Approved Professional Information for Medicines for Human Use:

Amitriptyline 10 mg Camox

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

Amitriptyline 10 mg Camox film-coated tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg amitriptyline (as hydrochloride).

Contains sugar (lactose monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Amitriptyline 10 mg Camox tablets are blue coloured, circular, biconvex, film-coated tablets with "IA" over "10" debossed on one side and plain on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amitriptyline is a tricyclic antidepressant used in the treatment of patients with endogenous depression. It possesses mild tranquillising and sedative properties which are helpful in alleviating anxiety or agitation that often accompany depression. It has been used with benefit in depression of long or short duration.

All patients do not respond to the same degree. Some may respond in 4 to 10 days while others may require up to 30 days to obtain benefit. A lack of response may occur occasionally.

4.2 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.

4.3 Contraindications

- Patients who have shown prior hypersensitivity to amitriptyline or any of the excipients listed in section 6.1.
- Patients using a monoamine oxidase inhibitor (see section 4.5). Hyperpyretic crises, severe convulsions and deaths have occurred in patients receiving tricyclic antidepressant and monoamine oxidase inhibiting medicines simultaneously. When it is desired to substitute Amitriptyline 10 mg Camox for a monoamine oxidase inhibitor, a minimum of 14 days should be allowed to elapse after the latter is discontinued. Amitriptyline 10 mg Camox should then be initiated cautiously with gradual increases in doses until optimum response is achieved.
- Patients concurrently using antihypertensive medicine, particularly adrenergic blocking medicines (see section 4.5).
- Patients in the acute-phase of myocardial infarction as dysrhythmias, sinus tachycardia and prolongation of conduction time have been reported.
- Children under 12 years of age.
- Lactation.
- Severe liver disease.

- Mania (see section 4.4).

Administration of Amitriptyline 10 mg Camox is not advised during the first trimester of pregnancy (see section 4.6).

4.4 Special warnings and precautions for use

This medicine should at all times be kept out of the reach of children, as even small doses may be fatal to them.

- In patients suffering from a depressive phase of manic depressive psychosis (bipolar disorder), caution should be observed as occasionally hypomania or mania can be precipitated in such patients. If the depression turns into a manic phase Amitriptyline 10 mg Camox should be withdrawn.
- Patients with suicidal tendencies should be carefully supervised during treatment.
- The use of Amitriptyline 10 mg Camox in patients suffering from acute forms of porphyria, especially variegate porphyria and to a lesser extent acute intermittent porphyria and hereditary coproporphyria, is contentious, and thus Amitriptyline 10 mg Camox should be used with caution in these patients.
- Amitriptyline 10 mg Camox should also be used with caution in patients with hyperthyroidism or with impaired liver function, in those with heart-block and in those with a history of epilepsy, untreated narrow-angle glaucoma, urinary retention, prostatic hypertrophy, or constipation.
- Peripheral anticholinergic side effects, notably dry mouth, constipation, urinary retention and pupillary dilatation with blurred vision and changes in visual accommodation. When anticholinergic effects are severe, Amitriptyline 10 mg Camox should be discontinued or reduced.
- Central nervous system depressants including alcohol and anticholinergic medicines can have their effects increased by Amitriptyline 10 mg Camox.
- The simultaneous administration of anticholinergic medicines may be dangerous.

- NOTE: Elderly patients are more prone to all these effects, and therapy should therefore be initiated at lower than standard doses in the elderly.
- In elderly male patients suffering from prostatism, urinary retention may be precipitated.
- Narrow-angle glaucoma may be aggravated.
- In patients suffering from cardiac disease, special caution should be observed because of the occasional problems of tachycardia, dysrhythmias, orthostatic hypotension and other unwanted effects on blood pressure, aggravation of conduction disturbances and electrocardiographic abnormalities. Regular cardiologic and electrocardiographic examinations are advised.
- Epilepsy may be aggravated.
- Amitriptyline 10 mg Camox should not usually be given to patients receiving other central nervous system depressants, for e.g. barbiturates, and to patients receiving monoamine oxidase inhibitors- only after a suitable interval has elapsed (these medicines may only be given together if the dosages are carefully controlled, preferably in hospital) (see section 4.5).
- Amitriptyline 10 mg Camox enhances the pressor effects of direct-acting sympathomimetic medicines, such as epinephrine (adrenaline) and nor-epinephrine (noradrenaline). Local anaesthetics containing these vasoconstrictors should be avoided as hypertensive reactions may occur. When possible, treatment with Amitriptyline 10 mg Camox should be discontinued several days before elective surgery. In addition, the hypotensive effect of certain antihypertensive medicines may be reduced (see section 4.5).
- Should allergic skin reactions occur, Amitriptyline 10 mg Camox should be withdrawn immediately.
- Drowsiness or excessive sedation may be caused in certain patients. On the other hand, disorientation and agitation, insomnia and restlessness can also occur with

normal doses. The risks of central nervous system depression are greater when administered together with other central nervous system depressants, e.g. alcohol, barbiturates.

