PACKAGE INSERT OF ACTI-LIFT

SCHEDULING STATUS:

S5

PROPRIETARY NAME AND DOSAGE FORM:

ACTI-LIFT 20 mg

COMPOSITION:

Each film coated tablet contains citalopram hydrobromide equivalent to citalopram 20 mg.

ACTI-LIFT also contains 114.5 mg of lactose monohydrate per tablet.

PHARMACOLOGICAL CLASSIFICATION:

A 1.2 Psychoanaleptics (antidepressants)

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

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 has little or no antidopaminergic, antiadrenergic, antiserotonergic, antihistaminergic 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 also 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 has been demonstrated in the elderly.

INDICATIONS:

ACTI-LIFT is indicated for the treatment of:-

- Depression and prevention of relapse
- Panic disorder 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 **ACTI-LIFT.**

  MAOIs should not be introduced for 7 days after discontinuation of **ACTI-LIFT** (see **INTERACTIONS**).

- Severe renal impairment (creatinine 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:

ACTI-LIFT 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 **ACTI-LIFT** 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 **ACTI-LIFT** should not be used (see **CONTRA-INDICATIONS**).
- Seizures or history thereof – There is an increased risk of seizures. **ACTI-LIFT** should be used with caution in patients with controlled epilepsy and be avoided in patients with poorly controlled epilepsy. Care is advised in patients receiving electroconvulsive therapy.
- Mania or history of mania – Condition may be re-activated. **ACTI-LIFT** should be discontinued if the patient enters the manic phase.
- **ACTI-LIFT** may cause a reduction in heart rate. Caution is advised in patients with pre-existing slow heart rates.
- Diabetes mellitus – Rare occurrences of hypoglycaemia have been reported.
- **ACTI-LIFT** should not be used with monoamine oxidase inhibitors; imipramine; other serotonergic medicines; moclobemide; alcohol; warfarin; and cimetidine (see **INTERACTIONS**).

- Risk of serotonin syndrome, a rare but potentially fatal hyperserotogenic state, if combined with other serotonergic medicines (see **INTERACTIONS**).

Patients with major depressive disorder 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 behavior has not been established. Patients being treated with **ACTI-LIFT** should, nevertheless, be observed closely for clinical worsening and suicidality, especially at the beginning of a course of therapy, or at anytime 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 disorder should be observed when treating patients with other psychiatric disorders and non-psychiatric disorders.

The following symptoms have been reported in patients being treated with antidepressants such as **ACTI-LIFT** 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 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 **ACTI-LIFT**, 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 with **ACTI-LIFT**, it is recommended that the dose should be decreased gradually to prevent the possibility of withdrawal symptoms (see **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 **ACTI-LIFT** 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 moclobemide and **ACTI-LIFT.**
- **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 **ACTI-LIFT** are increased when **ACTI-LIFT** is administered concurrently with cimetidine.

PREGNANCY AND LACTATION:

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

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 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.

If the decision is made to discontinue treatment with **ACTI-LIFT**, it is recommended that the dose should be decreased gradually to prevent possibility of withdrawal symptoms (see **WARNINGS**).

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.

ACTI-LIFT 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, headache, dizziness, fatigue, somnolence.

Less frequent

Agitation, confusion, impaired concentration, malaise, mania, convulsions, serotonin syndrome, neuroleptic malignant syndrome, akathisia, impulsivity, aggressiveness, anxiety, panic attacks, insomnia, irritability, hypomania.

Metabolism and Nutrition disorders:

Frequent

Weight changes

Gastrointestinal disorders:

Frequent

Nausea, constipation, diarrhea, dyspepsia, dry mouth

Less frequent

Salivation

Renal and Urinary disorders:

Frequent

Micturition 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 disorders:

Frequent

Sweating

Less frequent

Rash

General disorders and administration site conditions:

Less frequent

Yawning, hostility, suicidal ideation and self-harm.

Special Precautions:

- Patients should be monitored during early therapy until improvement in depression is observed because suicide is an inherent risk in depressed patients.
- Serotonin syndrome is more likely to occur after an increase in dose.

- If therapy with **ACTI-LIFT** 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.

Effect on the ability to drive and use machines:

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

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 **ACTI-LIFT.**

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

IDENTIFICATION:

Pink, oval shaped, biconvex tablets with "G" engraved on one side and "11" on the other side of the bisect on one face of the tablet and other face of the tablet being engraved with"20".

PRESENTATION:

Glenmark – Citalopram Tablets are packed in white opaque HDPE bottles containing 100 and 500 tablets.

STORAGE INSTRUCTIONS:

Store in tightly closed container, at or below 25 °C

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

41/1.2/0297

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

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Centurion

0157

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