PAXIL

SCHEDULING STATUS:

S5

PROPRIETARY NAME AND DOSAGE FORM:

PAXIL 20 tablets

COMPOSITION:

Each tablet contains paroxetine hydrochloride equivalent to paroxetine 20 mg free base.

Excipients:

Tablet core: dibasic calcium phosphate (dihydrate), sodium starch glycollate and magnesium stearate.

Film-coat: hypromellose, titanium dioxide (EEC No. 171), macrogol 400 and polysorbate 80.

Sugar-free.

PHARMACOLOGICAL CLASSIFICATION:

A 1.2 Psycho-analeptics (Antidepressants)

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Paroxetine is a selective inhibitor of serotonin (5-hydroxy-tryptamine, 5-HT) re-uptake and its antidepressant action and efficacy is thought to be related to its specific inhibition of serotonin re-uptake in brain neurones.

Pharmacokinetic properties:

Paroxetine is well absorbed after oral dosing and undergoes first pass metabolism.

The elimination half-life is variable but is generally about 1 day. Steady state systemic levels are attained 7-14 days after starting treatment and pharmacokinetics do not appear to change during long-term therapy.

Paroxetine is chemically unrelated to the tricyclic or tetracyclic antidepressants.

INDICATIONS:

Depression:

Major depressive disorders, such as single episodes and recurrent depression with associated anxiety, especially where sedation is not required.

Treatment at generally lower dosages may be continued for up to one year to prevent relapse and recurrence of further depressive episodes.

Safety and efficacy in children under 18 years of age has not been established.

Panic Disorder:

PAXIL has been shown to be effective in the treatment of panic disorder with and without agoraphobia.

The combination of PAXIL and a cognitive-behavioural therapy has been shown to be statistically significantly more effective than cognitive-behavioural therapy alone in the treatment of panic disorder.

In a placebo-controlled trial, the efficacy of PAXIL in the treatment of panic disorder has been maintained for up to one year.

Obsessive Compulsive Disorder:

For the short-term treatment of severe disabling obsessive compulsive disorder, where the obsessions or compulsions cause marked distress, are time-consuming or significantly interfere with social or occupational functioning.

Social Phobia:

PAXIL has been shown to be effective in the treatment of social phobia.

Generalised Anxiety Disorder:

PAXIL has been shown to be effective in the treatment of generalised anxiety disorder.

Children and adolescents (less than 18 years):

PAXIL is not indicated for use in children or adolescents aged less than 18 years (see WARNINGS AND SPECIAL PRECAUTIONS).

Controlled clinical studies in children and adolescents with major depressive disorder failed to demonstrate efficacy and do not support the use of PAXIL in the treatment of depression in this population (see CONTRA-INDICATIONS, WARNINGS AND SPECIAL PRECAUTIONS).

CONTRA-INDICATIONS:

Known hypersensitivity to paroxetine or any excipients of PAXIL.

Concomitant use with serotonin precursors (see WARNINGS AND SPECIAL PRECAUTIONS and INTERACTIONS).

PAXIL tablets should not be used in combination with monoamine oxidase (MAO) inhibitors or within 2 weeks of terminating treatment with MAO inhibitors. Likewise, MAO inhibitors should not be introduced within 2 weeks of cessation of therapy with PAXIL tablets (see INTERACTIONS).

Children under the age of 18 years (see WARNINGS AND SPECIAL PRECAUTIONS).

PAXIL tablets should not be used in combination with thioridazine, as PAXIL can elevate the plasma levels of thioridazine, leading to the prolongation of the QTc interval on the ECG.

PAXIL should not be used in combination with pimozide (see INTERACTIONS).

PAXIL should not be used in pregnancy (see PREGNANCY AND LACTATION).

WARNINGS AND SPECIAL PRECAUTIONS:

Children and Adolescents (less than 18 years):

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, suicide ideation and self-harm (see CONTRA-INDICATIONS).

Treatment with antidepressants is associated with an increased risk of suicidal thinking and behaviour in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders. In clinical trials of PAXIL in children and adolescents, adverse events related to suicidality (suicide attempts and suicidal thoughts) and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in patients treated with PAXIL compared to those treated with placebo.

Long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking.

Clinical worsening and suicide risk in adults:

Young adults, especially those with MDD, may be at increased risk for suicidal behaviour during treatment with PAXIL. An analysis of placebo controlled trials of adults with psychiatric disorders showed a higher frequency of suicidal behaviour in young adults (prospectively defined as aged 18-24 years) treated with paroxetine compared with placebo (17/776 [2,19 %] versus 5/542 [0,92 %]), although this difference was not statistically significant. In the older age groups (aged 25-64 years and ≥ 65 years), no such increase was observed.

