APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S5

PROPRIETARY NAME AND DOSAGE FORM

AURO-CITALOPRAM 10 mg (Tablet)

AURO-CITALOPRAM 40 mg (Tablet)

COMPOSITION

AURO-CITALOPRAM 10 mg:

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

AURO-CITALOPRAM 40 mg:

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

PHARMACOLOGICAL CLASSIFICATION

A 1.2 Psychoanaleptics (antidepressants).

PHARMACOLOGICAL ACTION

Citalopram is a bicyclic phthallane 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.

Pharmacokinetics:

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

AURO-CITALOPRAM 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 **AURO-CITALOPRAM**. MAOI's should not be introduced for 7 days after discontinuation of **AURO-CITALOPRAM**. (See **INTERACTIONS**).
- Severe renal impairment (creatine clearance less than 20 ml/min).
- Safety and efficacy in pregnancy and lactation has not been established.
- Children under the age of 18 years. (See **WARNINGS** and **SIDE-EFFECTS AND SPECIAL PRECAUTIONS.)**

WARNINGS

AURO-CITALOPRAM should be used with caution in:

- 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 **AURO-CITALOPRAM** is reduced. Cautious dosage titration and a lower maximum dose are recommended.
- Renal impairment— Elimination is decreased. If creatine clearance is less than 20 ml/min **AURO-CITALOPRAM** should not be used. **(See CONTRA-INDICATIONS)**

- Seizures or history thereof - There is an increased risk of seizures. **AURO-CITALOPRAM** 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.
- Mania or history of mania — Condition may be re-activated. **AURO-CITALOPRAM** should be discontinued if the patient enters the manic phase.
- **AURO-CITALOPRAM** may cause a reduction in heart rate. Caution is advised in patients with a pre-existing slow heart rate.
- Diabetes mellitus - Rare occurrences of hypoglycaemia have been reported.
- **AURO-CITALOPRAM** should not be used with monoamine oxidase inhibitors; imipramine; other serotonergic medicines; moclobemide; alcohol; warfarin; and cimetidine (See **INTERACTIONS**).

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 **AURO-CITALOPRAM** 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 antidepressants 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 **AURO-CITALOPRAM**, 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, **AURO-CITALOPRAM** should be tapered (See **PRECAUTIONS and DOSAGE AND DIRECTIONS FOR USE**).

Safety and efficacy in children under 18 years of age have not been established. (See **CONTRA-INDICATIONS and SIDE-EFFECTS AND SPECIAL PRECAUTIONS**).

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 **AURO-CITALOPRAM** 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.
- **Moclobemide** - Serotonin syndrome has developed after taking overdoses of moclobemide and

  AURO-CITALOPRAM.
- **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 **AURO-CITALOPRAM** are increased when **AURO-CITALOPRAM** is administered concurrently with cimetidine.

PREGNANCY AND LACTATION

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

DOSAGE AND DIRECTIONS FOR USE

<u>Depression</u>

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 60 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 60 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 60 mg a

day depending on the patient's response.

Special Populations

Elderly: 20 mg a day as a single dose. Depending on the patient's response the dose can be increased to a maximum of 30 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 AND SPECIAL PRECAUTIONS)**

AURO-CITALOPRAM may be taken with or without food in the morning or evening.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side Effects:

Cardiac disorders:

Frequent: Palpitations, tremor

Less frequent: Bradycardia

Nervous system disorders:

Frequent: Sleep disturbances, paraesthesia, restlessness, somnolence, headache, dizziness, fatigue.

Less frequent: Agitation, confusion, impaired concentration, malaise, mania, convulsions, serotonin syndrome, neuroleptic malignant syndrome

Endocrine disorders:

Frequent: Weight changes.

Gastrointestinal disorders:

Frequent: Nausea, constipation, diarrhoea, dyspepsia, dry mouth.

Less frequent: Salivation.

Renal and urinary disorders:

Frequent: Micturition disorders.

Reproductive system and breast disorders:

Less frequent: Sexual dysfunction including ejaculation disorder, decreased libido, anorgasmia

Hepato-biliary disorders:

Less frequent: Hepatitis.

Musculoskeletal, connective tissue and bone disorders:

Frequent: Asthenia.

Eye disorders:

Frequent: Accommodation disturbances.

Less frequent: Mydriasis.

Respiratory, thoracic and mediastinal disorders:

Less frequent: Nasal congestion.

Skin and subcutaneous tissue disorders:

Frequent: Sweating.

Less frequent: Rash.

Other:

Less frequent: Yawning.

Hostility, suicidal ideation and self harm have been reported in children.

Special Precautions

- Patients should be monitored during early therapy until improvement in depression is observed because suicide is an inherent risk in depressed patients.
- **AURO-CITALOPRAM** may impair performance of skilled tasks. If affected these patients should not operate machinery or drive.
- Serotonin syndrome is more likely to occur after an increase in dose.
- If therapy with **AURO-CITALOPRAM** is to be discontinued, it is recommended that the dose is decreased gradually in order to prevent the possibility of a withdrawal syndrome.
- Avoid alcohol. (See **INTERACTIONS**).
- 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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

(See **SIDE-EFFECTS AND SPECIAL PRECAUTIONS**)

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 **AURO-CITALOPRAM.**

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

AURO-CITALOPRAM 10 mg: White coloured, biconvex, round shaped, film coated tablets debossed with 'A' on one side and '05' on the other side.

AURO-CITALOPRAM 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

AURO-CITALOPRAM 10 mg:

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.

Tablets are packed in 40 ml white opaque HDPE container of 38 mm neck finish (OFC 51 ml) with 38 mm - 400 RS white opaque closure with induction seal wad. 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

AURO-CITALOPRAM 40 mg:

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.

Tablets are packed in 40 ml white opaque HDPE container of 33 mm neck finish (OFC 51 ml) with 33 mm-400 RS white opaque closure with induction seal wad. 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. Do not remove the blister strip from the carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER

AURO-CITALOPRAM 10 mg: 42/1.2/0850

AURO-CITALOPRAM 40 mg: 42/1.2/0851

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

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