Selegiline Hydrochloride Capsules

**INDICATIONS AND USAGE**

Selegiline is a non-selective MAO inhibitor. It is used to treat Parkinson's disease by delaying the deterioration of symptoms. It is also used in the prophylaxis of depression in patients with a history of recurrent depressive episodes. Selegiline is not a selective MAO inhibitor, but its action on MAO is selective, due to the presence of a phenelzine metabolite, MAO-B. Selegiline is available as 5 mg and 10 mg capsules.

**CONTRAINDICATIONS**

Selegiline should not be used in patients with a history of seizures, cardiovascular disease, or certain other medical conditions. Selegiline should also be used with caution in patients with a history of antidepressant use.

**WARNINGS**

Selegiline should be prescribed only by physicians who are familiar with the treatment of patients with Parkinson's disease. Selegiline should be discontinued if the patient experiences an increase in the severity of any symptoms, such as tremors, rigidity, or dyskinesia. Selegiline should be used with caution in patients with a history of ulcer disease.

**SIDE EFFECTS**

Selegiline may cause serious side effects, including cardiovascular problems, cerebrovascular accidents, and gastrointestinal problems. Selegiline may also cause a number of less serious side effects, including changes in heart rate, blood pressure, and blood laboratory tests.

**PHARMACOKINETICS**

Selegiline is rapidly absorbed after oral administration. The peak plasma concentration occurs within 1 to 2 hours. The plasma half-life of selegiline is approximately 8 hours. The oral bioavailability of selegiline is approximately 70%.

**DOSE AND ADMINISTRATION**

Selegiline is usually administered once or twice daily. The starting dose is 5 mg daily, and the dose may be increased by 5 mg daily every 2 weeks. The maximum recommended dose is 40 mg daily. Selegiline should be taken at the same time each day, preferably with or after a meal.

**HOW SUPPLIED**

Selegiline is supplied as 5 mg and 10 mg capsules. Each capsule contains selegiline hydrochloride, USP, as selegiline hydrochloride. Each capsule also contains the following inactive ingredients: lactose NF, citric acid anhydrous USP, microcrystalline cellulose NF, D&C Blue #1, FD&C Blue #1, and titanium dioxide. The capsule shell contains gelatin NF, FD&C Blue #1, FD&C Red #40, and FD&C Yellow #6.
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**INCIDENT OF TREATMENT-EMERGENT ADVERSE EXPERIENCES IN THE PLACEBO-CONTROLLED CLINICAL TRIAL**

<table>
<thead>
<tr>
<th>Incidence (Placebo)</th>
<th>N = 1250</th>
<th>Incidence (Selegiline) N = 1250</th>
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<tbody>
<tr>
<td>Nausea</td>
<td>14 (11%)</td>
<td>12 (9%)</td>
</tr>
<tr>
<td>Dizziness/Lightheadedness</td>
<td>7 (6%)</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>4 (3%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Confusion</td>
<td>3 (2%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Dyskinesia</td>
<td>2 (2%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (3%)</td>
<td>4 (3%)</td>
</tr>
</tbody>
</table>

**The following events were reported in either or both groups:**

- Ache: generalized
- Anorexia
- Tension
- Asthenia
- Dizziness
- Hair Loss
- Insomnia
- Lethargy
- Leg pain
- Hyperacusis
- Malaise
- Fatigue
- Unrelated

**All** in prospectively monitored clinical investigations, enrolling approximately 920 patients, the following adverse events, classified by body system, were reported:

**Central Nervous System**

- Motor/Coordination/Extrapyramidal: increased tremor, chorea, loss of balance, restlessness, blepharospasm, increased bradykinesia, facioglabellar movements, falling down, heavy leg, muscle twitch*, myoclonic jerks*, stiff neck, tardy dystonias, dystonic symptoms, dyskinesia, involuntary movements, freezing, festination, increased apraxia, muscle cramps.

**Mental Status/Behavior/Psychiatric:** hallucinations, dizziness, confusion, anxiety, depression, disorientation, lightheadedness, impared memory*, increased energy*, transient* high*, hallucinations, lethargy, malaise, apathy, oversedation*, vertigo, personality change, sleep disturbance, restlessness, weakness, transient irritability.

**Pain/Altered Sensation:** headache, back pain, leg pain, tinnitus, migraine, suralparesthesia, pain, breast burning, generalized ache, chills, numbness of legs/fingers, taste disturbance.

**Autonomic Nervous System:** dry mouth, hyperhidrosis, sexual dysfunction.

**Cardiovascular:** orthostatic hypertension, hypotension, arrhythmia, palpitations, new or increased angina pectoris, chest pain, syncope, hypertension, tachycardia, peripheral edema, sinus bradycardia, syncope.

**Gastrointestinal:** nausea, vomiting, constipation, weight loss, anorexia, poor appetite, dysphagia, diarrhea, heartburn, rectal bleeding, bruising*, gastrointestinal bleeding (exacerbation of preexisting ulcers).

**Genitourinary/Gynecologic/Endocrine:** slow urination, transient anorgasmia*, nocturia, prostate hypertrophy, urinary hesitancy, urinary retention, decreased penile sensation*, urinary frequency.

