SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

PAX-5, 5 mg tablets

PAX-10, 10 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of PAX-5 contains 5 mg of diazepam.

Contains sugar: Lactose monohydrate 113,1 mg.

Each tablet of PAX-10 contains 10 mg of diazepam.

Contains sugar: Lactose monohydrate 108,3 mg.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

PAX-5: A flat, round, pale orange tablet with bevelled edges, bisected on one side and embossed “C33” on the other side.

PAX-10: A flat, round, blue tablet with bevelled edges, bisected on one side and embossed “C34” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PAX is only indicated when the disorder is severe, disabling or when the individual is subject to extreme stress.

PAX is indicated for the following conditions:

Anxiety: symptomatic relief of anxiety, tension and other somatic or psychological complaints associated with the anxiety syndrome. It can also be used as an adjunct to the treatment of anxiety or excitation associated with psychiatric disorders.

Muscle relaxation: as an adjunct for the relief of reflex muscle spasm due to local trauma (injury, inflammation). It can also be used to combat spasticity arising from damage to spinal and supraspinal interneurons such as cerebral palsy and paraplegia, as well as athetosis and stiff-man syndrome.

Treatment should be as short as possible. The patient should be assessed regularly and the need for continued treatment should be re-evaluated especially when the patient is symptom-free. The overall duration of treatment of anxiety should not be more than 8 to 12 weeks, including a tapering off process. In certain cases, extension beyond the maximum treatment

period may be necessary. If so, it should not take place without re-evaluation of the patient's status.

4.2 Posology and method of administration

Posology

The duration of treatment should be as short as possible. The patient should be reassessed regularly and the need for continued treatment evaluated, especially if the patient is symptom free. It should not exceed 2 - 3 months, including the tapering-off period. Extension beyond this period should not take place without re-evaluation of the situation. It may be useful to inform the patient when treatment is started that it will be of limited duration and explain precisely how the dosage will be progressively decreased. Moreover, it is important that the patient be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms, should they occur during withdrawal. There is evidence that, in case of short-acting benzodiazepines, withdrawal phenomena can become manifest within the dosage interval especially when the dosage is high. When long-acting benzodiazepines such as PAX are being used, it is important to warn against changing to short-acting benzodiazepines as withdrawal symptoms may develop.

Standard adult dosage

For optimal effect, the dosage should be carefully individualised. Treatment should begin at the lowest effective dose appropriate to the particular condition and the maximum dose should not be exceeded.

Average adult dosage for oral administration: Initial dose: 5 - 10 mg. Depending on symptom severity, the usual dose is 5 - 20 mg daily. The maximum single oral dose for adults should not exceed 10 mg.

Special dosage instructions

Chronic respiratory depression, elderly and debilitated patients:

Elderly and debilitated patients who are at particular risk of oversedation, respiratory depression and ataxia should be given half of the usual adult dose. These patients should be checked regularly at the start of treatment in order to minimise the dosage and/or frequency of administration to prevent overdose due to accumulation.

Impaired hepatic or renal function:

Patients with impaired hepatic function should be given a reduced dose.

The usual precautions in treating patients with impaired renal function should be observed.

Method of administration

Oral administration.

4.3 Contraindications

- Hypersensitivity to diazepam or to any of the excipients listed in section 6.1
- Severe respiratory insufficiency
- Severe hepatic insufficiency
- Sleep apnoea syndrome
- Myasthenia gravis
- Dependence on other CNS depressants including alcohol, except in the acute withdrawal reactions (see section 4.4).
- PAX is not recommended for the primary treatment of psychotic illness.
- PAX should not be used alone to treat depression or anxiety associated with depression as suicide may occur in such patients.

4.4 Special warnings and precautions for use

Concomitant use of alcohol/CNS depressants

The concomitant use of PAX with alcohol or/and CNS depressants (e.g., barbiturates, narcotics, monoamine oxidase inhibitors) should be avoided. Such concomitant use has the potential to increase the clinical effects of PAX possibly including severe sedation, clinically relevant respiratory and/or cardiovascular depression (see section 4.5).

Psychiatric and 'paradoxical' reactions

Paradoxical reactions such as restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using PAX. Should this occur, the use of PAX should be discontinued. They are more likely to occur in the elderly.