However, the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24.

Patients with major depressive disorders, both adults and children, may experience worsening of their depression and/or the emergence of suicide ideation and behavior, whether or not they are taking antidepressant medication and this risk may persist until significant improvement occurs.

It is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which PAXIL is prescribed can also be associated with an increased risk of suicidal behaviour and these conditions may also be co-morbid with MDD.

Additionally, patients with a history of suicidal behaviour or thoughts, young adults, and those patients exhibiting a significant degree of suicidal ideation prior to commencement of

treatment, are at a greater risk of suicidal thoughts or suicide attempts and should receive careful monitoring during treatment.

All patients should be monitored for clinical worsening (including development of new symptoms) and suicidality throughout treatment and especially at the beginning of a course of treatment, or at the time of dose changes, either increases or decreases.

Patients (and caregivers of patients) should be alerted about the need to monitor for any worsening of their condition (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour or thoughts of harming themselves and to seek medical advice immediately if these symptoms present. It should be recognised that the onset of some symptoms, such as agitation, akathisia or mania, could be related either to the underlying disease state or to therapy (see Akathisia and Mania and Bipolar Disorder below; SIDE EFFECTS).

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing PAXIL, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Akathisia:

The use of PAXIL has been associated with the development of akathisia, which is characterised by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment.

Serotonin Syndrome/Neuroleptic Malignant Syndrome:

Development of a serotonin syndrome or neuroleptic malignant syndrome-like events may occur in association with PAXIL treatment, particularly when given in combination with other serotonergic and/or neuroleptic medicines. As these syndromes may result in potentially life-threatening conditions, treatment with PAXIL should be discontinued if such events (characterised by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic

instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated.

PAXIL should not be used in combination with serotonin precursors (such as L-tryptophan, oxitriptan) due to the risk of serotonergic syndrome (see CONTRA-INDICATIONS and INTERACTIONS).

Mania and Bipolar Disorder:

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone can increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Prior to initiating treatment with an antidepressant, patients should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that PAXIL is not approved for use in treating bipolar depression. PAXIL should be used with caution in patients with a history of mania.

Bone fracture:

Epidemiological studies on bone fracture risk following exposure to some antidepressants, including SSRIs such as PAXIL, have reported an association with fractures.

Symptoms seen on discontinuation of paroxetine treatment in adults:

In clinical trials in adults, adverse events seen on treatment discontinuation occurred in 30 % of patients treated with paroxetine compared to 20 % of patients treated with placebo. The occurrence of discontinuation symptoms is not the same as the medicine being addictive or dependence producing as with a substance of abuse.

Dizziness, sensory disturbances (including paraesthesia, electric shock sensations and tinnitus), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea have been reported. Generally these symptoms

are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that PAXIL should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs (see 'Discontinuation of PAXIL', DOSAGE AND DIRECTIONS FOR USE).

Symptoms seen on discontinuation of PAXIL treatment in children and adolescents:

In clinical trials in children and adolescents, adverse events seen on treatment discontinuation occurred in 32 % of patients treated with paroxetine compared to 24 % of patients treated with placebo. Events reported upon discontinuation of paroxetine at a frequency of at least 2 % of patients and which occurred at a rate at least twice that of placebo were: emotional liability (including suicidal ideation, suicide attempt, mood changes and tearfulness), nervousness, dizziness, nausea and abdominal pain (see SIDE EFFECTS).

Haemorrhage:

Skin and mucous membrane bleedings (including gastrointestinal bleeding) have been reported following treatment with PAXIL. PAXIL should therefore be used with caution in patients concomitantly treated with medicines that give an increased risk for bleeding and in patients with a known tendency for bleeding or those with predisposing conditions (see INTERACTIONS).

Risperidone:

Co-administration with risperidone may lead to increased toxicity thereof (see INTERACTIONS).

Cardiac Condition:

Administration of PAXIL to patients with a serious cardiovascular disorder such as (unstable) angina pectoris, poorly monitored cardiac decompensation, ventricular rhythm disorder and acute myocardial infarction, has not been studied and must therefore be avoided. If

antidepressant medication is nevertheless indicated for such patients, PAXIL should be administered with caution.

Epilepsy:

PAXIL should be used with caution in patients with epilepsy.

Seizures:

Seizures may occur in patients treated with PAXIL.

