Revised: October 2014 (8th version)

Standard Commodity Classification No. of Japan
875200

■10■

- Kampo-preparation-

TSUMURA Saikokeishito 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)3268
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986

DESCRIPTION

Composition	7.5 g of TSUMURA Saikokeishito extract granules (hereafter TJ-10) contains 4.0 g of a dried extract of the following mixed crude drugs. JP Bupleurum Root ..... 5.0 g JP Pinellia Tuber ..... 4.0 g JP Scutellaria Root ..... 2.0 g JP Glycyrrhiza …..... 2.0 g JP Cinnamon Bark ..... 2.0 g JP Peony Root ..... 2.0 g JP Jujube ..... 2.0 g JP Ginseng ..... 2.0 g JP Ginger ..... 1.0 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 sweet and astringent
	ID code	TSUMURA/10

INDICATIONS

TJ-10 is indicated for the relief of the following symptoms of those patients with fever, diaphoresis, rigors, physical pain, headache, and nausea:

Febrile diseases, such as common cold, influenza, pneumonia, and pulmonary tuberculosis; and stomach pit tension pain, such as gastric ulcer, duodenal ulcer, cholecystitis, cholelithiasis, hepatic dysfunction, and pancreatitis

DOSAGE AND ADMINISTRATION

The usual adult dose is 7.5 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. Important Precautions

(1) When TJ-10 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-10 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-10 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.

2. Drug Interactions

Precautions for coadministration (TJ-10 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.

3. Adverse Reactions

Summary of the incidence of adverse reactions

In the drug experience investigation (October 1993 to February 1994), 24 adverse reactions were reported in 20 of 2,641 patients (0.76%). The data shown here include adverse reactions (reported from the time of approval to July 1998) whose incidence could not be calculated.

(1) Clinically significant adverse reactions

1) **Interstitial pneumonia** (incidence unknown): If fever, cough, dyspnea, abnormal pulmonary sound (fine crackle), etc. are observed, administration of TJ-10 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-10 immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) **Pseudoaldosteronism** (incidence unknown): 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** (incidence unknown): 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** (incidence unknown): 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	5%> ≧0.1%	<0.1%
Hypersensitivity[1)]	Redness, Urticaria		Rash, Pruritus
Gastrointestinal		Diarrhea	Dyspepsia, Constipation
Urinary[2)]	Cystitis	Cystitis-like sympoms (Pollakiuria, Micturition pain, Hematuria, Feeling of residual urine)	

Note

1) In the event of such symptoms, administration should be discontinued.

2) Since these symptoms may occur. The patient should be carefully monitored, and if abnormalities are observed, administration of the drug should be discontinued and appropriate therapeutic measures taken.

4. Use in the Elderly

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

5. Use during Pregnancy, Delivery or Lactation

The safety of TJ-10 in pregnant women has not been established. Therefore, TJ-10 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.

6. Pediatric Use

The safety of TJ-10 in children has not been established. [Insufficient clinical data.]

7. Other Precautions

Adverse reaction of interstitial pneumonia has been reported frequently with a similar prescription "Shosaikoto" in the case of combined use with interferon-α.

PHARMACOLOGY

1. Anti-ulcer actions

Administration of Saikokeishito inhibited the development of acute gastric mucosal injury after the water immersion restraint stress in rats[1)].

2.Effects on hepatopathy

(1) Oral administration of Saikokeishito to rats inhibited increases in the serum AST (GOT), OCT, and γ-GTP levels and the liver triglyceride (TG) level which were induced by partial hepatectomy. Saikokeishito increased the liver DNA content (*in vivo*) [2)].

(2) Oral pre-administration of Saikokeishito to mice inhibited D-galactosamine -induced increases in the serum AST (GOT) level and the liver lipid peroxide (LPO) level. It also increased levels of glutathiones (GSH, GSSG) in liver[3)].

(3) Oral administration of Saikokeishito to rats relieved α-naphthylisothiocyanate (ANIT)-induced liver/biliary tract disorders, and inhibited an increase in the serum LPO level[4)].

2. Effects on pancreatitis

(1) Feeding a diet containing Saikokeishito to rats inhibited a decrease in the pancreatic amylase level induced by water-immersion/restraint stress loading and simultaneous administration of cerulein[5)].

(2) Oral pre-administration of Saikokeishito to rats inhibited cerulein-induced increases in the pancreatic fluid level, pancreatic trypsin level, and pancreatic LPO level as well as a decrease in the pancreatic SOD level. Saikokeishito also inhibited the intracellular redistribution of cathepsin B in pancreatic cells[5)]. Histologically, Saikokeishito inhibited the induction of interstitial

edema and vacuolation of acinar cells induced by an increase in pancreatic duct pressure[7].

3. Action mechanism

Saikokeishito shows pharmacological effects via the following actions:

(1)Suppressive on pancreatitis

In rat pancreatic gland cells, Saikokeishito inhibited high-level calcium treatment-induced decreases in the intracellular amounts of DNA (*in vitro*) [8].

(2) Immunological actions

In human peripheral blood monocytes, Saikokeishito promoted the production of granulocyte colony -stimulating factor (G-CSF) [9] and TNF-α (*in vitro*)[10].

(3) Deletion of active oxygen

Deletion of active oxygen by Saikokeishito was observed by using the spin trapping method with an electron spin resonance (ESR) device (*in vitro*) [11].

PACKAGING

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

REFERENCES

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6)Hirano, T. et al. KANPO IGAKU. 1995, 19(4), p.115.
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8)Wakasugi, H. et al. Iryo. 1996, 50(1), p.18.
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10)Yamashiki, M. et al. Drug Dev. Res. 1994, 31, p.170.
11)Takahashi, S. et al. Free Radic. Res. Commun. 1993, 19, p.S101.

REQUEST FOR LITERATURE SHOULD BE MADE TO:

Consumer Information Services Center
Tsumura & Co.
2-17-11 Akasaka, Minato-ku, Tokyo 107-8521, Japan
TEL:0120-329970 FAX:03-5574-6610

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