AcoEaze
(Acotiamide)

Tablet 100 mg

COMPOSITION

THERAPEUTIC INDICATIONS

Postprandial fullness, upper abdominal fullness, and early satiety in functional dyspepsia

DOSAGE AND METHOD OF ADMINISTRATION

The usual adult dosage is 100 mg of acotiamide hydrochloride hydrate orally administered three times a day before meals.

CONTRAINDICATIONS

Patients with a history of hypersensitivity to the ingredients of this drug

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Precautions Related to Dosage and Administration

Discontinuation of administration of this drug should be considered if symptoms do not improve after one month of administration of this drug.

If symptoms persist, the possibility of organic disease should be considered, and in addition to upper gastrointestinal endoscopy, other examinations should be considered if necessary.

Important Precautions

This drug is an acetylcholinesterase inhibitor and enhances the action of acetylcholine.

If the symptoms continue to improve, consider discontinuing the administration of this drug, and be careful not to administer it carelessly for a long period of time.

Children

No clinical trials have been conducted in children, etc.

Elderly

If any abnormalities are observed, appropriate measures such as suspension of administration should be taken. In general, physiological functions (renal function, liver function, etc.) are decreased.

DRUG INTERACTIONS

Precautions for co-administration (Pay attention to co-administration)

Drug name, etc.	Clinical symptoms/measures	Mechanism/risk factors
Drugs with anticholinergic effects o atropine sulfate hydrate o Butylscopolamine bromide, etc.	The action of this drug may be weakened.	Since this drug has an acetylcholinesterase inhibitory effect, concomitant use with anticholinergics suppresses the action of this drug.

choline enhancers and cholinesterase inhibitors o Acetylcholine chloride etc. o Neostigmine bromide,etc.	The effects of this drug and concomitant drugs may be enhanced.	Along with this drug, it has a receptor-stimulating or stimulating effect.

FERTILITY, PREGNANCY, AND LACTATION

Pregnant women

Pregnant women or women who may become pregnant should only be administered if the therapeutic benefits are judged to outweigh the risks.

Lactating women

Consider the therapeutic benefit and the benefit of breastfeeding and consider continuing or discontinuing breastfeeding. It has been reported that it is excreted in the milk of rats

EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES

ADVERSE DRUG REACTIONS

The following adverse reactions may occur. Patients should be carefully monitored, and if any abnormalities are observed, appropriate measures such as discontinuing administration should be taken.

	1 or more	0.5 to less than 1%	less than 0.5%
hypersensitivity			rash, urticaria
blood		Increased white blood cell count	
Digestive organ	diarrhea, constipation	nausea, vomiting	stomach ache
liver	ALT increase, AST increase, γ-GTP increase	Blood bilirubin increased, blood ALP increased	
metabolism/endocrine	Increased blood prolactin, increased blood triglycerides		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at pv@searlecompany.com

OVERDOSE

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics properties

Mechanism of Action

It showed acetylcholinesterase inhibitory action.

Gastrointestinal hypermotility

It was shown to enhance postprandial gastric antrum motility in dogs and rats. In addition, it was shown to improve clonidine-induced gastric antral hypomotility in dogs and rats.

Improvement of delayed gastric emptying

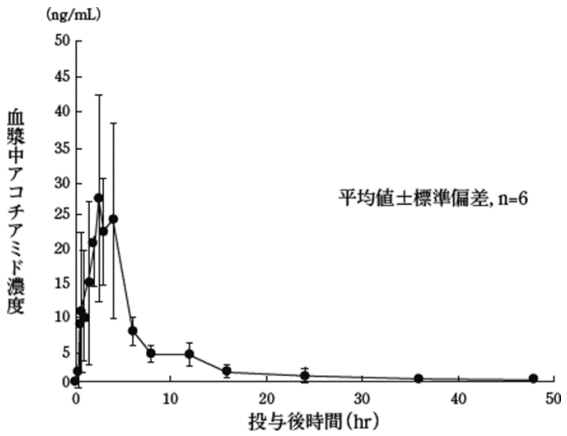
It was shown to improve clonidine-induced delayed gastric emptying in rats

Pharmacokinetic properties

Blood concentration

Single dose

When 1 tablet of this drug (100 mg of acotiamide hydrochloride hydrate) was administered orally in a single dose to healthy adult males under fasted conditions, the changes in plasma concentration of unchanged drug and pharmacokinetic parameters were as follows