PAXIL should be discontinued in any patient who develops seizures.

Electroconvulsive Therapy (ECT):

There is little clinical experience of the concurrent administration of PAXIL and electro-convulsive therapy.

Glaucoma:

PAXIL infrequently causes mydriasis and should be used with caution in patients with narrow angle glaucoma.

Hyponatraemia:

Hyponatraemia has been reported, predominantly in the elderly. The hyponatraemia generally reverses on discontinuation of PAXIL.

Alcohol:

The concomitant use of PAXIL and alcohol is not advised.

Effects on ability to drive and use machines:

Patients should be cautioned about their ability to drive a car and operate machinery.

INTERACTIONS:

Interactive Effects on PAXIL:

Clinical studies have shown the absorption and pharmacokinetics of PAXIL to be unaffected or only marginally affected (i.e. at a level which warrants no change in dosing regimen) by:

- **food**
- **antacids**

- **digoxin**
- **propranolol**
- **alcohol**: the concomitant use of PAXIL and alcohol is not advised.
- **lithium**: although there is no pharmacokinetic interaction, since there is limited experience in patients, the concurrent administration of PAXIL and lithium should be undertaken with caution.

Medicine metabolising enzymes:

The metabolism and pharmacokinetics of paroxetine may be affected by the induction or inhibition of medicine metabolising enzymes. For example, cimetidine, a known medicine metabolising enzyme inhibitor can increase the bioavailability of PAXIL.

When PAXIL is to be co-administered with a known medicine metabolising enzyme inhibitor (e.g. sodium valproate), consideration should be given to using doses at the lower end of the range.

No initial dosage adjustment is considered necessary when PAXIL is to be co-administered with known medicine metabolising enzyme inducers (e.g. carbamazepine, phenytoin). Any subsequent dosage adjustment should be guided by clinical effect (tolerability and efficacy).

Interactive Effects of PAXIL on Other Medicines:

- Daily administration of PAXIL increases significantly the plasma levels of **procyclidine**. If anti-cholinergic effects are seen, the dose of procyclidine should be reduced.
- **Anticonvulsants:** carbamazepine, phenytoin, sodium valproate. Concomitant administration showed no effect on pharmacokinetic/dynamic profile in epileptic patients.
- **P450 isoenzymes:**

  CYP2D6: Paroxetine inhibits the hepatic cytochrome P450 enzyme CYP2D6. Inhibition of CYP2D6 may lead to increased plasma concentrations of co-administered medicines metabolised by this enzyme. These include certain tricyclic antidepressants (e.g. amitriptyline, nortriptyline, imipramine and desipramine), phenothiazine neuroleptics (e.g.

perphenazine and thioridazine, see CONTRA-INDICATIONS), risperidone, atomoxetine, Type 1c antidysrhythmics (e.g. propafenone and flecainide) and metoprolol.

SSRI Class Interactions:

Co-administration with serotonergic medicines (e.g. MAO inhibitors (see CONTRA-INDICATIONS), L-tryptophan, triptans, tramadol, linezolid, SSRIs, lithium and St. John's Wort - *Hypericum perforatum* preparations) may lead to an incidence of 5HT associated effects (serotonin syndrome: see CONTRA-INDICATIONS, WARNINGS AND SPECIAL PRECAUTIONS and SIDE EFFECTS). The risk of using PAXIL in combination with other CNS active medicines has not been systematically evaluated. Consequently caution is advised if concomitant administration is required.

Pimozide:

Increased pimozide levels have been demonstrated in a study of a single low dose pimozide (2 mg) when co-administered with PAXIL. While the mechanism of this interaction is unknown, due to the narrow therapeutic index of pimozide and its known ability to prolong QT interval, concomitant use of pimozide and PAXIL is contra-indicated (see CONTRA-INDICATIONS).

Anticoagulants/Warfarin:

PAXIL should be administered with great caution to patients receiving oral anticoagulants (see WARNINGS AND SPECIAL PRECAUTIONS).

Preliminary data suggest that there may be a pharmacodynamic interaction between PAXIL and warfarin which may result in increased bleeding in the presence of unaltered prothrombin times/INRs.

PREGNANCY AND LACTATION:

Pregnancy:

PAXIL should not be used during pregnancy (see CONTRA-INDICATIONS).

Recent epidemiological studies of pregnancy outcomes following maternal exposure to antidepressants including PAXIL in pregnancy have reported an increase in risk of congenital

malformations, particularly cardiovascular (e.g. ventricular and atrial septal defects), associated with the use of paroxetine, as contained in PAXIL.

