Carbidopa and Levodopa Extended-Release Tablets 25 mg/100 mg and 50 mg/200 mg

SECTION 1 – PRODUCT AND COMPANY IDENTIFICATION

Product Name: Carbidopa and Levodopa Extended-Release Tablets
25 mg/100 mg and 50 mg/200 mg

Marketing Authorisation Holder
Accord Healthcare, Inc.,
1009 Slater Road,
Suite 210-B,
Durham, NC 27703, USA.
Telephone: 1-919-941-7878
Fax- 1-919-941-7881

Manufacturer
Intas Pharmaceuticals Ltd.
Plot No. 457, 458
Village-Matoda,
Bavla Road, Ta. Sanand,
Dist. Ahmedabad-382 210,
Gujarat, India

US Emergency Phone: Call CHEMTREC Day or Night: 1-800-424-9300

SECTION 2 – COMPOSITION, INFORMATION ON INGREDIENTS

Active: Carbidopa and Levodopa

Inactive: Microcrystalline cellulose, lactose monohydrate, hydroxypropyl methyl cellulose, hypromellose, colloidal anhydrous silica, magnesium stearate, ferric oxide red and ferric oxide yellow.

SECTION 3 - HAZARDS IDENTIFICATION

Emergency Overview: Irritant

Adverse Effects: Nausea; vomiting; agitation; confusion; hallucinations; unusual or uncontrolled movements of the body (including face, tongue, arms, hands, and upper body); clumsiness or unsteadiness; dizziness; difficulty swallowing; increased blinking or spasms of the eyelids; excessive watering of mouth; unusual tiredness or weakness; numbness; visual disturbances; irregular heartbeat; hot flashes; dilated pupils; mood or mental changes; skin rash; difficulty opening mouth; unusual weight gain or loss; loss of bladder control; difficulty urinating; abdominal pain; loss of appetite; dry mouth; gas; nightmares; constipation; diarrhea; flushing; headache; hiccups; increased sweating; trouble sleeping; changes in taste; burning of the tongue; and darkening of urine, saliva, or sweat.
Overdose Effects: Overdose effects may include some of the adverse effects listed above; such as confusion, agitation, unusual or uncontrolled body movements, trouble sleeping, nausea or vomiting, fast heartbeat, restlessness, change in blood pressure, and increased blinking or spasms of the eyelids.

Acute: Eye, skin, gastrointestinal and/or respiratory tract irritation.

Chronic: Eye, skin, gastrointestinal and/or respiratory tract irritation.

Medical Conditions Aggravated by Exposure: Hypersensitivity to material, lung or cardiovascular disease or disorders; previous heart attack; history of melanoma or undiagnosed skin lesions; peptic ulcer; psychotic disorders (including depression); liver or endocrine disease; impaired kidney function; and narrow angle, angle-closure, or open-angle glaucoma.

Cross Sensitivity: Not Found

Target Organs: Central nervous system, cardiovascular system.

SECTION 4 - EMERGENCY & FIRST AID MEASURES

Inhalation: Causes irritation. Avoid inhalation. Remove to fresh air.

Eye: Causes irritation. Avoid contact. Flush with copious quantities of water for at least 15 minutes.

Skin: Causes irritation. Avoid contact. Flush with copious quantities of soap and water.

Ingestion: May cause irritation, toxicity, and burning or bitter taste. Flush out mouth with water. This material is rapidly absorbed from the gastrointestinal tract.

General First Aid Procedures: Remove from exposure. Remove contaminated clothing. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. If person is not breathing give artificial respiration. If breathing is difficult give oxygen. Obtain medical attention.
Note to Physicians

**Overdose Treatment:** Treatment of statin overdose should be symptomatic and supportive and may include the following:

1. Perform gastric lavage soon after ingestion (within one hour). Protect airway by placement in Trendelenburg and left lateral decubitus position or by endotracheal intubation. Control any seizures first.
2. Administer activated charcoal as a slurry.
3. For dystonias and dyskinetic movements, administer deanol and/or pyridoxine.
4. Hypertension is generally transient and followed by hypotension. For severe or symptomatic hypertension, treat cautiously with nitroprusside and phentolamine, as needed.
5. For hypotension, infuse isotonic fluid. If hypotension persists, administer dopamine or norepinephrine.
7. The value of dialysis in treatment of overdose is unknown. [Meditext 2007 and USP DI 2007]

**SECTION 5 - FIRE FIGHTING MEASURES**

**Extinguisher Media:** Water spray, dry chemical, carbon dioxide, or foam as appropriate for surrounding fire and materials.

**Fire and Explosion Hazards:** This material is assumed to be combustible. As with all dry powders, it is advisable to ground mechanical equipment in contact with dry material to dissipate the potential buildup of static electricity.

**Firefighting Procedures:** As with all fires, evacuate personnel to a safe area. Firefighters should use self-contained breathing equipment and protective clothing.

