

Revised: July 2009 (9th version)

Standard Commodity Classification No. of Japan
871242

- Antispasmodic for the gastrointestinal tract -

**Coliopan<sup>®</sup> Capsules 5 mg****Coliopan<sup>®</sup> Tablets 10 mg****Coliopan<sup>®</sup> Granules 2 %**

&lt;Butropium bromide preparation&gt;

Powerful drug (Coliopan Tablets 10mg and Coliopan Granules 2 %)

Storage	Capsules 5 mg	Tablets 10 mg	Granules 2 %
COLIOPAN should be stored at room temperature. (See "PRECAUTIONS FOR HANDLING" section.)	Approval No. 21900AMX00057000	15400AMZ01759000	21900AMX00097000
	Date of listing in the NHI reimbursement price Jun 2007	Sep 1981	Jun 2007
	Date of initial marketing in Japan Apr 1974	Sep 1981	Sep 1981
Expiration date			
COLIOPAN should be used before the expiration date indicated on the package or label.			

**CONTRAINDICATIONS (COLIOPAN is contraindicated in the following patients.)**

1. Patients with glaucoma  
[COLIOPAN may increase intraocular pressure.]
2. Patients with micturition disorder due to prostatic hypertrophy  
[COLIOPAN may aggravate micturition disorder.]
3. Patients with serious heart disease  
[COLIOPAN may aggravate symptoms of heart disease.]
4. Patients with paralytic ileus  
[COLIOPAN may aggravate symptoms of paralytic ileus.]
5. Patients with a history of hypersensitivity to any ingredients of COLIOPAN

**DESCRIPTION****1. Composition****Capsules 5 mg:**

Each white hard capsule contains 5 mg of butropium bromide.

It also contains microcrystalline cellulose, gelatin, corn starch and sodium lauryl sulfate as inactive ingredients.

**Tablets 10 mg:**

Each white sugar-coated tablet contains 10 mg of butropium bromide.

It also contains carnauba wax, hydrated silicon dioxide, microcrystalline cellulose, titanium oxide, stearic acid, calcium stearate, sucrose, talc, precipitated calcium carbonate, corn starch, lactose hydrate, white shellac, hydroxypropylcellulose, pullulan, povidone and macrogol 6000 as inactive ingredients.

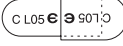



**Granules 2 %:**

Each gram of white to yellowish white coated granules contains 20 mg of butropium bromide.

It also contains light anhydrous silicic acid, microcrystalline cellulose, aminoalkyl methacrylate copolymer E, calcium stearate, talc, tocopherol, lactose hydrate, hy-

droxypropylcellulose, hypromellose and macrogol 6000 as inactive ingredients.

**2. Product description**

Brand Name	Dosage form and identification code	Appearance			Description
		Face	Reverse	Lateral	
COLIOPAN Capsules 5 mg	Hard capsules				Capsule Cap: White Body: White Contents: White powder
	CL05E	Length (mm) 14.5	Weight (mg) 140	Size No.4	
COLIOPAN Tablets 10mg	Sugar-coated tablets				White
	E 123	Diameter (mm) 6.2	Weight (mg) 100	Thickness (mm) 3.6	
COLIOPAN Granules 2%	Granules				White to yellowish white coated-granules

**INDICATIONS**

Remission of spasmodic pain in the following diseases:

Gastritis, enteritis, gastric ulcer, duodenal ulcer, cholelithiasis and cholecystopathy (including cholecystitis, and cholecystic and biliary dyskinesia)

**DOSAGE AND ADMINISTRATION****Capsules 5 mg:**

The usual adult dosage for oral use is 6 capsules (30 mg of butropium bromide) daily in three divided doses.

The dosage may be adjusted depending on the patient's age and symptoms.

**Tablets 10 mg:**

The usual adult dosage for oral use is 3 tablets (30 mg of butropium bromide) daily in three divided doses.

The dosage may be adjusted depending on the patient's age and symptoms.

**Granules 2 %:**

The usual adult dosage for oral use is 1.5 g (30 mg of butropium bromide) daily in three divided doses.

The dosage may be adjusted depending on the patient's age and symptoms.

**PRECAUTIONS****1. Careful Administration (COLIOPAN should be administered with care in the following patients.)**

- (1) Patients with prostatic hypertrophy  
[Micturition disorder may occur.]
- (2) Patients with congestive heart failure  
[COLIOPAN may aggravate symptoms of congestive heart failure.]
- (3) Patients with arrhythmia  
[COLIOPAN may aggravate arrhythmia.]
- (4) Patients with ulcerative colitis  
[Toxic megacolon colitis may occur.]
- (5) Patients with hyperthyroidism  
[COLIOPAN may aggravate palpitations and tachycardia accompanying hyperthyroidism.]
- (6) Elderly patients  
[See "Use in the Elderly" section.]
- (7) Patients exposed to high environmental temperature  
[Fever may occur.]

**2. Important Precautions**

Since COLIOPAN may produce visual accommodation disorder, drowsiness or dizziness, etc., patients should be cautioned against engaging in potentially hazardous activities requiring alertness, such as an operating machinery or driving a car.

**3. Drug Interactions**

**Precautions for coadministration (COLIOPAN should be administered with care when coadministered with the following drugs.)**

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Tricyclic antidepressants Phenothiazine derivatives Antihistamines	Adverse reactions due to anticholinergic action may occur.	May potentiate anticholinergic action of COLIOPAN.
Monoamine oxidase inhibitors		Inhibit the metabolism of COLIOPAN and may potentiate its anticholinergic action.