There have been reports of premature birth in pregnant women exposed to paroxetine or other SSRIs. PAXIL should not be used during pregnancy.

Neonates should be observed if maternal use of PAXIL continues into the later stages of pregnancy, because there have been reports of complications in neonates exposed to PAXIL or other SSRIs late in the third trimester of pregnancy. Reported clinical findings have included: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying and somnolence. In some instances the reported symptoms were described as neonatal withdrawal symptoms. In a majority of instances the complications were reported to have arisen either immediately or soon (< 24 hours) after delivery.

Lactation:

Small amounts of paroxetine are excreted into breastmilk. PAXIL should not be used during lactation.

DOSAGE AND DIRECTIONS FOR USE:

It is recommended that PAXIL is administered once daily in the morning with food. The tablet should be swallowed rather than chewed.

Morning dosing with PAXIL does not affect either the quality or duration of sleep. Patients are likely to experience improved sleep as they respond to PAXIL therapy.

Patients should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months for depression and for obsessive compulsive disorder and panic disorder can be even longer.

Depression:

The recommended dose is 20 mg daily. In some patients it may be necessary to increase the dose, which should be done gradually by 10 mg increments to a maximum of 50 mg daily, according to the patient's response.

Safety and efficacy in children under 18 years of age have not been established.

Panic Disorder:

The recommended dose is 40 mg daily. Patients should be started on 10 mg/day and the dose increased weekly in 10 mg increments according to the patient's response. Some patients may benefit from having their dose increased up to a maximum of 60 mg/day.

A low initial starting dose is recommended to minimise the potential worsening of panic symptomatology, which is generally recognised to occur early in the treatment of this disorder.

Obsessive Compulsive Disorder:

The recommended dose is 40 mg daily. Patients should start on 20 mg and the dose can be increased weekly in 10 mg increments. Some patients will benefit from having their dose increased up to a maximum of 60 mg/day.

Social Phobia:

The recommended dose is 20 mg daily. Some patients not responding to a 20 mg dose may benefit from having dose increases in 10 mg increments as required, up to a maximum of 40 mg/day according to the patient’s response.

Generalised Anxiety Disorder:

The recommended dose is 20 mg daily. Some patients not responding to a 20 mg dose may benefit from having dose increments as required, up to a maximum of 50 mg/day according to the patient’s response.

Other Populations:

Elderly:

Increased plasma concentrations of paroxetine occur in elderly subjects, but the range of concentrations overlaps with that observed in younger subjects.

Dosing should commence at the adult starting dose and may be increased gradually by 10 mg increments up to 40 mg daily.

***Children and adolescents (less than 18 years)*:**

PAXIL is not indicated for use in children or adolescents aged less than 18 years (see INDICATIONS and WARNINGS AND SPECIAL PRECAUTIONS).

***Renal/hepatic impairment*:**

Increased plasma concentrations of PAXIL occur in patients with severe renal impairment (creatinine clearance < 30 ml/min) or hepatic impairment. The dosage should be restricted to the lower end of the range.

***Discontinuation of PAXIL*:**

Abrupt discontinuation should generally be avoided (see WARNINGS AND SPECIAL PRECAUTIONS and SIDE EFFECTS). The taper phase regimen used in recent clinical trials involved a decrease in the daily dose by 10 mg/day at weekly intervals. When a daily dose of 20 mg/day was reached, patients were continued on this dose for one week before treatment was stopped. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the medical practitioner may continue decreasing the dose, but at a more gradual rate.

SIDE EFFECTS:

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1 000, < 1 /100), rare (≥ 1/10 000, < 1/1 000), very rare (< 1/10 000), including isolated reports.

Common and uncommon events were generally determined from pooled safety data from a clinical trial population of > 8 000 paroxetine-treated patients and are quoted as excess incidence over placebo.

Clinical Trials:

Blood & lymphatic system disorders:

Uncommon: abnormal bleeding, predominantly of the skin and mucous membranes (mostly ecchymosis but also in the gastrointestinal tract, central nervous system and eye)

Metabolism & nutrition disorders:

Common: decreased appetite

Psychiatric disorders:

Common: somnolence, insomnia, agitation

Uncommon: confusion, hallucinations

Nervous system disorders:

Common: dizziness, tremor

Uncommon: extrapyramidal disorders

Reports of extrapyramidal disorders including oro-facial dystonia have been received in patients sometimes with underlying movement disorders or who were using neuroleptic medication. In addition, akathisia has been rarely reported

Eye disorders:

Common: blurred vision

Respiratory, thoracic and mediastinal disorders:

Common: yawning

Gastrointestinal disorders:

Very common: nausea

Common: constipation, diarrhoea, dry mouth

Skin & subcutaneous tissue disorders:

Common: sweating

Uncommon: skin rashes

Renal & urinary disorders:

Uncommon: urinary retention, urinary incontinence

Reproductive system & breast disorders:

Very common: sexual dysfunction

General disorders & administration site conditions:

Common: asthenia.