**SECTION 6 - ACCIDENTAL RELEASE MEASURES**

**Spill Response:** Wear approved respiratory protection, chemically compatible gloves, and protective clothing. Wipe up spillage or collect spillage using a high-efficiency vacuum cleaner. Avoid breathing dust. Place spillage in appropriately labeled container for disposal. Wash spill site.
SECTION 7 - HANDLING AND STORAGE

Handling: Avoid all contact and inhalation of dust, mists, and/or vapours associated with the material. Wash thoroughly after handling.

Storage: Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F)

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Engineering Controls: Engineering controls such as exhaust ventilation are recommended.

Respiratory Protection: Use a NIOSH-approved respirator, if it is determined to be necessary by an industrial hygiene survey involving air monitoring. In the event that a respirator is not required, an approved dust mask should be used.

Gloves: Chemically compatible.

Eye Protection: Safety glasses or goggles.

Protective Clothing: Protect exposed skin.

Exposure Limits: Not found.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Description of Tablets:

The 25 mg/100 mg tablets are peach to light peach coloured with mosaic appearance, oval shaped, biconvex tablets, debossed with ‘L100’ on one side and plain on other.

The 50 mg/200 mg tablets are peach to light peach coloured with mosaic appearance, oval shaped, biconvex tablets, debossed with ‘L200’ on one side and breakline on other.

SECTION 10 - STABILITY AND REACTIVITY

Stability: The product is stable

Conditions to Avoid: Heat and light.
Incompatibilities: Oxidizing agents and alkaline solutions.

Polymerization: No

SECTION 11 - TOXICOLOGY INFORMATION

Oral Rat: For Carbidopa: LD50: 4810 mg/kg
For Levodopa: LD50: 1780 mg/kg

Oral Mouse: For Carbidopa: LD50: 1750 mg/kg
For Levodopa: LD50: 2363 mg/kg

Other Toxicity Data: Oral Rabbit LD50: 609 mg/kg (For Levodopa),
Not found (For Carbidopa)

Irritancy Data: Eye/Rabbit: mild; Skin/Rabbit: non-irritating (For Levodopa),
Not found (For Carbidopa)

Listed as a Carcinogen by: NTP: No IARC: No OSHA: No

Other Carcinogenicity Data: No

Mutagenicity Data:

Carbidopa was positive for mutagenicity in the Ames S. typhimurium test, with and without metabolic activation. It was negative for unscheduled DNA synthesis in rat hepatocyte, without metabolic activation.

Levodopa was positive mutagenicity test with Chinese hamster cells; positive Ames tests with Salmonella typhimurium strains TA104 with and without activation and TA100 with activation; negative Ames test with Salmonella typhimurium strain TA100 without activation.

Reproductive and Developmental Effects:

For Carbidopa: Offspring of pregnant rats given oral doses of 100 mg/kg carbidopa had an increased frequency of hemorrhages in their brown adipose tissue.

For Levodopa: Reproduction studies in rodents have shown that levodopa, when given in doses in excess of 200 mg/kg of body weight per day, depresses fetal and postnatal growth and viability. At doses of 125 and 250 mg/kg, levodopa caused malformations of the circulatory system in rabbits. Early postnatal loss occurred in rats administered levodopa during pregnancy at a dose of 10 mg/kg/day, and fetal stunting occurred in mice given doses up to 500mg/kg/day.
SECTION 12 - ENVIRONMENTAL IMPACT INFORMATION

Ecological Information:

Levodopa: This material is barely toxic for fish, strongly toxic for algae, and barely toxic for planktonic crustaceans.

Carbidopa: Daphnia magna LC50: 35.3 mg/L.

SECTION 13 - DISPOSAL INFORMATION

Waste must be disposed of in accordance with state, local and other environmental control regulations.

SECTION 14 - TRANSPORTATION INFORMATION

This product is not subject to the regulations for the safe transport of hazardous chemicals.

DOT: Not regulated
TDG: Not regulated
IATA: Not regulated
IMDG: Not regulated

SECTION 15 - REGULATORY INFORMATION

U.S. Regulatory Information:
For Carbidopa: Not found.
For Levodopa: California Proposition 65: Developmental Toxicity

International Regulatory Information:
For Carbidopa: Not found
For Levodopa: Hazard Code: Xn
SECTION 16 - OTHER DATA

The information above is believed to be accurate and represents the best information currently available to us. However, we make no warranty of merchantability or any other warranty, express or implied, with respect to such information, and we assume no liability resulting from its use. Users should make their own investigations to determine the suitability of the information for their particular purposes. In no event shall INTAS be liable for any claims, losses, or damages of any third party or for lost profits or any special, indirect, incidental, consequential or exemplary damages, howsoever arising, even if INTAS has been advised of the possibility of such damages.