SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

ADCO PAROXETINE 20 mg, (20 mg film-coated tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains paroxetine mesylate equivalent to 20 mg of paroxetine base.
Contains sugar (lactose monohydrate): 3,81 mg.
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.
A yellow to orange, round shaped, film-coated tablet. The tablet is debossed with "POT 20" on one side. The tablet is scored on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Depression

ADCO PAROXETINE 20 mg is indicated for the treatment of major depressive disorders with associated anxiety and especially where sedation is not required. It is appropriate for the treatment of single episodes as well as recurrent depression.
It is also indicated as prophylactic treatment for relapse and recurrence of depressive episodes. In these cases treatment at lower doses may be continued for up to one year.

Panic disorder

Panic disorder with and without agoraphobia has been shown to be responsive to treatment with paroxetine. This has been established in a placebo controlled trial where paroxetine was effective in treating panic disorder for up to one year. It has further been shown that panic disorder is treated more effectively with a combination of paroxetine and cognitive-behavioural therapy rather than cognitive-behavioural therapy alone.

Obsessive compulsive disorder

ADCO PAROXETINE 20 mg is indicated in the short-term treatment of severe disabling obsessive compulsive disorder. These obsessions or compulsions may be time consuming, may significantly impair social or occupational functioning, or cause significant distress.

Social phobia

ADCO PAROXETINE 20 mg is indicated for the treatment of social phobia.

4.2 Posology and method of administration

Posology

Depression

The recommended initial dose is 20 mg daily. It may be necessary in some patients to increase the dose. This should be done gradually by 10 mg increments (half a tablet) to a maximum of 50 mg daily, according to the patient's response.

Panic disorder

The recommended dose is 40 mg per day. Patients should start on 10 mg (half a tablet) per day to avoid a possible worsening of the panic symptomatology during early treatment of panic disorders; a low initial starting dose is therefore recommended. The dose may be increased weekly in 10 mg increments (half a tablet), according to the patient's response, to a maximum of 60 mg per day.

Obsessive compulsive disorder

The recommended dose is 40 mg per day. Patients should start on 20 mg per day and the dose may be increased weekly in 10 mg increments (half a tablet) according to the patient's response to a maximum of 60 mg per day.

Social phobia

The recommended dose is 20 mg per day. The dose may be increased weekly in 10 mg increments (half a tablet) according to the patient's response to a maximum of 40 mg per day.

General information

It is recommended that a course of antidepressant treatment should continue for a sufficient period, which may be several months for depression and may be even longer for obsessive compulsive disorder and panic disorder to ensure that patients are symptom free.
When treatment is discontinued, the dosage must be tapered down slowly over several weeks in order to reduce withdrawal symptoms (see section 4.4 and 4.8).

Special populations

Elderly

Increased plasma concentrations occur in the elderly. The recommended dose is 20 mg per day. In some patients it may be necessary to increase the dose. This should be done gradually by 10 mg increments to a maximum of 40 mg according to the patient's response.

Renal/hepatic impairment

The dosage given to patients with severe renal (creatinine clearance < 30 ml/min) or severe hepatic impairment should be restricted to the lower end of the dosage range as elevated plasma concentrations of paroxetine have occurred in such patients.

Paediatric population
Safety and efficacy in children under 18 years of age have not been established. In clinical trials in Major Depressive Disorder, there were increased reports of hostility and suicide-related adverse events such as suicidal ideation and self-harm (see section 4.3, 4.4 and 4.8).

Method of administration
ADCO PAROXETINE 20 mg is administered orally.
The tablets must be swallowed and not chewed.
The tablets should preferably be taken once daily in the morning with food, as it has been shown that a morning dose does not affect duration or quality of sleep. Sleep patterns are likely to improve in patients as they respond to **ADCO PAROXETINE 20 mg** therapy.