**4. Adverse Reactions**

Adverse reactions were reported in 189 of 2,057 patients (9.19%). (At the end of the investigation for incidence of adverse reactions)

	≥5%	5% > ≥0.1%	<0.1%	Incidence unknown
Ophthalmic		Visual accommodation disorder		
Gastrointestinal	Thirst	Constipation and nausea/vomiting		
Urinary		Micturition disorder		
Psyconeurologic		Sleepiness and headache	Dizziness	
Cardiovascular		Palpitations		Decrease in blood pressure
Hypersensitivity <sup>(note)</sup>				Rash
Others		Facial hot flushes	Malaise	

Note) In the event of such symptoms, treatment should be discontinued.

**5. Use in the Elderly**

Since the elderly often develop adverse reactions such as micturition disorder, visual accommodation disorder, thirst or constipation, etc. due to the anticholinergic action of COLIOPAN, they should take it under careful supervision.

**6. Use during Pregnancy, Delivery or Lactation**

COLIOPAN should only be used in pregnant women or women suspected of being pregnant, if the expected therapeutic benefits are evaluated to outweigh the possible risk of treatment.

[The safety of COLIOPAN in pregnant women has not been established.]

**7. Pediatric Use**

Safety in children has not been established (insufficient clinical experience).

**8. Precautions concerning Use**

Caution in handing over drug (tablets and capsules)

For drugs that are dispensed in a press-through package (PTP), instruct the patient to remove the drug from the package prior to use. [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in serious complications such as mediastinitis.]

**CLINICAL STUDIES****Clinical efficacy**

The usefulness of COLIOPAN for spasmodic pain has been established in double blind clinical trials.<sup>1,2)</sup>

Relief of abdominal pain was achieved in 39 min after oral administration of 10 mg of COLIOPAN, and this effect was sustained for 214 min.<sup>1)</sup>

**PHARMACOLOGY****1. Inhibition of gastrointestinal motility**

Butropium bromide reduces the motility of smooth muscle of the gastrointestinal tract by acting on the acetylcholine receptors at the parasympathetic nerve endings.

Experiments in isolated rat stomach, isolated rabbit jejunum, isolated rat and guinea pig proximal colon and isolated guinea pig gallbladder indicated that butropium bromide was more effective than atropine in inhibiting the

motility and tone of smooth muscle. In an experiment with isolated mouse ileum, butropium bromide exhibited stronger papaverine-like action than atropine.<sup>3)</sup>

## 2. Inhibition of gastric secretion

When butropium bromide was administered orally to rats with pyloric ligation-induced ulceration, it was shown to decrease the incidence of ulcers, increase the intragastric pH, reduce the volume of gastric juice, lower the total acidity and suppress pepsin secretion.<sup>4)</sup>

The oral administration of COLIOPAN was found to significantly inhibit gastric secretion (in the stomach tube method) in healthy adult male volunteers.<sup>5)</sup>

## PHYSICOCHEMISTRY

**Nonproprietary name:** Butropium Bromide (JAN, INN)

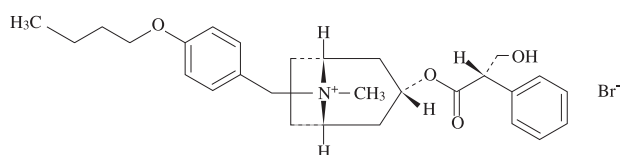
**Chemical name:**

(1*R*,3*r*,5*S*)-8-(4-Butoxybenzyl)-3-[(2*S*)-hydroxy-2-phenylpropanoyloxy]-8-methyl-8-azoniabicyclo [3.2.1] octane bromide

**Molecular formula:** C<sub>28</sub>H<sub>38</sub>BrNO<sub>4</sub>

**Molecular weight:** 532.51

**Structural formula:**



**Description:**

Butropium Bromide occurs as white crystals or crystalline powder. It is very soluble in formic acid, freely soluble in methanol, soluble in ethanol (95), slightly soluble in water, and practically insoluble in diethyl ether and in acetic anhydride.

## PRECAUTIONS FOR HANDLING

1. PTP packages of tablets should be protected from light after opening outer box.
2. Bottle packages of tablets should be protected from light and moisture after opening cap.
3. Bottle packages of granules should be protected from moisture after opening cap.

## PACKAGING

**COLIOPAN Capsules 5 mg:**

Boxes of 100 and 1,000 in press-through packages

**COLIOPAN Tablets 10 mg:**

Boxes of 100 and 1,000 in press-through packages, and bottles of 500

**COLIOPAN Granules 2 %:**

Bottles of 100 g

## REFERENCES

- 1) Nakano T. et al.: Jpn. J. Clin. Exp. Med., **51**, 2001, 1974.
- 2) Miyoshi A. et al.: Jpn. Arch. Int. Med., **20**, 31, 1973.
- 3) Wakabayashi T. et al.: Folia pharmacol. japon., **69**, 257, 1973.
- 4) Wakabayashi T. et al.: *ibid.*, **69**, 269, 1973.
- 5) Matsuo Y. et al.: Clin. Report, **9**, 277, 1975.

## REQUEST FOR LITERATURE SHOULD BE MADE TO:

Safety Management Department

Fax: 03-3811-2710

Eisai Co., Ltd.

## REQUEST FOR PRODUCT INFORMATION SHOULD BE MADE TO:

Customer Information Service

Free Dial: 0120-419-497

Eisai Co., Ltd.

## Manufactured and marketed by:

Eisai Co., Ltd.

6-10, Koishikawa 4-chome, Bunkyo-ku, Tokyo, 112-8088