Hypotension

PAX should be administered with caution to patients in whom a drop in blood pressure might lead to cardiac or cerebral complications. This is particularly important in elderly patients.

Amnesia

PAX may induce anterograde amnesia. Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages. Amnestic effects may be associated with inappropriate behaviour.

Acute narrow-angle glaucoma

Caution should be used in the treatment of patients with acute narrow-angle glaucoma (because of atropine-like side effects).

Use in hepatic impairment

Use with caution when administering PAX to patients with mild to moderate hepatic impairment (see section 4.2).

Periodic liver function tests are recommended.

Use in renal impairment

Patients with impaired renal function should use benzodiazepine (as contained in PAX) with caution and dosage reduction may be advisable (see section 4.2).

Blood dyscrasias

Patients taking benzodiazepines as contained in PAX have developed blood dyscrasias. Periodic blood counts are recommended.

Tolerance

Some loss of response to the effects of PAX may develop after repeated use for a prolonged period of time.

Depression, psychosis and schizophrenia

PAX is not recommended for the primary treatment of psychotic illness. PAX should not be used alone to treat depression or anxiety with depression (suicide may be precipitated in such patients) (see section 4.3). PAX should be used with extreme caution in patients with a history of alcohol or drug abuse.

Caution should be observed in patients suffering from anxiety accompanied by an underlying depressive disorder.

Respiratory insufficiency

Caution in the use of PAX is recommended in patients with respiratory depression. In patients with chronic obstructive pulmonary disease, PAX can cause increased arterial carbon dioxide tension and decreased oxygen tension (see section 4.3).

A lower dose is recommended for patients with chronic respiratory insufficiency, due to the risk of respiratory depression.

Medical history of alcohol or drug abuse

PAX should be used with extreme caution in patients with a history of alcohol or drug abuse, see Dependence below.

PAX should not be used in patients with dependence on CNS depressants including alcohol (see section 4.3).

An exception to the latter is the management of acute withdrawal reactions.

A lower dose is recommended for patients with chronic respiratory insufficiency, due to the risk of respiratory depression (see section 4.3). Lower doses should also be used for elderly and debilitated patients.

Dependence

There is a potential for abuse and the development of physical and psychological dependence, especially with prolonged use and high doses. The risk of dependence is also greater in patients with a history of alcohol or drug abuse.

Withdrawal

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability.

In severe cases the following symptoms may occur; derealisation, depersonalisation, hyperacusis, numbness and tingling of extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. Withdrawal symptoms may occur after long periods of ordinary therapeutic doses.

PAX may increase the frequency and severity of attacks of grand mal epilepsy, during treatment or abrupt withdrawal.

Rebound anxiety

A transient syndrome whereby the symptoms that led to treatment with PAX recur in an enhanced form, may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness.

Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment it is recommended that the dosage is decreased gradually.

Duration of treatment

The duration of treatment should be as short as possible (see section 4.2), but should not exceed eight to twelve weeks, including tapering off process. Extension beyond this period should not take place without re-evaluation of the situation. It may be useful to inform the

patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover it is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms, should they occur while the product is being discontinued.

PAX should be given with caution to the elderly and to patients with arteriosclerosis.

Avoid in porphyria as PAX is considered unsafe although there is conflicting evidence of porphyrogenicity**.**

Lactose warning:
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take PAX.

4.5 Interactions with other medicines and other forms of interaction

Pharmacodynamic Interactions

The response to treatment with oral anticoagulants may be variable in patients taking PAX.
Enhanced effects of sedation, respiration, and haemodynamics may occur when PAX is coadministered with other centrally acting depressants such as antipsychotics (e.g. clozapine, phenothiazines, levomepromazine, olanzapine), anxiolytics or sedatives, antidepressants, hypnotics, anticonvulsants, narcotic analgesics (e.g. methadone), and sedative antihistamines, or alcohol.
Concomitant use of barbiturates, alcohol or other central nervous system depressants increases cardio-respiratory depression with increased risk of apnoea.

Alcohol should be avoided in patients receiving PAX (see section 4.4 and 4.9).
Reversible loss of control of Parkinson’s disease has been seen in some patients treated with combined levodopa and PAX.

