Revised: February 2018 (8th version)

Standard Commodity Classification No. of Japan
875200

■90■

- Kampo-preparation-

TSUMURA Seihaito Extract Granules for Ethical Use

Storage
Store in light-resistant, air-tight containers.

Expiration date
Use before the expiration date indicated on the container and the outer package.

Approval No.	(61AM)3320
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986

DESCRIPTION

Composition	9.0 g of TSUMURA Seihaito extract granules (hereafter TJ-90) contains 6.0 g of a dried extract of the following mixed crude drugs. JP Japanese Angelica Root ..... 3.0 g JP Ophiopogon Root ..... 3.0 g JP Poria Sclerotium ..... 3.0 g JP Scutellaria Root ..... 2.0 g JP Platycodon Root ..... 2.0 g JP Apricot Kernel ..... 2.0 g JP Gardenia Fruit ..... 2.0 g JP Mulberry Bark ..... 2.0 g JP Jujube ..... 2.0 g JP Citrus Unshiu Peel ..... 2.0 g JP Asparagus Root …… 2.0 g JP Fritillaria Bulb ……... 2.0 g JP Glycyrrhiza …… 1.0 g JP Schisandra Fruit …… 1.0 g JP Ginger …… 1.0 g Bamboo Culm..……..... 2.0 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Light Anhydrous Silicic Acid JP Magnesium Stearate JP Lactose Hydrate
Description	Dosage form	Granules
	Color	Yellow-brown
	Smell	Characteristic smell
	Taste	Sweet and bitter
	ID code	TSUMURA/90

INDICATIONS

Coughing accompanied by frequent expectoration

DOSAGE AND ADMINISTRATION

The usual adult dose is 9.0 g/day orally in 2 or 3 divided doses before or between meals. The dosage may be adjusted according to the patient's age and body weight, and symptoms.

PRECAUTIONS

1. Careful administration (TJ-90 should be administered with care in the following patients.)

(1) Patients with an extremely weak gastrointestinal tract [Anorexia, epigastric distress, nausea, diarrhea, etc. may occur.]

(2) Patients with anorexia, nausea or vomiting [These symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-90 is used, the patient's "SHO" (constitution/symptoms) should be taken into account. The patient's progress should be carefully monitored, and if no improvement in symptoms/findings is observed, continuous treatment should be avoided.

(2) Since TJ-90 contains Glycyrrhiza, careful attention should be paid to the serum potassium level, blood pressure, etc., and if any abnormality is observed, administration should be discontinued.

(3) Long-term administration of a gardenia fruit-containing preparation (usually 5 years or longer) may cause mesenteric phlebosclerosis accompanied by discoloration, edema, erosion, ulceration, and stenosis of the colon. Periodical examinations such as CT scanning and colonoscopy would be desirable in cases of its long-term administration.

(4) When TJ-90 is co-administered with other Kampo-preparations (Japanese traditional herbal medicines), etc., attention should be paid to the duplication of the contained crude drugs.

SHO: The term "SHO" refers to a particular pathological status of a patient evaluated by the Kampo diagnosis, and is patterned according to the patient's constitution, symptoms, etc. Kampo-preparations (Japanese traditional herbal medicines) should be used after confirmation that it is suitable for the identified "SHO" of the patient.

3. Drug Interactions

Precautions for coadministration (TJ-90 should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
(1) Preparations containing Glycyrrhiza (2) Preparations containing glycyrrhizinic acid or glycyrrhizinates	Pseudoaldosteronism is likely to occur. Besides, myopathy is likely to occur as a result of hypokalemia. (Refer to the section "Clinically significant adverse reactions".)	Since glycyrrhizinic acid has an accelerating action on the potassium excretion at the renal tubules, an acceleration of decrease in the serum potassium level has been suggested.

4. Adverse Reactions

TJ-90 has not been investigated (drug use investigations, etc.) to determine the incidence of adverse reactions. Therefore, the incidence of adverse reactions is not known.