Special precautions relating to excipients

Amitriptyline 10 mg Camox tablets contain lactose. Patients with the rare hereditary conditions of galactose intolerance, e.g. galactosaemia, Lapp lactase deficiency or glucose-galactose malabsorption should not take Amitriptyline 10 mg Camox.

4.5 Interaction with other medicines and other forms of interaction

Monoamine oxidase inhibitors (MAOI)

Concurrent use of tricyclic antidepressants, such as Amitriptyline 10 mg Camox and monoamine oxidase inhibiting medicines has resulted in hyperpyretic crises, severe convulsions and deaths. When it is desired to substitute Amitriptyline 10 mg Camox for a monoamine oxidase inhibitor, a minimum of 14 days should be allowed to elapse following discontinuation of the MAOI. Amitriptyline 10 mg Camox should then be initiated cautiously with gradual increases in doses until optimum response is achieved (see section 4.3).

Sympathomimetic medicines

The pressor effects of the direct-acting sympathomimetic medicines, epinephrine (adrenaline) and nor-epinephrine (noradrenaline), are enhanced by amitriptyline, and local anaesthetics containing these vasoconstrictors should be avoided as hypertensive reactions may occur. When possible, treatment should be discontinued several days before elective surgery.

Antihypertensives

The hypotensive effect of certain antihypertensive medicines may be reduced by Amitriptyline 10 mg Camox (see section 4.4). Concurrent use of antihypertensive adrenergic blocking medicines such as Guanethidine and Amitriptyline 10 mg Camox is contraindicated (see section 4.3).

Central nervous system depressants

Concurrent use of central nervous system depressants including alcohol and anticholinergic medicines can have their effects increased by amitriptyline. Amitriptyline 10 mg Camox should not usually be given to patients receiving other central nervous system depressants, for e.g. barbiturates, and to patients receiving monoamine oxidase inhibitors

- only after a suitable interval has elapsed (the drugs may be given together if the dosages are carefully controlled, preferably in hospital) (see section 4.4).

Cytochrome P450 enzyme inducers

Rifampicin may increase the metabolism of amitriptyline and may lower plasma concentrations and reduce the antidepressant response of Amitriptyline 10 mg Camox.

Cytochrome P450 enzyme inhibitors

Cimetidine, antipsychotics, antivirals and calcium-channel blockers can reduce the metabolism of tricyclic antidepressants, such as amitriptyline, leading to the possibility of increased plasma concentrations of Amitriptyline 10 mg Camox and accompanying toxicity.

Medicines which prolong the QT interval

Medicines such as antidysrhythmics (amiodarone or quinidine), antihistamines (astemizole and terfenadine), some antipsychotics (notably pimozide and thioridazine), cisapride, halofantrine and sotalol may increase the likelihood of prolonged QT interval and ventricular dysrhythmias when taken concomitantly with tricyclic antidepressants, such as amitriptyline. This effect may be exacerbated where the interacting drug (such as quinidine or some antipsychotics) also reduces the metabolism of amitriptyline. Caution is advised during concurrent use with Amitriptyline 10 mg Camox.

4.6 Fertility, pregnancy and lactation

Safety of Amitriptyline 10 mg Camox during pregnancy and lactation has not been established (see section 4.3).

Amitriptyline 10 mg Camox is contraindicated in breastfeeding.

4.7 Effects on ability to drive and use machines

Drowsiness and impairment of decision making skills may occur at the start of therapy with amitriptyline. Hence, 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 as impaired decision making could lead to accidents.

4.8 Undesirable effects

The following side effects have been reported with use of Amitriptyline 10 mg Camox. Many of the side effects of Amitriptyline 10 mg Camox are related to its anticholinergic actions. When anticholinergic effects are severe, Amitriptyline 10 mg Camox should be discontinued or reduced.

Blood and lymphatic system disorders

Blood disorders: eosinophilia, bone-marrow depression, thrombocytopenia, leucopenia, agranulocytosis.

Immune system disorders

Angiodema, urticaria.

Endocrine disorders

Changes in blood sugar concentrations, inappropriate secretion of antidiuretic hormone.

Metabolism and nutrition disorders

Anorexia with mass loss, or mass gain, increased appetite.

Psychiatric disorders

Confusion or delirium (particularly in the elderly), hallucinations, mania.

