APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S5

PROPRIETARY NAME AND DOSAGE FORM

RECITA 10 mg (Tablet)

RECITA 20 mg (Tablet)

RECITA 40 mg (Tablet)

COMPOSITION

RECITA 10 mg:

Each film-coated tablet contains citalopram hydrobromide corresponding to 10 mg of citalopram.

RECITA 20 mg:

Each film-coated tablet contains citalopram hydrobromide corresponding to 20 mg of citalopram.

RECITA 40 mg:

Each film-coated tablet contains citalopram hydrobromide corresponding to 40 mg of citalopram.

The other ingredients of the formulation include lactose, maize starch, copovidone, croscarmellose sodium, cellulose microcrystalline, and magnesium stearate. **RECITA** is coated with Opadry White which consists of hypromellose, macrogol and titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION

A 1.2 Psychoanaleptics (antidepressants).

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Citalopram is a bicyclic phthalane derivative with antidepressant effect. Its effect is linked to the selective inhibition of specific serotonin (5-HT) reuptake. Citalopram, primarily through its (S)-enantiomer, blocks 5-HT reuptake, leading to potentiation of serotonergic activity in the central nervous system (CNS). Neither citalopram nor its metabolites have an effect on noradrenaline, dopamine and GABA reuptake. Citalopram also has little or no antidopaminergic, antiadrenergic, antiserotonergic, anthistaminergic or anticholinergic properties.

Pharmacokinetic properties:

Oral bioavailability is about 80 % with maximum plasma levels being reached in 4 hours (range 1 to 6 hours). Volume of distribution is about 14 ℓ/kg (range 9 to 17 ℓ/kg). Time to reach steady state concentration is 1 to 2 weeks. Protein binding is about 80 %. Elimination half-life is 36 hours (range 28- 42 hours). Citalopram undergoes hepatic metabolism primarily involving the cytochrome P450 (CYP3A4) and 2C19 (CYP2C19) isoenzymes and to a small extent cytochrome P450 2D6 (CYP2D6) isoenzymes. The metabolites inhibit the reuptake of serotonin, but are less potent than the parent molecule. Citalopram is excreted mainly via the liver with the remainder via the kidneys (approximately 20 % of which 12 % is unchanged medicine). Longer half-lives and decreased clearance due to a reduced rate of metabolism have been demonstrated in the elderly.

INDICATIONS

RECITA is indicated for the treatment of:

- Depression and prevention of relapse
- Panic disorders with or without agoraphobia
- Obsessive-compulsive disorder (OCD)

CONTRA-INDICATIONS

- Hypersensitivity to citalopram or any of the ingredients in the formulation.

- Concurrent use with a monoamine oxidase inhibitor (MAOI). At least 14 days should elapse between discontinuing the MAOI and initiating therapy with **RECITA**. MAOI's should not be introduced for 7 days after discontinuation of **RECITA** (see **INTERACTIONS**).
- Severe renal impairment (creatine clearance less than 30 ml/min).
- Safety and efficacy in pregnancy and lactation has not been established.
- Children under the age of 18 years. (See **WARNINGS AND SPECIAL PRECAUTIONS** and **SIDE-EFFECTS)**
- **RECITA** is contraindicated in patients with congenital long QT syndrome (see **WARNINGS AND SPECIAL PRECAUTIONS**, **SIDE EFFECTS**, and **INTERACTIONS**).
- Concomitant use with products that prolong QT interval.

WARNINGS AND SPECIAL PRECAUTIONS:

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 causal role, however, for antidepressant medicines in inducing such behaviour has not been established. Patients being treated with **RECITA** 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 disorders and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric and non-psychiatric disorders.

The following symptoms have been reported in patients being treated with **RECITA** for major depressive disorders 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 causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing **RECITA**, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patients presenting symptoms.
If the decision is made to discontinue treatment, **RECITA** should be tapered in order to avoid the possibility of a withdrawal syndrome.

RECITA should also be used with caution in:

- Patients suffering from seizures or history thereof - There is an increased risk of seizures. **RECITA** should be used with caution in patients with controlled epilepsy and avoided in patients who are poorly controlled epileptics. Care is advised in patients receiving electroconvulsive therapy.
- Elderly patients — Longer half-life and decreased clearance due to a reduced rate of metabolism. A lower dose is recommended in the elderly.
- Hepatic impairment — Clearance of **RECITA** is reduced. Cautious dosage titration and a lower maximum dose are recommended.
- Renal impairment— Elimination is decreased. If creatine clearance is less than 30 ml/mm **RECITA** should not be used. (See **CONTRA-INDICATIONS**)
- Mania or history of mania — Condition may be re-activated. **RECITA** should be discontinued if the patient enters the manic phase.
- **RECITA** may cause a reduction in heart rate. Caution is advised in patients with a pre-existing slow heart rate.
- Diabetes mellitus - Occurrences of hypoglycaemia have been reported.
- **RECITA** should not be used with monoamine oxidase inhibitors; imipramine; other serotonergic medicines; moclobemide; alcohol; warfarin; and cimetidine (See **INTERACTIONS**).