(1) Clinically significant adverse reactions

1) Interstitial pneumonia: If fever, cough, dyspnea, abnormal pulmonary sound (fine crackle), etc. are observed, administration of TJ-90 should be discontinued, and examinations such as X-ray should be performed immediately and appropriate measures such as administration of adrenocortical hormones taken. Besides, the patient should be advised to discontinue TJ-90 immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) Pseudoaldosteronism: Pseudoaldosteronism such as hypokalemia, increased blood pressure, retention of sodium/body fluid, edema, increased body weight, etc. may occur. The patient should be carefully monitored (measurement of serum potassium level, etc.), and if any abnormality is observed, administration should be discontinued and appropriate measures such as administration of potassium preparations should be taken.

3) Myopathy: Myopathy may occur as a result of hypokalemia. The patient should be carefully monitored, and if any abnormality such as weakness, convulsion/paralysis of limbs, etc. are observed, administration should be discontinued and appropriate measures such as administration of potassium preparations should be taken.

4) Hepatic dysfunction and jaundice: Hepatic dysfunction and/or jaundice with remarkable elevation of AST (GOT), ALT (GPT), Al-P and γ-GTP etc. may occur. The patient should be carefully monitored for abnormal findings. Administration should be discontinued and appropriate therapeutic measures should be taken, if abnormalities are observed.

5) Mesenteric phlebosclerosis: Mesenteric phlebosclerosis may occur with long-term administration. If symptoms such as abdominal pain, diarrhea, constipation, and abdominal distension repeatedly occur, or if the patient tests positive for fecal occult blood, administration should be discontinued. At the same time, tests such as CT and colonoscopy should be performed, and appropriate measures should be taken. Intestinal resection has been reported in some cases.

(2) Other adverse reactions

	Incidence unknown
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Diarrhea, etc.

5. Use in the Elderly

Because elderly patients often have reduced physiological function, careful supervision and measures such as reducing the dose are recommended.

6. Use during Pregnancy, Delivery or Lactation

The safety of TJ-90 in pregnant women has not been established. Therefore, TJ-90 should be used in pregnant women, women who may possibly be pregnant only if the expected therapeutic benefits outweigh the possible risks associated with treatment.

7. Pediatric Use

The safety of TJ-90 in children has not been established. [Insufficient clinical data]

PHARMACOLOGY

1. Promotion of tracheal mucosal ciliary transport (expectorant effect)

(1) Oral administration of Seihaito to pigeons promoted mucous ciliary transport (MCT) on the tracheal mucosa. It also promoted the activation of MCT induced acetylcholine spraying[1)].

(2) In tracheal mucosal epithelial cells from rabbits, Seihaito increased the ciliary beat frequency involved in airway fluid transportation (*in vitro*) [2)].

2. Action mechanism

Seihaito shows pharmacological effects via the following actions:

(1) Actions on the mucociliary transport system

- In the cultured canine tracheal mucosal epithelium, administration of Seihaito on the serous membrane side increased the short-circuit current reflecting active ion transport. This reaction was not influenced by a Na channel blocker, amyloride, but was inhibited by a Cl transport inhibitor, furosemide (*in vitro*) [3)].
- Oral administration of Seihaito to rabbits with subacute bronchitis promoted an increase in the level of saturated phosphatidylethanolamine, which promotes mucociliary transport in sputum, and inhibited an increase in the level of sphingomyelin, which inhibits mucous ciliary transport[1)].

(2) Actions on active oxygen and chemical mediators

In the lungs of ovalbumin–sensitized guinea pigs, Seihaito inhibited the release of slow reacting substance of anaphylaxis (SRS-A) on antigen stimulation (*in vitro*) [4)].

PACKAGING

Bottles of 500 g
3.0 g × 42 packets
3.0 g × 189 packets

REFERENCES

1) Miyata, T. KAMPO IGAKU. 1988, 12(9), p.234.
2) Chiyotani, A. et al. Kampo and Immuno-allergy vol.8. PharMa International Inc., 1994, p.44.
3) Chiyotani, A. et al. Jpn. J. Allergol. 1994, 43(9), p.1210.
4) Miyamoto, K. et al. Jpn. J. Oriental Medicine. 1987, 38(1), p.25.

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