Revised: March 2013 (5th version)

Standard Commodity Classification No. of Japan
875200

■35■

- Kampo-preparation-

TSUMURA Shigyakusan 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)1118
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 Shigyakusan extract granules (hereafter TJ-35) contains 2.25 g of a dried extract of the following mixed crude drugs. JP Bupleurum Root ..... 5.0 g JP Peony Root ..... 4.0 g JP Immature Orange ..... 2.0 g JP Glycyrrhiza ..... 1.5 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	Bitter
	ID code	TSUMURA/35

INDICATIONS

TJ-35 is indicated for the relief of the following symptoms of those patients with a comparatively strong constitution:
Cholecystitis, cholelithiasis, gastritis, hyperacidity, gastric ulcer, nasal catarrh, bronchitis, nervousness, and hysteria

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. Careful Administration (TJ-35 should be administered with care in the following patients.)

Patients with greatly declined constitution [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

2. Important Precautions

(1) When TJ-35 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-35 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-35 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-35 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-35 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) 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.

(2) 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.

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-35 in pregnant women has not been established. Therefore, TJ-35 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-35 in children has not been established. [Insufficient clinical data]

PHARMACOLOGY

1. Antiulcer actions

(1) Oral pretreatment with of Shigyakusan to rats prevented post-ischemia reperfusion-induced gastric mucosal injury, and then inhibited an increase of thiobarbituric acid-reactive substances (TBA-RS) level in the gastric mucosa[1].

(2) Oral administration of Shigyakusan to rats with Compound 48/80-induced gastric mucosal lesion reduced the area of disordered mucosa in the glandular gastric region[2].

2. Inhibitory effects on hepatic/biliary injury

Oral administration of Shigyakusan inhibited the elevation of serum AST (GOT), ALT (GPT), LDH, and Al-P activities in rats with α-naphthylisothiocyanate (ANIT)-induced hepatic/biliary injury, and also inhibited increases of the serum levels of total bile acid, total cholesterol, lipid peroxide, T-Bil, and D-Bil[3].

3. Action mechanism

Shigyakusan shows pharmacological effects via the following actions:

(1) Antiulcer actions

Oral administration of Shigyakusan inhibited an increase of lipid peroxide level, the elevation of myeloperoxidase activity, and the reduction of Se-containing glutathione peroxidase activity in the gastric mucosa of rats with Compound 48/80-induced gastric mucosal lesion[2].

(2) Active oxygen-scavenging actions

The spin trapping method with an electron spin resonance (ESR) device showed oxygen-scavenging actions of Shigyakusan (*in vitro*)[1].

(3) Inhibitory effects on proton pump activity

Shigyakusan inhibited the activity of H^+, K^+-ATPase purified from the pig gastric mucosa (*in vitro*)[4].

PACKAGING

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

REFERENCES

1) Yoshikawa, T. et al. J. Clin. Biochem. Nutr. 1991, 10, p.189.
2) Ohta, Y. et al. KAMPO IGAKU. 1995, 19(5), p.148.
3) Ohta, Y. et al. J. Traditional Med. 1997, 14(2), p.143.
4) Ono, K. et al. Prog. Med. 1995, 15(10), p.2188.

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