The xanthines, theophylline and caffeine, oppose the sedative and possibly anxiolytic effects of PAX partially through blocking of adenosine receptors.

Diazepam (as contained in PAX) pre-treatment changes the pharmacodynamics and pharmacokinetics of the anaesthetic ketamine. Ketamine N-demethylation was inhibited leading to a prolonged half-life and prolonged ketamine-induced sleeping time. In the presence of diazepam, a reduced ketamine concentration is required to achieve adequate anaesthesia.

The anti-cholinergic effects of other medicines including atropine and similar medicines, anti-histamines and antidepressants may be potentiated.

Interactions have been reported between some benzodiazepines (as contained in PAX) and anti-convulsants (e.g., diazepam with phenytoin or with carbamazepine), with changes in the serum concentration of the benzodiazepine or anticonvulsant. It is recommended that patients be observed for altered responses when PAX and anti-convulsants are prescribed together and that serum level monitoring of the anti-convulsant is performed more frequently.

Pharmacokinetic Interactions

Pharmacokinetic medicine interactions

The metabolism of diazepam (as contained in PAX) and its main metabolite, desmethyldiazepam depends on the cytochrome P450 isozymes CYP3A4 and CYP2C19. Modulators of these enzymes may lead to changes in diazepam disposition and effects. Stronger interactions are seen with compounds that affect more than one of diazepam's oxidative metabolic pathways. Inhibitors of CYP3A4 and CYP2C19 decrease metabolic rate and may lead to higher than normal concentrations of diazepam and the desmethyl metabolite and consequently to increased/ prolonged sedation and anxiolytic effects. Such changes may exacerbate diazepam's effects in patients with increased sensitivity, e.g. due to their age, reduced liver function or treatment with other medicine that impair oxidation. Inducers of CYP3A4 and CYP2C19 may lead to lower than expected concentrations and hence to a lack of desired efficacy.

Effect of other medicines on the pharmacokinetics of PAX

Enzyme inhibitors

Grapefruit juice contains strong inhibitors of CYP3A4. Diazepam (as contained in PAX) exposure was strongly increased (AUC 3,2-fold; C_{max} 1,5-fold) and time to reach maximum concentration was delayed when diazepam was given with grapefruit juice instead of water. This may result in excessive or prolonged sedation. Patients should be advised to avoid grapefruit juice while taking PAX.

Antimycotic azole derivatives inhibit CYP3A4 and CYP2C19 pathways and lead to increased exposure to diazepam (as contained in PAX). The increased exposure to diazepam may result in greater and more prolonged sedation. Therefore, it is recommended to avoid concomitant use of these medicines (including ketoconazole) with PAX or reduce the dose of PAX.

The serotonin reuptake inhibitor fluvoxamine also inhibits both of diazepam's (as contained in PAX) CYP3A4 and CYP2C19 degradation pathways. Fluoxetine is a moderate inhibitor of CYP3A4. Fluoxetine showed a more moderate effect on diazepam AUC (approximately 50 % increase) and did not affect psychomotor response because combined concentrations of diazepam and desmethyldiazepam were similar with and without fluoxetine. Fluvoxamine and fluoxetine may lead to increased and prolonged sedation. For patients taking fluvoxamine, a benzodiazepine metabolised via a non-oxidative pathway is recommended. Patients receiving fluoxetine with PAX should be monitored closely.
Combined hormonal contraceptives appear to reduce the clearance (by 40 %) and prolong elimination half-life (by 47 %) of diazepam (as contained in PAX). Diazepam-induced psychomotor impairment in women on contraceptives may be higher during the 7-day menstrual pause when off the hormone preparation than when taking the contraceptive. Monitor the clinical response to PAX in women taking concomitant oral contraception. There is some limited evidence that PAX can increase the incidence of break-through bleeding in women with hormonal contraceptives.

The proton pump inhibitor omeprazole, a CYP2C19 and CYP3A4 inhibitor, increase diazepam (as contained in PAX) AUC and the half-life. The elimination of desmethyldiazepam is reduced as well. The effect of omeprazole was seen in extensive, but not slow, metabolisers of CYP2C19.
Esomeprazole (but not lansoprazole or pantoprazole) has the potential to inhibit the metabolism of diazepam to a similar degree as omeprazole. Patients being administered these medicines with PAX should be monitored closely and the dose of PAX should be reduced if necessary.