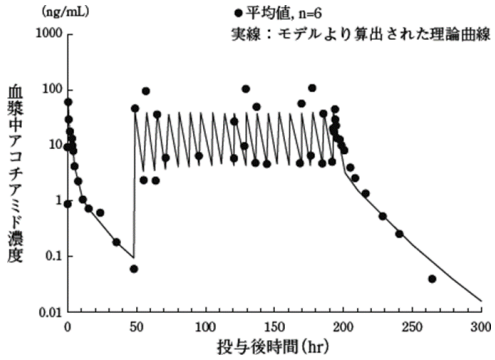


Single-dose pharmacokinetic parameters

Dosage (mg)	T_{max} (hr)	C_{max} (ng/mL)	AUC_{inf} (ng・hr/mL)	$T1_{/2}$ (hr)
100	2.42±0.97	30.82±13.33	171.3±59.43	13.31±6.91
Mean ± standard deviation, n = 6 AUC_{inf} : AUC calculated by extrapolating from the last measurement point to infinity				

Repeated doses

Administer 1 tablet (100 mg of acotiamide hydrochloride hydrate) to healthy adult men three times a day for 9 days (single dose on day 1, before each meal on days 3 to 8, single dose on day 9), and when repeatedly administered orally before meals, the plasma concentration reached a steady state after the third administration on day 3. In addition, the pharmacokinetics of repeated administration hardly changed.



Absorption

Dietary Effects

When one tablet of this drug (100 mg of acotiamide hydrochloride hydrate) was orally administered to healthy adult males under fasting conditions, before meals, or after meals, Cmax was the highest when administered before meals and increased by 62.7% compared to when administered under fasted conditions. In addition, the C max of postprandial administration was 59.6% of that of preprandial administration. AUC last was the lowest with postprandial administration, and decreased to 76.8% and 80.0%, respectively, in fasting and preprandial administration.

Distribution

Plasma protein binding rate

The plasma protein binding rate obtained by the in vitro equilibrium dialysis method was 84.21% to 85.95% for human plasma and 82.64% to 85.10% for human serum albumin. thought to be albumin

Metabolism

Metabolism

When [14 C] acotiamide solution (600 mg/103 μCi) was orally administered to 6 healthy adult male subjects under fasting conditions, unchanged drug accounted for 60.0% of the plasma radioactivity. In addition, de-isopropyl glucuronide, unchanged glucuronide, and de-isopropyl glucuronide conjugate were found in plasma (non-Japanese data).

Metabolic Enzymes

In vitro metabolism studies using human CYP-expressing microsomes indicate that this drug is metabolized to deisopropyl by CYP2C8, CYP1A1, or CYP3A4. In addition, an in vitro metabolism test using human UGT-expressing

microsomes suggests that this drug is metabolized to the unchanged glucuronide conjugate by UGT1A8 or UGT1A9.

Excretion

Acotiamide solution (600 mg/103 μCi) was orally administered to 6 healthy adult male subjects under fasted conditions. 5.3% were excreted (foreign data).

PRECLINICAL SAFETY DATA

Information Based on Nonclinical Studies

In a 24-month carcinogenicity study in rats, endometrial adenocarcinoma was observed in 5/50, 8/50, and 5 of the 200 mg/kg/day, 600 mg/kg/day, and 2,000 mg/kg/day groups, respectively. /50 cases, and significantly increased in the 600 mg/kg/day group (approximately 100 times the clinical dose in terms of dosage). On the other hand, no genotoxicity or estrogenic effects were observed with this drug. In addition, up to 2,000 mg/kg/day (approximately 330 times the clinical dose) in a 24-month carcinogenicity study in mice, and up to 2,000 mg/kg in a two-stage uterine carcinogenesis study using genetically modified animals.

PRESENTATION

ACOEAZE 100mg Tablets are available in Alu-Alu blister in a pack size of 20’s (2x10’s) tablets.

STORAGE

Do not store and transport above 30°C.

INSTRUCTIONS

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

Protect from sunlight, moisture and heat.

Keep all medicines out of sight & reach of children.

Product contains Lactose.

REGISTRATION NUMBER

ACOEAZE 100mg Tablets : 123123

MANUFACTURING LICENSE NUMBER : 000016

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