Nervous system disorders

Drowsiness, nervousness, insomnia, headache, peripheral neuropathy, tremor, ataxia, epileptiform seizures, extrapyramidal symptoms including speech difficulties.

Eye disorders

Pupillary dilatation: blurred vision, disturbances in visual accommodation, increased intra-ocular pressure.

Ear and labyrinth disorders

Tinnitus.

Cardiac disorders

Palpitations, tachycardia, effects on the myocardium: conduction defects and cardiac dysrhythmias; an increased risk of sudden death has been suspected in cardiac patients receiving tricyclic antidepressants, such as Amitriptyline 10 mg Camox.

Vascular disorders

Orthostatic hypotension, hypertension.

Gastrointestinal disorders

Dry mouth, sour or metallic taste, constipation which may lead to paralytic ileus, stomatitis and gastric irritation with nausea and vomiting.

Hepato-biliary disorders

Cholestatic jaundice.

Skin and subcutaneous tissue disorders

Allergic skin reactions, photosensitisation.

Renal and urinary disorders

Urinary retention.

Reproductive system and breast disorders

Interference with sexual function: changes in libido, impotence, gynaecomastia, breast enlargement, galactorrhoea, testicular swelling.

General disorders and administrative site conditions

Dizziness, sweating, weakness, fatigue.

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. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form",** found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

Symptoms

Overdosage and poisoning may be characterised by central nervous system depression or excitation, severe anticholinergic effects and cardiotoxicity.

The following symptoms and signs are characteristic of acute overdosage: drowsiness, restlessness, ataxia, stupor, coma, pyrexia, palpitations, tachycardia, cardiac arrhythmias, hypotension, and in severe cases, respiratory depression. Epileptiform seizures may occur.

Mixed poisoning with other central nervous system depressants is not uncommon.

Management

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.1.2 Psychoanaleptics (antidepressants)

Pharmacotherapeutic group: Antidepressants - Non-selective monoamine reuptake inhibitor (tricyclic antidepressant).

ATC Code: N 06 AA 09

Amitriptyline is a tricyclic antidepressant.

Amitriptyline causes inhibition of the membrane pump mechanism which is responsible for the reuptake of noradrenaline into adrenergic neurons. As the re-uptake of noradrenaline is physiologically important in terminating the transmitting actions of noradrenaline, inhibition of the re-uptake may potentiate or prolong sympathetic activity. The antidepressant action of amitriptyline is believed to be due to this interference with re-uptake of noradrenaline. The precise mechanism of action in man has not yet been confirmed. Amitriptyline is not a monoamine oxidase inhibitor nor does it act primarily by stimulation of the central nervous system.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, amitriptyline is well absorbed from the gastrointestinal tract and peak plasma concentrations occur within 6 hours.

Distribution

Both amitriptyline and its primary active metabolite, nortriptyline are distributed throughout the body and are extensively bound to plasma and tissue protein. Plasma concentrations of both amitriptyline and nortriptyline differ widely between patients.

Biotransformation

Amitriptyline undergoes extensive liver metabolism. It is demethylated to form its primary active metabolite, nortriptyline by cytochrome P450 isoenzymes CYP3A4, CYP2C9 and CYP2D6. Other paths of metabolism include hydroxylation by CYP2D6 and N-oxidation; nortriptyline follows similar paths.

Elimination

The elimination half-life of amitriptyline has been estimated to range from about 9 to 25 hours which may be considerably extended in overdosage. Excretion is via urine mainly in as metabolites either in free or conjugated form.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose monohydrate

Microcrystalline cellulose

Crospovidone

Maize starch

Anhydrous colloidal silica

Purified talc

Magnesium stearate

Film coating

Hypromellose

Purified talc

Titanium dioxide (E171)

Macrogol 6000

Brilliant blue FCF CI42090

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

HDPE bottle pack and PVC/aluminium blister pack

Store at or below 25 °C in well closed container (in the case of HDPE bottle pack).

Store in the original packaging until required for use.

Store in a cool dry place.

6.5 Nature and contents of container

Tablets are packed in

- HDPE bottles in pack sizes of 100, 500 or 1000 tablets.
- White opaque PVC/aluminium blister pack of 28, 30, 56, 60 and 100 tablets.

Not all pack sizes are marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

1 Sherborne Road

Parktown

JOHANNESBURG

2193

South Africa

Tel: 0860287835

8. REGISTRATION NUMBER

1. Amitriptyline 10 mg Austell - 49/1.2/1017

2. Amitriptyline 10 mg Apex - 49/1.2/1018

3. Amitriptyline 10 mg Camox - 49/1.2/1019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 November 2020

10. DATE OF REVISION OF THE TEXT