The histamine H2-receptor antagonist cimetidine, an inhibitor of multiple CYP isozymes, including CYP3A4 and CYP2C19, reduces the clearance of diazepam (as contained in PAX) and of desmethyldiazepam by 40 to 50 %. Enhanced sedation was seen with co-administration of cimetidine. Therefore, when used with cimetidine, a reduction in the dose of PAX may be necessary. Ranitidine and famotidine do not affect the hepatic elimination of diazepam.

Disulfiram inhibits the metabolism of diazepam (as contained in PAX) and probably the further metabolism of diazepam's active metabolites. Enhanced sedative effects may result.

Antituberculosis therapy may change the disposition of diazepam (as contained in PAX). When used with isoniazid, monitor patients and reduce the dose of PAX if necessary.

The calcium channel blocker diltiazem, a substrate for the same CYP isozymes as diazepam and an inhibitor of CYP3A4, increased AUC (by approximately 25 %) and prolonged half-life (by 43 % in extensive CYP2C19 metabolisers) of diazepam. Exercise caution when using PAX with diltiazem, irrespective of CYP2C19 metaboliser status.

The psychostimulants modafinil and armodafinil induce CYP3A4 and inhibit CYP2C19; they may prolong the elimination of diazepam (as contained in PAX) and cause excessive sedation. When used with these psychostimulants, monitor patients and reduce the dose of PAX if necessary.

The use of other CYP3A or CYP2C19 inhibitors (such as clarithromycin, erythromycin, ritonavir and verapamil) with PAX may lead to increased and prolonged sedation.

Enzyme inducers
Rifampicin potently induces CYP3A4 and diazepam (as contained in PAX), therefore PAX should only be used together with rifampicin if no therapeutic alternative exists.

Carbamazepine is a known inducer of CYP3A4 and accelerated elimination (increased clearance, reduced half-life) of diazepam 3-fold while increasing concentrations of desmethyldiazepam. This can result in a reduced effect of PAX.

Food, antacids and medicine affecting gut motility
Food may lower the rate but will not lower the extent of diazepam (as contained in PAX) absorption from the tablet; this may lead to attenuated effects after a single dose but not influence steady-state concentrations during multiple-dose therapy.
Antacids may lower the rate but will not lower the extent of diazepam absorption from the tablet; this may lead to attenuated effects after a single dose but not influence steady-state concentrations during multiple-dose therapy.
Prokinetic medicine e.g., cisapride, may lead to a temporary increase in the sedative effects of PAX due to faster absorption.

Intravenous but not oral metoclopramide increases the rate of absorption of diazepam (as contained in PAX) and increases the maximum concentration achieved after oral dosing.

Narcotics (morphine, pethidine) decrease the absorption rate and lower peak concentrations of diazepam (as contained in PAX). However, due to the additive CNS depressant effect, the concomitant use of PAX and opioids should be avoided.

If a decision is made to prescribe PAX concomitantly with opioids, prescribe the lowest effective dose and minimum duration of concomitant use. Follow patients closely for signs and symptoms of respiratory depression and sedation (see section 4.4 and 4.9).
Advise both patients and caregivers about the risks of respiratory depression and sedation when PAX is used with opioids. Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the opioid have been determined (see section 4.7).

Effect of PAX on the pharmacokinetics of other medicines
Monitor serum levels of phenytoin when initiating or discontinuing PAX.

4.6 Fertility, pregnancy and lactation
Pregnancy
The safety of PAX for use in pregnancy has not been established. An increased risk of congenital malformation associated with the use of benzodiazepines during the first trimester of pregnancy has been suggested. Continuous administration of benzodiazepines during pregnancy may give rise to the so-called floppy-infant syndrome, manifested by hypotension, reduced respiratory function and hypothermia in the newborn child. Withdrawal symptoms in newborn infants have been reported with PAX.
Special care must be taken when PAX is used during labour and delivery, as high single doses may produce irregularities in the foetal heart rate and hypotonia, poor sucking, hypothermia and moderate respiratory depression in the neonate. With newborn infants it must be remembered that the enzyme system involved in the breakdown of the medicine is not yet fully developed (especially in premature infants).