4.3 Contraindications
ADCO PAROXETINE 20 mg is contraindicated in patients known to have a hypersensitivity to paroxetine or to one of the excipients used in the tablet.
MAO inhibitors
Concomitant use of **ADCO PAROXETINE 20 mg** in patients receiving monoamine oxidase (MAO) inhibitors is contraindicated and a washout period of at least 2 weeks is recommended when changing from MAO inhibitor therapy to **ADCO PAROXETINE 20 mg** or vice versa.
Children under the age of 18 years (see section 4.2, 4.4 and 4.8).

4.4 Special warnings and precautions for use
Patients with major depressive disorder, both adults and children, may experience worsening of their depression and or the emergence of suicidal ideation and behaviour, whether or not they are taking antidepressant medicines. This risk may persist until significant remission occurs. A casual role, however, for antidepressant medicine in inducing such behaviour has not been established. Patients being treated with **ADCO PAROXETINE 20 mg** should, nevertheless, be observed closely for clinical worsening and suicidality, especially at the beginning of a course of therapy or at any time of dose changes, either increases or decreases. Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorders should be observed when treating patients with other psychiatric and non-psychiatric disorders. The following symptoms have been reported in patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric: anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness), impulsivity, akathisia, hypomania, and mania. Although a casual link between the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing **ADCO PAROXETINE 20 mg**, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms. If the decision is made to discontinue treatment, **ADCO PAROXETINE 20 mg** should be tapered (see section 4.2).

Following abrupt discontinuation of paroxetine, symptoms including dizziness, confusion, nausea, sleep disturbance, insomnia, sensory disturbances, tremor and sweating have been reported (see section 4.8).

History of mania
Patients with a history of mania should use **ADCO PAROXETINE 20 mg** cautiously. Patients receiving a combination of paroxetine and neuroleptics have reported symptoms indicative of neuroleptic malignant syndrome. Caution is therefore advised in patients on neuroleptic treatment.

Oral anticoagulants
There is evidence of a pharmacodynamic interaction between paroxetine and warfarin, which may cause an increase in bleeding even though prothrombin times might remain unaltered. Patients taking oral anticoagulants should therefore use **ADCO PAROXETINE 20 mg** with extreme caution.

Cardiac condition
No studies have been conducted on the administration of **ADCO PAROXETINE 20 mg** to patients with serious cardiovascular disorders and it must therefore be avoided. The serious cardiovascular disorders include acute myocardial infarction, (unstable) angina pectoris, ventricular rhythm disorder and poorly monitored cardiac decompensation. If, however, **ADCO PAROXETINE 20 mg** is indicated for such patients, it should be administered with caution.

Epilepsy
Patients with epilepsy or a history of such a disorder should use **ADCO PAROXETINE 20mg** with caution.

Seizures
Patients receiving **ADCO PAROXETINE 20 mg** may experience seizures. Treatment should be discontinued immediately in such cases.

Electro-convulsive therapy (ECT)
Clinical experience regarding the concomitant administration of paroxetine with electro-convulsive therapy is limited.

Glaucoma
Caution should be exercised in patients with narrow angle glaucoma as **ADCO PAROXETINE 20 mg** may infrequently cause mydriasis.

Haemorrhage
Selective serotonin reuptake inhibitors (SSRIs)/serotonin-norepinephrine reuptake inhibitors (SNRIs) may increase the risk of postpartum haemorrhage (see section 4.6 and 4.8).

Safety and efficacy in children under 18 years of age have not been established. In clinical trials in Major Depressive Disorder, there were increased reports of hostility and suicide-related adverse events such as suicidal ideation and self-harm (see section 4.2, 4.3 and 4.8).

ADCO PAROXETINE 20 mg contains the sugar lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take **ADCO PAROXETINE 20 mg.**

4.5 Interaction with other medicines and other forms of interaction

Food and antacids do not alter the absorption or pharmacokinetics of **ADCO PAROXETINE 20 mg.**

Co-administration of medicines known to be drug metabolising enzyme inhibitors or inducers may affect the metabolism and pharmacokinetics of **ADCO PAROXETINE 20 mg.**

Cimetidine, which is a drug metabolising enzyme inhibitor, can increase the plasma levels of paroxetine. The dosage of **ADCO PAROXETINE 20 mg** may need to be restricted to the lower end of the dosage range when it is to be administered concomitantly with drug metabolising enzyme inhibitors.

