Gesondheidsverskaffers word gevra om enige vermoedens van newe-effekte aan te meld by SAHPRA deur die "**6.04 Adverse Drug Reaction Reporting Form**", wat aanlyn gevind word onder SAHPRA se publikasies: https://www.sahpra.org.za/Publications/Index/8

Oordosering
Oordosering en vergiftiging kan gekenmerk word deur sentrale senuweestelsel depressie of eksitasie, ernstige anticholinergiese effekte en kardiotoksisiteit. Die tekens en simptome van 'n oordosis sluit in: lomerigheid, rusteloosheid, ataksie, koma, stupor, kardiale disritmieë, pireksie, hartkloppings, hipotensie, tagikardie, stuiptrekkings en respiratoriese depressie. Gemengde vergiftiging met ander sentrale senuweestelsel-depressante is nie ongewoon nie.
Behandeling vir oordosis is simptomaties en ondersteunend.

4 FARMAKOLOGIESE EIENSKAPPE
Farmakodinamiese eienskappe
Kategorie en Klas: A 1.2 Psigoanaleptika (antidepressante).
Farmakoterapeutiese groep: Antidepressante – Nie-selektiewe monoamien heropname inhibeerder (trisikliese antidepressant)
ATC kode: N06AA09

Amitriptilien is 'n trisikliese antidepressant. Dit het merkbare anticholinergiese en kalmerende eienskappe. Dit verhoed die heropname, en dus die inaktivering van noradrenalien en serotonien by senuwee-terminale. Heropname voorkoming van hierdie monoamien neurotransmitters versterk hul werking in die brein. Dit blyk geassosieer te word met die antidepressante aktiwiteit.

Farmakokinetiese eienskappe
Absorpsie
Amitriptilien word geabsorbeer na orale toediening en bereik die maksimum plasmakonsentrasie ongeveer 6 uur na toediening.
Verspreiding
Amitriptilien en nortriptilien word wyd deur die liggaam versprei met 'n hoë binding aan plasmaproteïene en weefsels. 'n Eliminasie-halfleeftyd wat wissel van 9 – 25 uur is beraam.
Amitriptilien en nortriptilien gaan oor die plasentaskans. By borsvoedende moeders word amitriptilien en nortriptilien in die borsmelk uitgeskei.
Biotransformasie
Amitriptilien word omvattend gedemetieleer in die lewer tot sy primêre aktiewe metaboliet, nortriptilien. Die metabolismeweg sluit N-oksidasie en konjugasie met glukuroonsuur in.
Eliminasie
Amitriptilien word uitgeskei as glukuronied of gekonjugeerde sulfaatmetaboliete en min medisyne verskyn onveranderd in die urine.

5 FARMASEUTIESE BESONDERHEDE
Lys van hulpstowwe
Kern tablet:
Kolloïdale silikondioksied
Mieliestysel
Kroskarmellose natrium
Laktosemonohidraat
Magnesiumstearaat
Mikrokristallyne sellulose
Talk

Tablet bedekking AMDERIP 10:
Hipromellose
Makrogol 6000
Makrogol (E1521)
Poliviniel alkohol (E1203)
Talk (E553b)
Titaandioksied (E171)
FD&C Blou #1/Briljante Blou FCF Aluminiummeer (E133)

Tablet bedekking AMDERIP 25:
Hipromellose
Ysteroksied geel (E172)
Makrogol 6000
Makrogol (E1521)
Poliviniel alkohol (E1203)
Talk (E553b)
Titaandioksied (E171)

Tablet bedekking AMDERIP 50:
Hipromellose
Ysteroksied geel (E172)
Ysteroksied rooi (E172)
Makrogol 6000
Makrogol (E1521)
Poliviniel alkohol (E1203)
Talk (E553b)
Titaandioksied (E171)

Onverenigbaarhede
Nie van toepassing.

Raklewe
2 Jaar. Bêre by of onder 25 ° C.

Spesiale voorsorgmaatreëls vir berging
AMDERIP benodig geen spesiale bergingsvoorwaardes nie.

Aard en inhoud van houer
AMDERIP 10 word verpak in PVC/PVdC/Aluminium stulpstroke en bevat 30 filmbedekte tablette. Die stulpstroke word in 'n gedrukte karton verpak.

AMDERIP 25 word verpak in PVC/PVdC/Aluminium stulpstroke en bevat 30 of 60 filmbedekte tablette. Die stulpstroke word in 'n gedrukte karton verpak.

AMDERIP 50 word verpak in PVC/PVdC/Aluminium stulpstroke en bevat 30 filmbedekte tablette. Die stulpstroke word in 'n gedrukte karton verpak.

Nie alle verpakkingsgroottes word moontlik bemark nie.

Spesiale voorsorgmaatreëls vir wegdoening <en ander behandeling>
Geen spesiale vereistes nie.

7 HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE
Strides Pharma SA (Edms.) Bpk.
16de Weg 106
Gebou 2
Midrand

8 REGISTRASIE NOMMER(S)
AMDERIP 10: 54/1.2/0684.681
AMDERIP 25 54/1.2/0684.682
AMDERIP 50: 54/1.2/0684.683

9 DATUM VAN EERSTE MAGTIGING/HERNUWING VAN DIE MAGTIGING
29 Maart 2022

10 DATUM VAN HERSIENING VAN DIE TEKS xxxxxxx
N.A

Strides

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