Fertility
No data is currently available.

Breastfeeding
PAX is excreted in breastmilk and should not be administered to breastfeeding mothers.

4.7 Effects on ability to drive and use machines
Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or operate machinery. These symptoms may be aggravated by simultaneous intake of alcohol, opioids or other central nervous system depressant medicines (see section 4.5).
Prior to receiving PAX, the patient should be warned not to operate dangerous machinery or motor vehicles until completely recovered. The medical practitioner should decide when these

activities may be resumed. Abilities may be impaired on the day following use.

4.8 Undesirable effects

The side effects most frequently encountered with PAX are drowsiness, muscle weakness, oversedation, dizziness, light-headedness, mental depression, fatigue, apathy, constipation, irritability.

Tabulated summary of adverse reactions

Blood and lymphatic system disorders	
Less frequent	Occasional blood disorders, isolated instances of neutropenia.
Psychiatric disorders	
Less frequent	Drowsiness, confusion, numbed emotions, depression. Paradoxical reactions such as restlessness, acute disorientation, agitation, irritability, aggressiveness, nervousness, hostility, anxiety, delusion, rage, nightmares, abnormal dreams, hallucinations, psychoses, hyperactivity, inappropriate behaviour and other adverse behavioural effects are known to occur when using PAX. If these occur, PAX should be discontinued.
There is potential for abuse. Withdrawal symptoms (including convulsions) have occurred following abrupt cessation, especially in patients who have received large doses for prolonged periods. Physical and psychological dependence, (see section 4.4).	
Nervous system disorders	
Less frequent:	Fatigue, headache, lethargy, ataxia, dizziness, slurred speech or dysarthria, tremor, numbed emotions, anterograde amnesia – (see section 4.4), reduced alertness. PAX may increase the frequency and severity of attacks of grand mal epilepsy, during treatment or abrupt withdrawal.
Cardiac disorders	
Less frequent:	Cardiac failure including cardiac arrest, variations in pulse rate. Large doses may produce syncope.
Vascular disorders	
Less frequent:	Hypotension.
Respiratory, thoracic and mediastinal disorders	
Less frequent:	Circulatory depression, respiratory depression including respiratory failure due to a depressant effect on the respiratory centre and cardiovascular collapse.
Eye disorders	
Less frequent:	Diplopia, visual disturbances such as blurred vision.

Gastrointestinal disorders	
Less frequent:	Indigestion, nausea, dry mouth, changes in salivation e.g., hypersalivation, constipation and gastrointestinal disturbances such as diarrhoea.
Hepato-biliary disorders	
Less frequent:	Elevated transaminases and blood alkaline phosphatase, jaundice, hepatic dysfunction.
Renal and urinary disorders	
Less frequent:	Incontinence, urinary retention.
Skin and subcutaneous tissue disorders	
Less frequent:	Skin reactions such as rashes.
Ear and labyrinth disorders	
Less frequent:	Vertigo.
Reproductive system and breast disorders	
Less frequent:	Increase or decrease in libido, menstrual irregularities.
Injury and poisoning	
Less frequent:	There have been reports of falls and fractures in benzodiazepine users, including PAX. The risk is increased in those taking concomitant sedatives (including alcoholic beverages), and in the elderly.

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.

Reporting can also be done directly to Adcock Ingram Limited at:

Adcock Ingram Limited:

E-mail: Adcock.aereports@adcock.com

Tel: 011 635 0134

4.9 Overdose

Symptoms

Manifestations of overdosage include somnolence, confusion, coma, respiratory and cardiovascular depression and hypotension.

PAX commonly causes drowsiness, ataxia, dysarthria and nystagmus. Overdose of PAX may be life-threatening if the medicine is taken alone, and may lead to areflexia, apnoea,

hypotension, cardio-respiratory depression and coma. Coma, if it occurs, usually lasts a few hours but it may be more protracted and cyclical, particularly in elderly patients. PAX's respiratory depressant effects are more serious in patients with respiratory disease. PAX increases the effects of other central nervous system depressants, including alcohol.

Treatment

There is no specific treatment and recovery usually follows symptomatic and supportive therapy, with particular attention being paid to the maintenance of cardiovascular, respiratory and renal functions, and to the maintenance of electrolyte balance.

Further absorption should be prevented using an appropriate method e.g. treatment within 1 – 2 hours with activated charcoal. If activated charcoal is used airway protection is imperative for drowsy patients.

If CNS depression is severe, consider the use of flumazenil, a benzodiazepine antagonist. This should only be administered under closely monitored conditions. It has a short half-life (about an hour), therefore patients administered flumazenil will require monitoring after its effects have worn off. Flumazenil is to be used with extreme caution in the presence of medicines that reduce seizure threshold (e.g. tricyclic antidepressants). Refer to the prescribing information for flumazenil, for further information on the correct use of this medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 2.6 Tranquillisers

Pharmacotherapeutic group: Anxiolytics, benzodiazepine derivatives, ATC code: N05BA01.

Diazepam is a long-acting benzodiazepine hypnotic with anxiolytic, sedative, muscle-relaxant, anticonvulsant and amnesic properties.

The major sites of action of diazepam on the spinal reflexes are supraspinal. However, this action is in part mediated by the brain stem reticular system. It depresses the duration of electrical after discharge in the limbic system, including the septal region, amygdala and hippocampus. These actions result from potentiation of the neural inhibition that is mediated by Gamma-aminobutyric acid (GABA).

5.2 Pharmacokinetic properties

Absorption

After oral administration peak plasma concentrations are reached in one to four hours.

Distribution

Diazepam and its metabolites are extensively bound to plasma proteins (98 %).

Diazepam and its metabolites cross the blood-brain and placental barriers and are also found in breastmilk. The volume of distribution at steady state is 0,8 - 1,0 ℓ/kg. The half-life of distribution is up to 3 hours.

Biotransformation

Diazepam is mainly metabolised to the pharmacologically active metabolites such as N-desmethyldiazepam, temazepam and oxazepam.

The oxidative metabolism of diazepam is mediated by CYP3A and CYP2C19 isoenzymes.

Oxazepam and temazepam are further conjugated to glucuronic acid.

Elimination

The decline in the plasma concentration-time profiles after oral administration of diazepam is biphasic; an initial rapid and extensive distribution phase being followed by a prolonged terminal elimination phase (half-life up to about 48 hours). The terminal elimination half-life of the active metabolite N-desmethyldiazepam is up to 100 hours. Diazepam and its metabolites are excreted mainly into the urine, predominantly in their conjugated forms. The clearance of diazepam is 20 – 30 mL/min.

Pharmacokinetics in special populations

The elimination half-life may be prolonged in the newborn, in the elderly and in patients with liver disease. In renal impairment the half-life of diazepam is unchanged.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dye lennon lake yellow no.127 (C.I. 15985) (Pax-5)

Dye Indigo Carmine Lake (CI 73015) (Pax-10)

Lactose monohydrate

Microcrystalline cellulose

Powdered vegetable stearine

Starch maize

6.2 Incompatibilities

Not applicable

6.3 Shelf life

PAX-5:

HDPE container: 60 months

Blister packs: 24 months

PAX-10: 60 months

6.4 Special precautions for storage

Store at or below 25 °C, in a well-closed container.

Protect from light.

Keep in original packaging until required for use.

6.5 Nature and contents of container

PAX-5: 30 tablets are packed in a clear polyvinylchloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

100, 500 or 1 000 tablets are packed in a white cylindrical polypropylene container with a white linear low density polyethylene cap, together with a polyurethane foam insert and leaflet.

PAX-10: 30 tablets are packed in a clear polyvinylchloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

500 tablets are packed in a white polypropylene container with a white low density polyethylene cap, together with a white polyurethane foam insert.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

1 New Road

Erand Gardens

Midrand, 1685

Customer Care: 0860 ADCOCK/ 232625

8. REGISTRATION NUMBER(S)

PAX-5: J/2.6/267

PAX-10: J/2.6/250

DATE OF APPROVAL: 26 SEPTEMBER 2024

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration:

PAX-5: 20 April 1977

PAX-10: 20 April 1977

10. DATE OF REVISION OF THE TEXT

26 September 2024

Namibia		
NS3	Pax-10	90/2.6/001099

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