Co-administration of paroxetine and phenytoin, a drug metabolising enzyme inducer, is associated with decreased plasma concentrations of paroxetine, and an increase in undesirable effects (diarrhoea, nervousness, imbalance, vertigo, ataxia and indifference) which may be seen with other anticonvulsants as well. Concomitant administration of **ADCO PAROXETINE 20 mg** with drug metabolizing enzyme inducers may not require dosage adjustments initially. However, if the patient displays decreased tolerability or efficacy then the dosage should be adjusted.

Concomitant administration of paroxetine with the medicines debrisoquine and sparteine leads to elevated plasma levels of these medicines. This is due to the inhibitory effect of paroxetine on hepatic cytochrome P450 isozyme CYP 2D6, which is responsible for the metabolism of debrisoquine and sparteine. Other medicines metabolised by this isozyme include phenothiazine neuroleptics (e.g. perphenazine and thioridazine), Type 1C antiarrhythmics (e.g. propafenone) and certain tricyclic antidepressants (e.g. nortriptyline, amitriptyline, imipramine and desipramine).

Preliminary data has shown that the sedation and drowsiness associated with haloperidol, amylobarbitone or oxazepam use, is not increased by the concomitant administration of paroxetine.

The “serotonin syndrome” may occur when **ADCO PAROXETINE 20 mg** is co-administered with monoamine oxidase (MAO) inhibitors (see section 4.3) or other tryptophan medication.

Caution should be exercised when lithium is to be co-administered with **ADCO PAROXETINE 20 mg** as it has been known to interact with other serotonin re-uptake inhibitors. The lithium levels of patients taking this combination should be monitored.

Plasma concentrations of procyclidine and other anticholinergic agents are markedly elevated by daily administration of paroxetine. The dose of procyclidine should be reduced if patients experience any anticholinergic effects.

Anticoagulants/Warfarin: See section 4.4.

Alcohol
It is advisable to avoid the use of alcohol during therapy with **ADCO PAROXETINE 20 mg.**

4.6 Fertility, pregnancy and lactation
The safety of **ADCO PAROXETINE 20 mg** in human pregnancy has not been established. Paroxetine is excreted in breast milk, and therefore should not be used during lactation. Observational data indicate an increased risk (less than 2-fold) of postpartum haemorrhage following SSRI/SNRI exposure within the month prior to birth (see section 4.4 and 4.8).

No data on fertility is available.

4.7 Effects on ability to drive and use machines
Patients taking **ADCO PAROXETINE 20 mg** should exercise caution when driving a car or operating machinery.

4.8 Undesirable effects
A decrease in the intensity and frequency of adverse events may be expected with continued treatment.
The most frequently reported adverse events are: nausea, vomiting, dyspepsia, constipation, diarrhoea, sexual dysfunction, somnolence, sweating, tremor, asthenia, dry mouth, insomnia, dizziness, anxiety, decreased appetite and headaches.
Abnormal liver function tests (elevated levels of hepatic enzymes) have occurred, with isolated cases of serious liver function abnormalities. Treatment should be discontinued in these cases.
There have been reports of extrapyramidal symptoms associated with the use of paroxetine and of aggravation of Parkinson's disease in patients taking paroxetine. It should therefore be avoided in patients with extrapyramidal disorders or who were using neuroleptic medication.
ADCO PAROXETINE 20 mg should be used with caution in patients already receiving neuroleptics, since symptoms suggestive of neuroleptic malignant syndrome cases have been reported with this combination.
Hyponatraemia possibly due to inappropriate secretion of antidiuretic hormone, has been associated with the use of antidepressants, particularly in the elderly.
The hyponatraemia generally reverses on discontinuation of paroxetine.
Bruising, rash, acute glaucoma, urinary retention, peripheral and facial oedema, neuroleptic malignant syndrome, confusion, abnormal bleeding (mostly ecchymosis and purpura) and symptoms suggestive of hyperprolactinaemia/galactorrhoea have been reported.
"**Serotonin syndrome**": which includes symptoms of confusion, hallucinations, agitation, incoordination, excessive sweating, hyperreflexia, tachycardia, myoclonus, diarrhoea, shivering, fever and tremor (see section 4.5).
In children, reports of hostility, suicidal ideation and self-harm (see section 4.2, 4.3 and 4.4).
Postpartum haemorrhage has been reported (frequency unknown) for the therapeutic class of SSRIs/SNRIs (see section 4.4 and 4.8).

