BETAHISTINE HYDROCHLORIDE

EXIGO® 8 mg, 16 mg, 24 mg Tablet
Anti-Vertigo

FORMULATION
Each tablet contains:
Betahistine hydrochloride..... 8 mg, 16 mg or 24 mg

PRODUCT DESCRIPTIONS
Betahistine 8 mg is an off-white tablet, round, flat tablet, bisected on one side and plain on the other.

Betahistine 16 mg is an off-white tablet, round, biconvex, bisected on one side and plain on the other.

Betahistine 24 mg is an off-white tablet, round, flat tablet, bisected on one side and plain on the other.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS
The exact mechanism of action of betahistine is unclear. However, animal studies have shown that betahistine improves blood flow in the striae vascularis of the inner ear, resulting in reduced endolymphatic pressure.

Pharmacologic evaluation showed that betahistine may exert weak H_1 receptor agonistic activity and H_3 antagonistic properties in the central and autonomic nervous systems. Betahistine also appears to inhibit spike generation of neurons in the lateral and medial vestibular nuclei in a dose-dependent manner.

PHARMACOKINETICS
Betahistine is rapidly and completely absorbed after oral administration. It is rapidly and almost completely metabolized into 2-pyridylacetic acid (2-PAA), its main metabolite which has no pharmacological activity. Since plasma betahistine levels are very low, pharmacokinetic analyses are therefore based on 2-PAA measurements in plasma and urine. Peak plasma concentrations of 2-PAA achieved one hour after oral administration in fasting subjects and declines with a half-life of about 3.5 hours. Tissue distribution of betahistine in humans is unknown. The drug has little or no binding to either serum albumin, or other plasma proteins.

It is not known to what extent the drug crosses the placenta. The effects of hepatic and renal disease on the kinetics of betahistine are unknown.

Betahistine is eliminated in the kidney with 85 to 90% of the radioactivity of an 8 mg dose appearing in the urine over 56 hours. The maximum rates of excretion are reached within 2 hours of administration. The drug is excreted in the urine as 2-PAA with no unchanged betahistine being detected

INDICATIONS
- For the treatment of vertigo, tinnitus and hearing loss associated with Meniere's syndrome.
- For the symptomatic treatment of vertigo of peripheral origin.

DOSAGE AND ADMINISTRATION
Orally, to be taken preferably with meals.

Recommended Initial Dose: 8 to 16 mg given three times a day; OR 24 mg given two times a day
Maintenance Dose: 24 to 48 mg per day given in divided doses
Maximum dose: 48 mg per day

- Individualize dosage according to patient's response and tolerance.
- Re-assess patient periodically to determine the need for maintenance treatment with an appropriate dose.
  Or, as prescribed by a physician.

CONTRAINDICATIONS
- Hypersensitivity to betahistine or any component of the product.
- Patients with pheochromocytoma since betahistine, a synthetic histamine analog, may provoke release of epinephrine and/or norepinephrine from the tumor, precipitating a hypertensive crisis.
- Active peptic ulcer or a history of this condition

WARNINGS AND PRECAUTIONS
Use with caution in patients with the following conditions:
- Bronchial asthma and COPD with bronchospastic component
- History of allergic skin conditions
- Porphyria

Avoid concurrent use with antihistamines. (see ***Drug Interactions***)
Mild gastrointestinal irritation may be expected with betahistine. Patients should be advised to take the drug with food. Otherwise, dose may be reduced.

INTERACTIONS WITH OTHER MEDICAMENTS
There have been no reports of potentially hazardous interactions with other drugs.

No *in vivo* studies have been performed. *In vitro* data revealed no inhibition of cytochrome P450 enzymes.

In vitro data showed an inhibition of betahistine metabolism by drugs that inhibit monoamine-oxidase (MAO) including MAO subtype B (e.g., Selegiline). Caution is recommended when using betahistine and MAO inhibitors (including MAO-B selective) concomitantly.

Although antagonism between betahistine and antihistamines may be expected theoretically, no such interactions have been reported.

The effects of $Beta_2$ agonists may be decreased by betahistine.

There is a case report of potentiation of betahistine with salbutamol and a case report of interaction with ethanol and maloprim.

STATEMENT ON USAGE FOR HIGH RISK GROUPS
Pregnancy
Clinical data regarding the safe use of betahistine during pregnancy are unavailable. Betahistine should not be used during pregnancy unless clearly necessary.
Lactation
It is not known whether betahistine is excreted in human breast milk. The benefits of the drug to the mother should be weighed against the potential risk to the baby when considering betahistine treatment.
Children
The safety and efficacy of betahistine in pediatric patients less than 18 years old have not been established.
Geriatric
There is no special precaution required for treatment of the elderly; therefore, the same dosage as in the general population may be used.
Effect on Ability to Drive and Use Machines
Betahistine does not affect driving or psychomotor ability.

UNDESIRABLE EFFECTS
In general, betahistine is well tolerated. However, a few adverse effects associated with the drug have been reported:
Gastrointestinal: Vomiting, diarrhea, gastrointestinal pain, nausea, dyspepsia, abdominal cramps, abdominal distention, bloating
Body as a Whole: Tiredness, malaise
CNS: Dizziness, headache, drowsiness, insomnia, and throbbing pulsation; rarely, convulsions, somnolence, confusions, hallucinations
Skin and Subcutaneous Tissue Disorders: Angioneurotic edema, rash, pruritus, and urticaria; Stevens Johnson syndrome
Cardiovascular: Vasodilation, postural hypotension, tachycardia, and ventricular extrasystoles
Respiratory: Dyspnea, asthma, bronchospasms
Immune System: Rare cases of hypersensitivity reactions such as anaphylaxis

OVERDOSAGE & MANAGEMENT
Few cases of overdose have been reported with some patients experiencing mild to moderate symptoms with doses above 200 mg. Clinical features of betahistine overdose may include nausea, dry mouth, vomiting, dyspepsia, abdominal pain, headache, somnolence, hypotension, itching; convulsion, pulmonary or cardiac complications, ataxia, and seizures at higher doses. A case of convulsion was reported at a dose of 728 mg.

There is no specific antidote to betahistine overdose; gastric lavage and symptomatic treatment are recommended.

Store at temperatures not exceeding 30°C.

Caution: Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY
Betahistine hydrochloride (Exigo) 8 mg Tablet - Box of 30 Tablets (in flex foil)
Betahistine hydrochloride (Exigo) 16 mg Tablet - Box of 30 Tablets (in flex foil)
**Betahistine hydrochloride (Exigo) 24 mg Tablet - Box of 30 Tablets (in flex foil)

Manufactured by Amherst Laboratories, Inc.
UNILAB Pharma Campus, Barangay Mamplasan
Biñan, Laguna, Philippines
for UNILAB, Inc.
No. 66 United Street, Mandaluyong City, Metro Manila, Philippines

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