- Serotonin syndrome is more likely to occur after an increase in dose.
- 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.
- Concomitant administration of pimozide with citalopram has been associated with a mean increase in QTc values compared to when pimozide was given alone.
- A rare but potentially fatal hyperserotonergic state may occur when **RECITA** is co-administered with other drugs that may affect the serotonergic neurotransmitter systems such as linezolid or St. John's Wort.

QT-Prolongation and Torsade de Pointes

RECITA causes dose-dependent QT prolongation and should not be dosed above 40 mg/day. **RECITA** should not be used in patients with congenital long QT syndrome. Hypokalaemia and hypomagnesaemia should be corrected prior to initiation of treatment and periodically monitored. ECG monitoring is recommended in patients with congestive heart failure, bradydysrhythmias, or patients on concomitant medications that prolong the QT interval. Dose escalations over 20 mg/day in CYP2C19 poor metabolisers or patients taking concomitant cimetidine or another CYP2C19 inhibitor is not recommended.

Effects on ability to drive and use machines

RECITA may impair performance of skilled tasks. If affected these patients should not operate machinery or drive.

Lactose

RECITA contains lactose and should not be given to patients with rare hereditary problems or a history of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

INTERACTIONS:

- Monoamine oxidase inhibitors (MAOI) - Concurrent use is contra-indicated. Serious and potentially fatal reactions have occurred such as: hyperthermia, rigidity, myoclonus, autonomic instability with rapid fluctuation of vital signs and mental status changes including extreme agitation progressing to delirium and coma. (See **CONTRA-INDICATIONS**)
- **Imipramine** - An increase in the concentration of desimipramine (the active metabolite of imipramine) may occur. It appears that **RECITA** does not cause a marked increase in plasma levels of some tricyclic antidepressants.
- **Other serotonergic medicines or medicines with serotonergic activity** - Increased risk of developing the serotonin syndrome, a rare but potentially fatal hyperserotonergic state may occur when **RECITA** is co-administered with other drugs that may affect the serotonergic neurotransmitter systems such as linezolid or St. John's Wort.
- **Moclobemide** - Serotonin syndrome has developed after taking highdoses of moclobemide and **RECITA**.
- **Alcohol** - The effects of alcohol may be increased.
- **Warfarin** - The anticoagulant activity of warfarin may be increased.
- **Cimetidine** - The AUC and the maximum plasma concentration of **RECITA** are increased when **RECITA** is administered concurrently with cimetidine.
- **Medicines that prolong the QT Interval** - ECG monitoring is recommended with concomitant medications that have demonstrated prolongation of the QT interval.
- **Pimozide** – concurrent administration of pimozide with citalopram has been associated with a mean increase in QTc values compared to when pimozide was given alone.

PREGNANCY AND LACTATION

Safety and efficacy in pregnancy and lactation has not been established. **RECITA** is excreted into the breast milk.

Effects on neonates

Neonates exposed to citalopram and other selective serotonin reuptake inhibitors (SSRIs) or serotonin–norepinephrine reuptake inhibitors (SNRIs), late in the third trimester, have developed complications requiring prolonged hospitalisation, respiratory support, and tube feeding. Reported clinical findings have included respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn. When treating a pregnant woman with citalopram during the third trimester, the medical practitioner should carefully consider both the potential risks and benefits of treatment.

DOSAGE AND DIRECTIONS FOR USE

Depression

20 mg a day as a single dose. Dosage may be increased by 20 mg a day at intervals of at least one week to a maximum of 40 mg depending on the patient's response.

Panic disorder

10 mg a day as a single dose for the first week then increasing to 20 mg a day. The dose may be increased thereafter as required to a maximum of 40 mg a day depending on the patient's response.

Obsessive compulsive disorder

20 mg a day as a single dose. This dose can be increased by 20 mg increments to a maximum of 40 mg a day depending on the patient's response.

Special populations

Elderly: 10 - 20 mg a day as a single dose. Depending on the patient's response the dose can be increased to a maximum of 20 mg a day.

Reduced hepatic function: Dose should be halved.

Reduced renal function: Dose adjustment is not necessary in cases of mild or moderate renal impairment.

The onset of action is seen within 2 to 4 weeks. Treatment should be continued for an appropriate length of time (up to six months) after recovery in order to prevent relapse. The medicine should be gradually withdrawn during a couple of weeks when stopping therapy (See **SIDE-EFFECTS**)

RECITA may be taken with or without food in the morning or evening.

