Revised: October 2014 (10th version)

Standard Commodity Classification No. of Japan
875200

■19■

- Kampo-preparation-

TSUMURA Shoseiryuto 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)3284
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986
Date of latest reevaluation	March 1996
Date of latest reevaluation	April 2014

CONTRAINDICATIONS (TSUMURA Shoseiryuto extract granules (hereafter TJ-19) is contraindicated in the following patients.)

1. Patients with aldosteronism
2. Patients with myopathy
3. Patients with hypokalemia

[1-3: These diseases or symptoms may be aggravated.]

DESCRIPTION

Composition	9.0 g of TJ-19 contains 5.0 g of a dried extract of the following mixed crude drugs. JP Pinellia Tuber..... 6.0 g JP Processed Ginger ..... 3.0 g JP Glycyrrhiza ..... 3.0 g JP Cinnamon Bark ..... 3.0 g JP Schisandra Fruit ..... 3.0 g JP Asiasarum Root ..... 3.0 g JP Peony Root ..... 3.0 g JP Ephedra Herb ..... 3.0 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate Sucrose Esters of Fatty Acids
Description	Dosage form	Granules
	Color	Light brown
	Smell	Characteristic smell
	Taste	Slightly acid and sweet
	ID code	TSUMURA/19

INDICATIONS

Watery sputum, watery nasal discharge, nasal obstruction, sneezing, stridor, coughing, lacrimation in the following diseases:

Bronchitis, bronchial asthma, rhinitis, allergic rhinitis, allergic conjunctivitis, and common cold

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-19 should be administered with care in the following patients.)

(1) Patients in a period of weakness after disease or with greatly declined constitution [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

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

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

(4) Patients showing a remarkable tendency of sweating [Excess sweating and/or generalized weakness may occur.]

(5) Patients with cardiovascular disorders including angina pectoris and myocardial infarction, etc. or those with a history of such disorders.

(6) Patients with severe hypertension

(7) Patients with severe renal dysfunction

(8) Patients with dysuria

(9) Patients with hyperthyroidism

[(5)-(9): These disease and symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-19 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-19 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) When TJ-19 is coadministered 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-19 should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
(1) Preparations containing Ephedra Herb (2) Preparations containing ephedrine-related compounds (3) Monoamine oxidase (MAO) inhibitors (4) Thyroid preparations Thyroxine Liothyronine (5) Catecholamine preparations Adrenaline Isoprenaline (6) Xanthine preparations Theophylline Diprophylline	Insomnia, excessive sweating, tachycardia, palpitation, general weakness, mental excitation, etc. are likely to occur. In such cases, TJ-19 should be administered with care by measures such as reducing the dosage.	An enhancement of the sympathetic nerve-stimulating action has been suggested.
(1) Preparations containing Glycyrrhiza (2) Preparations containing glycyrrhizinic acid or glycyrrhizinates (3) Loop diuretics Furosemide Etacrynic acid (4) Thiazide diuretics Trichlormethiazide	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 and diuretics have 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-19 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-19 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-19 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 elevation of AST (GOT), ALT (GPT), Al-P and γ-GTP or other symptoms 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.

(2) Other adverse reactions

	Incidence unknown
Hypersensitivity Note 1)	Rash, Redness, Pruritus, etc.
Autonomic	Insomnia, Excess sweating, Tachycardia, Palpitation, Generalized weakness, Mental excitation, etc.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Vomiting, Abdominal pain, Diarrhea, etc.
Urinary	Urination disorder, etc.

Note 1) If such symptoms are observed, administration should be discontinued.

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-19 in pregnant women has not been established. Therefore, TJ-19 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-19 in children has not been established. [Insufficient clinical data.]

CLINICAL STUDIES

TJ-19 improved paroxysmal sneezing, nasal discharge, and nasal obstruction in a double-blind comparative study on perennial nasal allergy. The final global improvement rate is shown below[1].

	Rate of improvement :%, (n)	
	"Moderately improved" or better evaluations	"Slightly improved" or better evaluations
TJ-19 group	44.6 (41/92)	83.7 (77/92)
Placebo group	18.1 (17/94)	43.6 (41/94)

PHARMACOLOGY

1. Anti-allergic and anti-inflammatory actions

(1) Oral pre-administration of Shoseiryuto to rats inhibited passive cutaneous anaphylaxis (PCA) for 48 hours [2].

(2) Oral administration of Shoseiryuto to rats inhibited the histamine-induced skin inflammatory reaction[2].

(3) Oral pre-administration of Shoseiryuto inhibited nasal symptoms/scratching, eosinophils infiltration in the nasal mucosa, decrease in the nasal cavity volume and the increase in dye leakage to the nasal cavity induced by a topical antigen challenge in the dinitrophenil-ascaris-sensitized nasal allergy guinea pigs[3].

(4) Oral administration of Shoseiryuto suppressed the increase of eosinophils in bronchoalveolar lavage in airway inflammation mouse model. Shoseiryuto also suppressed the increase of respiratory resistance caused by the inhalation of methacholine (methylated derivative of Ach)[4].

(5) Administration of TJ-19 with feed reduced the counts of histamine-induced sneezing and nose scratching in rats[5].

2. Action mechanism

Shoseiryuto exhibits pharmacological effects via the following actions:

(1) Inhibition of the production/release of chemical mediators

1) Histamine

Shoseiryuto inhibited the histamine release from rat peritoneal mast cells induced by Compound 48/80[10] and antigen[4] (*in vitro*).

2) Arachidonic acid metabolism

In porcine tracheal smooth muscle cells, Shoseiryuto increased the production of cyclooxygenase and lipoxygenase derivatives (*in vitro*) [7].

(2) Actions on neuropeptides

Administration of Shoseiryuto with feed inhibited the increases in substance P, calcitonin gene-related peptide (CGRP) and nerve growth factor (NGF) in nasal lavage fluid caused by nasal drop of toluene-2,4-diisocyanate in rats[8].

(3) Actions on inflammatory cells

Shoseiryuto inhibited human eosinophils degranulation induced by ovalbumin, human IgG, human secretory IgA GM-CSF, and PAF[9]. It suppressed the expressions of adhesion molecules/ CD11b/CD18 on eosinophils[10]. Furthermore, it reduced eosinophils viability induced by the rhIL-5 (*in vitro*) [9)10].

(4) Actions on cytokines

In the splenocytes isolated Shoseiryuto-administered mice, the ovalbumin-induced IL-4 production was decreased, while IFN-γ production was not. Furthermore, it inhibited an increase in the number of IL-4 producing $CD4^+$ T cells (Th2 cells), but not the number of IFN-γ producing $CD4^+$ T cells (Th1 cells) (*in vitro*) [11].

(5) Actions on acetylcholine stimulation

In nasal gland acinar cells from guinea pigs, Shoseiryuto inhibited of the elevation in intracellular Na^+ induced by acetylcholine. In addition, it inhibited the ionic currents augmented by acetylcholine (*in vitro*) [12].

PACKAGING

Bottles of 500 g and boxes of 5 kg (500 g × 10 bottles)
3.0 g × 42 packets
3.0 g × 189 packets

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