Revised: February 2018 (9th version)

Standard Commodity Classification No. of Japan
875200

■15■

- Kampo-preparation-

TSUMURA Orengedokuto 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)3278
Date of listing in the NHI reimbursement price	October 1986
Date of initial marketing in Japan	October 1986
Date of latest reevaluation	April 2014

DESCRIPTION

Composition	7.5 g of TSUMURA Orengedokuto extract granules (hereafter TJ-15) contains 1.5 g of a dried extract of the following mixed crude drugs. JP Scutellaria Root .....….... 3.0 g JP Coptis Rhizome …… 2.0 g JP Gardenia Fruit ..... 2.0 g JP Phellodendron Bark .....….... 1.5 g (JP : The Japanese Pharmacopoeia)	
	Inactive ingredients	JP Magnesium Stearate JP Lactose Hydrate
Description	Dosage form	Granules
	Color	Yellow-brown
	Smell	Characteristic small
	Taste	Bitter
	ID code	TSUMURA/15

INDICATIONS

TJ-15 is for the relief of the following symptoms of those patients who have ruddy face with comparatively strong constitution, a touch of hot flushes, and a tendency to irritability: nose bleeding, hypertension, insomnia, neurosis, gastritis, alcoholic hangover , climacteric disturbance and automatic imbalance syndrome peculiar to women resembling climacteric disturbance, dizziness, palpitation, eczema or dermatitis and pruritus cutaneous

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-15 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-15 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) 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.

(3)When TJ-15 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. Adverse Reactions

TJ-15 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-15 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-15 immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) Hepatic dysfunction and jaundice: 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.

3) 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
Hypersensitivity Note 1)	Rash, Urticaria, etc.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Vomiting, Abdominal pain, Diarrhea, etc.

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

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-15 in pregnant women has not been established. Therefore, TJ-15 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-15 in children has not been established. [Insufficient clinical data.]

PHARMACOLOGY

1. Actions on circulatory system

Oral administration of Orengedokuto to rats increased regional cerebral blood flow (CBF) in the hippocampus[1].

2. Actions on injury to the gastric mucosa

Oral administration of Orengedokuto to rats reduced the area of mucosal injury in the glandular stomach induced by single-dose or repeated administration of compounds 48/80, and inhibited increases in the gastric mucosal levels of lipid peroxide (LPO), the elevation of xanthine oxidase (XOD) activity, and the reduction of glutathione peroxidase activity[2)3)].

3. Anti-inflammatory actions

(1) Oral administration of Orengedokuto to rats inhibited ovalbumin-, or bradykinin-induced paw oedema and bradykinin-induced enhancement of capillary permeability. Furthermore, oral administration of Orengedokuto to mice inhibited xylene-induced ear oedema [4].

(2) Oral administration of Orengedokuto to rats inhibited formation of cotton pellet granuloma[5].

4. Mechanisms of action

Orengedokuto shows pharmacological effects via the following actions:

Inhibitory effects on platelet aggregation

In human platelets, Orengedokuto inhibited platelet aggregation and the release of ATP by collagen, adrenaline, ADP, STA_2, or arachidonic acid, and the thrombin-, ADP-, or STA_2- induced release of Platelet factor 4 and β-thromboglobulin (*in vitro*) [6].

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

1)Kogure, H. et al. Pharma Medica. 1988, 6(suppl.2), p.33.
2)Otsuji, K. et al. J. Med. Pharm. Soc. WAKAN-YAKU. 1992, 9(2), p.101.
3)Kobayashi, T. et al. J. Med. Pharm. Soc. WAKAN- YAKU. 1993, 10(3), p.222.
4)Wang, L. M. et al. J. Pharma. Pharmacol. 1996, 48(3), p.327.
5)Mizukawa, H. et al. Am. J. Chin. Med. 1993, 21(1), p.71.
6)Yang, L. B. et al. Jpn. J. Clin. Exp. Med. 1992, 69(9), p.3005.

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