Revised: October 2016 (12th version)

Standard Commodity Classification No. of Japan
875200

■68■

- Kampo-preparation -

TSUMURA Shakuyakukanzoto 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)1139
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986
Date of latest reevaluation	April 2014

CONTRAINDICATIONS (Shakuyakukanzoto 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	7.5 g of TSUMURA Shakuyakukanzoto extract granules (hereafter TJ-68) contains 2.5 g of a dried extract of the following mixed crude drugs. JP Glycyrrhiza ..... 6.0 g JP Peony Root ..... 6.0 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate
Description	Dosage form	Granules
	Color	Light grayish-brown
	Smell	Characteristic smell
	Taste	Slightly sweet
	ID code	TSUMURA/68

INDICATIONS

TJ-68 is indicated for the relief of pain, myalgia or arthralgia, gastric pain and abdominal pain accompanied by sudden muscle spasms

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.

<Precaution>

The duration of administration of TJ-68 should be limited to the minimum period required for the treatment of the patient's condition.

PRECAUTIONS

1. Careful Administration (TJ-68 should be administered with care in the following patients.)

Elderly patients (Refer to the section “Use in the Elderly”)

2. Important Precautions

(1) When TJ-68 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-68 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-68 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-68 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 (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[1)]

In a clinical survey of adverse reactions of 2,975 patients treated with TJ-68 (October 2013 - September 2014), 37 adverse reactions including abnormal laboratory values were reported for 32 patients (1.1%).

(1) Clinically significant adverse reactions

1) Interstitial pneumonia (incidence unknown) : If cough, dyspnea, fever, abnormal pulmonary sound, etc. are observed, administration of TJ-68 should be discontinued, and examinations such as X-ray or chest CT should be performed immediately and appropriate measures such as administration of adrenocortical hormones taken.

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) Congestive heart failure, ventricular fibrillation, ventricular tachycardia (including Torsades de Pointes) (incidence unknown) : The possibility that congestive heart failure, ventricular fibrillation, ventricular tachycardia (including Torsades de Pointes) may occur cannot be ruled out, and the patient should be carefully monitored (measurement of serum potassium levels, etc.). If any abnormal findings such as palpitations, breathlessness, malaise, dizziness, syncope, etc. are observed, administration of the drug should be discontinued and appropriate therapeutic measures taken.

4) Myopathy (incidence unknown) : As a result of hypokalemia, myopathy/ rhabdomyolysis may occur. If weakness, muscle weakness, myalgia, convulsion/paralysis of limbs, increased CK (CPK), increased blood/urinary myoglobin are observed, administration should be discontinued and appropriate measures such as an administration of a potassium preparation taken.

5) Hepatic dysfunction and jaundice (incidence unknown): Hepatic dysfunction and/or jaundice with remarkable 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

	5% > ≥0.1%	<0.1%	Incidence unknown
Hypersensitivity Note 1)		Rash	Redness, Pruritus, etc.
Hepatic		Abnormality of hepatic function	
Gastrointestinal		Nausea	Vomiting, Diarrhea, etc.
Others	Hypokalemia, Edema, High blood pressure [containing increased blood pressure]		

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-68 in pregnant women has not been established. Therefore, TJ-68 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-68 in children has not been established. [Insufficient clinical data]

PHARMACOLOGY

1. Anti-allodynia* effect

Oral administration of Shakuyakukanzoto for 6 days from the day before induction suppressed the occurrence of allodynia and hyperalgesia in mice with paclitaxel-induced painful peripheral neuropathy[2)].

* Allodynia: Pathology in which innocuous mechanical stimuli and tactile stimuli are mistakenly recognized as severe pain.

2. Action mechanism

Shakuyakukanzoto shows pharmacological effects via the following actions:

(1) Activation of noradrenergic nervous system Shakuyakukanzoto activated the descending noradrenergic system in the spinal cord of diabetes mice, those with an increased α_2-adrenoceptor function in its spinal cord[3)].

(2) Inhibition of uterine contraction

-Shakuyakukanzoto inhibited the prostaglandin (PG) F2a-induced uterine contraction in mice (*in vitro*)[4].

-Shakuyakukanzoto inhibited the productions of PGE_2、$PGF_2\alpha$、6-keto$PGF_1\alpha$ in cultured human myometrium cells in vitro by suppressing the activity of cytosolic phospholipase A_2 ($cPLA_2$) (*in vitro*)[5].

PACKAGING

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

REFERENCES

1) Maki A. et. al. Diagnosis and Treatment. 2016, 104(7), P947.
2) Hidaka, T. et al. Eur. J. Pain. 2009, 13, P.22.
3) Omiya, Y. et al. J. Pharmacol. Sci. 2005, 99(4), p.373.
4) Kushihiki, M. et al. Bulletin of College of Allied Medical Science Akita University. 1998, 6(2), p.141.(in Japanese)
5) Shibata, T. et al. Acta Obstetrica Et Gynaecologica Japonica. 1996, 48(5), p.321.

■ **REQUEST FOR LITERATURE SHOULD BE MADE TO:**

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