Description of selected adverse reactions

Following abrupt discontinuation of paroxetine, symptoms including dizziness, confusion, nausea, sleep disturbance, insomnia, sensory disturbances, tremor and sweating have been reported (see section 4.4).

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: http://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Experience of paroxetine in overdose has shown symptoms including nausea, vomiting, tremor, dilated pupils, dry mouth and irritability. Death, ECG abnormalities, coma or convulsions have not been reported following overdosage with paroxetine alone.
No specific antidote is known. Treatment of overdose is supportive and symptomatic. Gastric emptying either by the induction of emesis, lavage or both should be performed. After evacuation, 20 to 30 grams of activated charcoal may be administered every 4 to 6 hours during the first 24 hours after ingestion to delay absorption of paroxetine.
Supportive care, including frequent monitoring of vital signs and careful observation is indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 1.2 Psychoanaleptics (antidepressants)
Pharmacotherapeutic group: Antidepressants, selective serotonin reuptake inhibitors, ATC code: N06AB05.
Paroxetine, a phenylpiperidine derivative, is a selective 5-hydroxytryptamine (5-HT, serotonin) re-uptake inhibitor. The antidepressant action is presumably linked to potentiation of serotonergic activity in the central nervous system resulting from inhibition of neuronal re-uptake of serotonin (5-HT).

5.2 Pharmacokinetic properties

Paroxetine is well absorbed from the gastrointestinal tract. Paroxetine undergoes extensive first-pass metabolism in the liver. The principle metabolites of paroxetine are polar and conjugated products of oxidation and methylation, which are readily cleared. The metabolites of paroxetine do not compromise the selective action of paroxetine on neuronal 5-HT uptake. Paroxetine is widely distributed throughout the body tissues and is about 95 % bound to plasma proteins. The elimination half-life is variable but is generally about one day. Steady state concentrations of paroxetine are reached within 1 to 2 weeks after commencing therapy and pharmacokinetics do not appear to change during long-term therapy.

5.3 Preclinical safety data
No information available.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Calcium hydrogen phosphate anhydrous
Iron oxide yellow (E172)
Iron oxide red (E172)
Lactose monohydrate
Magnesium stearate
Methylhydroxypropyl cellulose
Polyethylene glycol 4000
Sodium starch glycolate
Titanium dioxide (E171)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
ADCO PAROXETINE 20 mg should be stored at or below 25 °C.
Keep blister strips in outer carton until required for use.
Protect from light and moisture.

6.5 Nature and contents of container
Carton boxes with 1, 2, 3 or 5 PVC/PE/PVDC/Al-blisters or PVC/TE/PVDC/Al-blisters or Alu/Alu-blisters with 10 tablets each, resulting in total pack sizes of 10, 20, 30 or 50 tablets
or
carton boxes with 1, 2 or 4 PVC/PE/PVDC/Al-blisters or PVC/TE/PVDC/Al-blisters or Alu/Alu-blisters with 14 tablets each, resulting in total pack sizes of 14, 28 or 56 tablets
or
300 ml white, opaque HDPE container with child-resistant closure containing 500 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION
Adcock Ingram Limited
1 New Road
Erand Gardens
Midrand,1685

Customer Care: 0860 ADCOCK / 232625

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