SIDE EFFECTS:

Immune system disorders:

The following side effects have been reported and frequencies are unknown: Anaphylaxis, angioedema.

Endocrine disorders:

Frequent: Weight changes.

Psychiatric disorders:

Frequent: Sleep disturbances, somnolence.

Less frequent: Hostility, suicidal ideation and self harm have been reported in children, agitation, confusion and mania.

Nervous system disorders:

Less frequent: Paraesthesia, fatigue, serotonin syndrome.

The following side effects have been reported and frequencies are unknown: restlessness, headache, dizziness, impaired concentration, malaise, convulsions, neuroleptic malignant syndrome.

Eye disorders:

The following side effects have been reported and frequencies are unknown: Accommodation disturbances, mydriasis.

Cardiac disorders:

Less frequent: Bradycardia, tremor, QT prolongation, tosades de pointes.

The following side effects have been reported and frequencies are unknown: Palpitations.

Respiratory, thoracic and mediastinal disorders:

The following side effects have been reported and frequencies are unknown: Nasal congestion.

Gastrointestinal disorders:

Frequent: Nausea, dry mouth.

Less frequent: diarrhoea, dyspepsia, salivation.

The following side effects have been reported and frequencies are unknown: constipation.

Hepato-biliary disorders:

The following side effects have been reported and frequencies are unknown: Hepatitis.

Skin and subcutaneous tissue disorders:

Less frequent: Sweating, rash.

Renal and urinary disorders:

Less frequent: Micturition disorders.

Reproductive system and breast disorders:

Frequent: Sexual dysfunction including ejaculation disorder, decreased libido, anorgasmia.

General disorders and administration site conditions:

Less frequent: Yawning, asthenia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

(See **SIDE-EFFECTS**)

Symptoms of overdose:

Tiredness, weakness, sedation, dizziness, tremor, nausea, somnolence and sinus tachycardia.

Treatment of overdose:

Treatment is symptomatic and supportive.

There is no specific antidote to **RECITA.**

The stomach should be emptied as soon as possible by emesis or gastric lavage. Monitoring of cardiac and vital signs is necessary and medical surveillance is advisable for about 24 hours.

IDENTIFICATION

RECITA 10 mg: White coloured, biconvex, round shaped film coated tablets debossed with ‘A’ on one side and ‘05’ on the other side.

RECITA 20 mg: White coloured, biconvex, capsule shaped film coated tablets debossed with ‘A’ on one side and with a score line in between ‘0’ and ‘6’ on the other side.

RECITA 40 mg: White coloured, biconvex, capsule shaped film coated tablets debossed with ‘A’ on one side and with a score line in between ‘0’ and ‘7’ on the other side.

PRESENTATION

RECITA 10 mg:

1. Blisters:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC and Printed Aluminium foil with 7 gsm Heat seal Lacquer. Each blister contains 10 and 14 tablets.

Pack size: 30's & 28's – Each carton contains 3 blisters of 10 tablets and 2 blisters of 14 tablets each.

2. Containers:

Tablets are packed in 40 ml white opaque colour HDPE container of 33 mm neck finish (OFC 51 ml) with a white opaque polypropylene stock ribbed closure with wad having induction sealing liner. The void space of the container is filled with Rayon Coil. Each container contains 30 tablets.

Pack size: 30's - One HDPE container of 30 tablets

RECITA 20 mg:

Tablets are packed in Clear PVC (250 microns) coated with PVdC (60 gsm) as the forming material and aluminium foil (25 microns) as the lidding material. Each blister contains 14 tablets.

Pack size: **28's** – Each carton contains 2 blisters of 14 tablets each.

RECITA 40 mg:

1. Blisters:

Tablets are packed in clear 250 micron PVC film coated with 60 gsm PVdC (width 188 mm) and Printed Aluminium foil with 7 gsm Heat seal Lacquer coating. Each blister contains 10 and 14 tablets.

Pack size: 30's & 28's – Each carton contains 3 blisters of 10 tablets and 2 blisters of 14 tablets each.

2. Containers:

Tablets are packed in 40 ml white opaque colour HDPE container of 33 mm neck finish (OFC 51 ml) with a white opaque polypropylene stock ribbed closure with wad having induction sealing liner. The void space of the container is filled with Rayon Coil. Each container contains 30 tablets.

Pack size: 30's: One HDPE container of 30 tablets.

STORAGE INSTRUCTIONS

Store in a cool, dry place, at or below 25 °C.

Keep the HDPE container well closed. The blister strips must not be removed from the carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER

RECITA 10 mg: 42/1.2/0855

RECITA 20 mg: 42/1.2/0531

RECITA 40 mg: 42/1.2/0856

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

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