Post-marketing Data:

The frequency of the following adverse events are unknown:

Blood & lymphatic system disorders: thrombocytopenia

Immune system disorders: allergic reactions (including urticaria and angioedema)

Endocrine disorders: syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Metabolism and nutritional disorders: hyponatraemia

Hyponatraemia has been reported predominantly in elderly patients and is sometimes due to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Psychiatric disorders: manic reactions

Nervous system disorders*:* convulsions, akathisia, serotonin syndrome (symptoms may include agitation, confusion, diaphoresis, hallucinations, hyperreflexia, myoclonus, shivering tachycardia and tremor)

Eye disorders: acute glaucoma

Gastrointestinal disorders: gastrointestinal bleeding

Hepatobiliary disorders: elevation of hepatic enzymes, hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure).

Post-marketing reports of hepatic events (such as hepatitis, sometimes associated with jaundice, and/or liver failure), which may be fatal, have also been received. Discontinuation of PAXIL should be considered if there is prolonged elevation of liver function test results.

Skin & subcutaneous tissue disorders: photosensitivity reactions

Reproductive system & breast disorders: hyperprolactinaemia/galactorrhoea

General disorders & administration site conditions: peripheral oedema.

Symptoms seen on discontinuation of paroxetine treatment:

Common: dizziness, sensory disturbances, sleep disturbances, anxiety.

Uncommon: agitation, nausea, sweating.

Abrupt discontinuation of PAXIL (particularly when abrupt) may lead to symptoms such as dizziness, sensory disturbances (including paraesthesia, electric shock sensations and tinnitus), sleep disturbances (including intense dreams), insomnia, tremor, confusion, agitation or anxiety, headache, nervousness, vertigo, nausea, diarrhoea and sweating. In the majority of patients, these events are mild to moderate and are self-limiting. No particular patient group appears to be at higher risk of these symptoms; it is therefore advised that when PAXIL treatment is no longer required, gradual discontinuation by dose tapering be carried out (see DOSAGE AND DIRECTIONS FOR USE and WARNINGS AND SPECIAL PRECAUTIONS).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Experience of PAXIL overdosage has indicated that, in addition to those symptoms mentioned under SIDE EFFECTS, vomiting, dilated pupils, fever, blood pressure changes, headache, involuntary muscle contractions, agitation, anxiety and tachycardia have been reported. Events such as coma or ECG changes have occasionally been reported and less frequently a fatal outcome, but generally when PAXIL was taken in conjunction with other psychotropic medicines, with or without alcohol.

No specific antidote is known.

The treatment should consist of those general measures employed in the management of overdose with any antidepressant. Where appropriate, the stomach should be emptied either by the induction of emesis, lavage or both. Following evacuation, 20 to 30 g of activated

charcoal may be administered every 4 to 6 hours during the first 24 hours after ingestion. Supportive care with frequent monitoring of vital signs and careful observation is indicated.

IDENTIFICATION:

A white, film-coated, oval-shaped, biconvex tablet, engraved 20 on one side and a break bar on the other side.

PRESENTATION:

Child-resistant blisters comprised of white, opaque polyvinyl chloride (PVC) backed with aluminium foil laminated with paper, packed in a cardboard carton. Cartons containing 28 tablets packed in blister strips of 14 tablets.

OR

Blister comprised of transparent polyvinyl chloride (PVC) coated with polyvinylidene chloride (PVdC) backed with aluminium (AL) foil, packed in a cardboard carton. Cartons containing 28 tablets packed in blister strips of 14 tablets.

STORAGE INSTRUCTIONS:

PAXIL blister packs should be stored at room temperature (at or below 30 °C).

Keep out of reach of children.

REGISTRATION NUMBER:

A39/1.2/0078

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

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date of registration: 29 July 2005

Date of most recent revision: 6 June 2014

GDS 30+34

Trademarks are owned by or licensed to the GSK group of companies.

© 2022 GSK group of companies or its licensor.