**Skin and Appendages:** increased sweating, diaphoresis, facial hair, hair loss, hirsutism, rash, photosensitivity.

**Miscellaneous:** asthma, diplopia, shortness of breath, speech affected.

**Postmarketing Reports:**

The following experiences were described in spontaneous postmarketing reports. These reports do not provide sufficient information to establish a clear causal relationship with the use of selegiline.

** CNS**

Seizure in a drowsy chronic renal failure patient on concomitant medications.

*indicates events reported only at doses greater than 10 mg/day.

**OVERDOSAGE**

Selegiline

No specific information is available about clinically significant overdoses of selegiline. However, experience gained during selegiline’s development reveals that some individuals exposed to doses of 600 mg of d-selegiline suffered severe hypotension and psychomotor agitation. The selective inhibition of MAO B by selegiline hydrochloride is achieved only at doses in the range recommended for the treatment of Parkinson’s disease (e.g., 10 mg/day). Overdoses are likely to cause significant inhibition of both MAO A and B. Consequently, the signs and symptoms of overdose may resemble those observed with non-selective MAO inhibitors (e.g., tranylcypromine, isocarboxazid, and phenelzine).

**Overdose with Non-Selective MAO Inhibition**

NOTE: This section is provided in order to describe events that have actually been observed with selegiline in overdose.

Characteristically, signs and symptoms of non-selective MAOI overdoses may not appear immediately. Delays of up to 12 hours between ingestion of drug and the appearance of signs may occur. Importantly, the peak intensity of the syndrome may not be reached for upwards of a day following the overdose. Death has been reported following overdosage. Therefore, immediate hospitalization, with continuous patient observation and monitoring for a period of at least two days following the ingestion of such drugs in overdose, is strongly recommended.

The clinical picture of MAOI overdose varies considerably; its severity may be a function of the amount of drug consumed. The central nervous and cardiovascular systems are prominently involved.

Signs and symptoms of overdose may include, alone or in combination, any of the following: drowsiness, dizziness, faintness, irritability, hyperventilation, hypotension, severe headache, hallucinations, tremors, insomnia, convulsions, and coma; rapid, shallow, irregular respiration, convulsions, cardiovascular collapse. Further management of respiratory depression and hyperpyrexia, hypotension, and cardiovascular collapse: (e.g., 10 mg/day), overdoses are likely to cause significant hypotension, hypertension and vascular collapse; convulsions, respiratory depression and hyperpyrexia, hypotension, and cardiovascular collapse.

**TREATMENT SUGGESTIONS FOR OVERDOSE**

**NOTE:** Because there is no recorded experience with selegiline overdose, the following suggestions are offered based upon the assumption that selegiline overdose may be modeled by non-selective MAOI poisoning. In any case, up-to-date information about the treatment of overdose can be obtained through contacting the certified Regional Poison Control Center. Telephone numbers of certified Poison Control Centers are listed in the Physicians’ Desk Reference (PDR).

Treatment of overdose with non-selective MAOIs is symptomatic and supportive. Induction of emesis or gastric lavage with instillation of charcoal slurry may be helpful in early poisoning, provided the airway has been protected against aspiration. Signs and symptoms of central nervous system stimulation, including convulsions, should be treated with diazepam, given slowly intravenously. Phenolamine derivatives and central nervous system stimulants should be avoided. Hypotension and vascular collapse should be treated with intravenous fluids and, if necessary, pressor agents. Convulsions should be treated with intravenous infusion of a dilute pressor agent. It should be noted that adrenergic agents may produce a markedly increased intracranial pressure.

Respiration should be supported by appropriate measures, including management of the airway, use of supplemental oxygen, and mechanical ventilatory assistance, as required.

Body temperature should be monitored closely. Intensive management of hyperpyrexia may be required. Maintenance of fluid and electrolyte balance is essential.

**DOSAGE AND ADMINISTRATION**

Selegiline hydrochloride capsules are intended for administration to Parkinsonian patients receiving levodopa/carbidopa therapy who demonstrate a deteriorating response to this treatment. The recommended regimen for the administration of selegiline hydrochloride is 10 mg per day administered as divided doses of 5 mg each taken at breakfast and lunch. There is no evidence that additional benefit will be obtained from the administration of higher doses. Moreover, higher doses should ordinarily be avoided because of the increased risk of side effects.

After two to three days of selegiline treatment, an attempt was made to reduce the dose of levodopa/carbidopa. A reduction of 10 to 30% was achieved with the typical participant in the domestic placebo controlled trials who was assigned to selegiline treatment. Further reductions of levodopa/carbidopa may be possible during continued selegiline therapy.

**HOW SUPPLIED**

Selegiline Hydrochloride Capsules are available containing 5 mg of selegiline hydrochloride. Each capsule consists of a white opaque body and an aqua blue opaque cap, printed ‘APO 505’ in black ink.

They are available as:

NDC 65055-0051-1 bottles of 60 capsules.
NDC 65055-0052-1 bottles of 50 capsules
NDC 65055-0052-10 bottles of 100 capsules

**STORAGE**

Store at controlled room temperature 15° - 30°C (59° - 86°F).

**TOLLPHARM**

SELEGINLE HYDROCHLORIDE CAPSULES 5 MG

Manufactured for:

Teijin Pharma

Manufactured by:

Apotex Corp.

Elinkho, Ontario

Canada M9W 6Y3

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