Revised: October2014 (9th version)

Standard Commodity Classification No. of Japan
875200

■107■

- Kampo-preparation-

TSUMURA Goshajinkigan 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 pacakage.

Approval No.	(61AM)3267
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 Goshajinkigan extract granules (hereafter TJ-107) contains 4.5 g of a dried extract of the following mixed crude drugs. JP Rehmannia Root ..... 5.0 g JP Achyranthes Root ..... 3.0 g JP Cornus Fruit ..... 3.0 g JP Dioscorea Rhizome ..... 3.0 g JP Plantago Seed ..... 3.0 g JP Alisma Rhizome ..... 3.0 g JP Poria Sclerotium ..... 3.0g JP Moutan Bark ..... 3.0 g JP Cinnamon Bark ..... 1.0 g JP Powdered Processed Aconite Root … 1.0 g (JP: The Japanese Pharmacopoeia)	
	Inactive ingredient	JP Magnesium Stearate JP Lactose Hydrate Sucrose Esters of Fatty Acids
Description	Dosage form	Granules
	Color	Grayish-brown
	Smell	Characteristic smell
	Taste	Slightly sweet and acid
	ID code	TSUMURA/107

INDICATIONS

TJ-107 is indicated for the relief of the following symptoms of those patients with decreased urine volume or polyuria sometimes having dry mouth who are easily fatigued and easily feel cold in the extremities:

Leg pain, low back pain, numbness, blurred vision in old patients, pruritus, dysuria, frequent urination and edema

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-107 should be administered with care in the following patients.)

(1) Patients with strong constitution [Adverse reactions are likely to occur, and the symptoms may be aggravated.]

(2) Patients with sensitivity to heat, a tendency towards hot flush and red face. [Palpitation, hot flush, numbness of the tongue, nausea, etc. may occur.]

(3) Patients with an extremely weak gastrointestinal tract [Anorexia, epigastric distress, nausea, vomiting, feeling of enlarged abdomen, abdominal pain, diarrhea, constipation, etc. may occur.]

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

2. Important Precautions

(1) When TJ-107 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) When TJ-107 is coadministered with other Kampo-preparations (Japanese traditional herbal medicines) etc., attention should be paid to the duplication of the contained crude drugs. