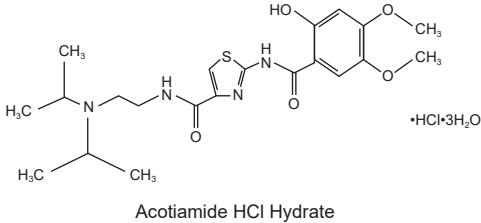


Acogest™

(Acotiamide HCl Hydrate)
Film-coated Tablets 100mg

DESCRIPTION

Acogest contains Acotiamide HCl Hydrate, a drug for functional gastrointestinal disorders. The chemical name of Acotiamide is N- [2- [Bis (1-methylethyl) amino] ethyl] - 2 - [(2-hydroxy-4,5-dimethoxybenzoyl) amino] thiazole - 4 - carboxamide monohydrochloride trihydrate. Its molecular formula is $C_{21}H_{30}N_4O_5S \cdot HCl \cdot 3H_2O$ and the structural formula is:



QUALITATIVE AND QUANTITATIVE COMPOSITION

Acogest (Acotiamide HCl Hydrate) is available for oral administration as:

Acogest Tablets 100mg
Each film-coated tablet contains:
Acotiamide HCl Hydrate... 100mg

CLINICAL PHARMACOLOGY

Mechanism of Action

Acotiamide inhibits acetylcholinesterase (AChE) activity by a mixed type of inhibition comprising competitive inhibition and noncompetitive inhibition. AChE inhibition by Acotiamide suppresses the degradation of acetylcholine (ACh) released from cholinergic nerve terminals, which results in enhancement of ACh-induced contraction and motility of the gastric antrum and gastric body, thereby increasing postprandial antral motility and improving antral hypomotility and delayed gastric emptying.

Pharmacokinetics

Absorption

Single Dose: When 1 tablet (100mg Acotiamide HCl Hydrate) was administered orally on an empty stomach to a healthy adult, the drug pharmacokinetic parameters were as follows:

Dosage (mg)	T _{max} (hr)	C _{max} (ng/mL)	AUC _{inf} (ng·hr/mL)	T _{1/2} (hr)
100	2.42±0.97	30.82±13.33	171.3±59.43	13.31±6.91

Repeated Dose: When 1 tablet (100mg as Acotiamide HCl Hydrate) was administered orally 3 times a day for 9 days (single dose on day 1, before every meal on days 3~8, and once on day 9 before meals, the plasma concentration reached almost steady state from the third dose on day 3. In addition, there was almost no change in pharmacokinetics with repeated administration.

Effects of food

When one tablet (100mg Acotiamide HCl Hydrate) was administered orally on an empty stomach, before or after meals to healthy adult, C_{max} was highest in preprandial administration and increased by 62.7% compared to fasting administration. In addition, the C_{max} administered after meals was 59.6% of the

preprandial administration. AUC_{last} was lowest in postprandial administration and decreased to 76.8% and 80.0%, respectively, compared to fasting and preprandial administration.

Distribution

The plasma protein binding rate obtained by in vitro equilibrium dialysis was 84.21%~85.95% for human plasma and 82.64%~85.10% for human serum albumin, and the binding rate was similar, so albumin was considered to be the main binding protein.

Metabolism

In vitro metabolism tests using human CYP-expressing microsomes suggest that the drug is metabolized to deisopropyl form by CYP2C8, CYP1A1 or CYP3A4. In addition, in vitro metabolism tests using human UGT-expressing microsomes suggest that the drug is metabolized to an unchanged glucuronate conjugate by UGT1A8 or UGT1A9. When oral fasting of [¹⁴C] Acotiamide solution (600mg/103μCi) was administered orally on an empty stomach to six healthy adult, 60.0% of the radioactivity in plasma was due to unchanged form. In addition, deisopropyl forms, unchanged glucuronic acid conjugates, and glucuronidates of deisopropyl forms were found in plasma.

Excretion

When oral administration of [¹⁴C] Acotiamide solution (600mg/103μCi) on an empty stomach to six healthy adult, 92.7% and 5.3% of the total radioactivity were excreted in feces and urine, respectively, by 216 hours after administration.

THERAPEUTIC INDICATIONS

Acogest (Acotiamide HCl Hydrate) is indicated for the treatment of postprandial bloating, epigastric distention, and early satiety in functional dyspepsia.

DOSAGE AND ADMINISTRATION

The usual adult dosage is 100mg of Acogest (Acotiamide HCl Hydrate) administered orally three times daily before a meal.

ADVERSE REACTIONS

Rash, urticaria, increased white blood cell count, dizziness, diarrhea, constipation, nausea, vomiting, stomach ache, stomatitis, ALT increase, AST increase, γ-GTP increase, increased blood bilirubin, increased blood ALP, increased prolactin in the blood and increased triglycerides in the blood.

“To report SUSPECTED ADVERSE REACTIONS to Getz Pharma’s pharmacovigilance Section, please contact at dsafety@getzpharma.com or +92-21-38636363”

CONTRAINDICATIONS

Acotiamide HCl Hydrate is contraindicated in patients with known hypersensitivity to the active substance or to any excipient of the product.

PRECAUTIONS

- If symptoms do not improve after 1 month of treatment with Acotiamide, consideration should be given to treatment discontinuation.
- If symptoms persist, the possibility of organic disease (including malignant diseases such as gastric cancer) should be taken into account and consideration should be given to

performing other tests in addition to upper gastrointestinal endoscopy, as necessary.

- Acotiamide is an acetylcholinesterase inhibitor and enhances the action of acetylcholine, caution is warranted.
- If symptoms improve continuously, consider discontinuing administration of this drug. Acotiamide should not be administered without careful consideration for a long period of time.
- Acotiamide should be used with caution in elderly patients with renal or hepatic impairment.

Pregnancy & Nursing Mothers

Acotiamide should be used during pregnancy and lactation only if the potential benefit justifies the potential risk.

DRUG INTERACTIONS

Drugs with anticholinergic effect

Atropine Sulfate Hydrate, Butylscopolamine, Bromide, etc, there is a possibility that the action of the drug may be attenuated. Since Acotiamide has an acetylcholinesterase inhibitory effect, the action of this drug is suppressed by concomitant use of anticholinergic agents.

Choline activators and cholinesterase inhibitors

Drugs like Acetylcholine Chloride, Neostigmine, Bromide alone or in combination may enhance the effect or has an acetylcholine receptor stimulating effect.

OVERDOSAGE

In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

STORAGE

Do not store above 30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Acogest (Acotiamide HCl Hydrate) Tablets 100mg are available in blister pack of 20's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.

This package insert is continually updated from time to time.

Manufactured by:



29-30/27,
K.I.A., Karachi,
Pakistan

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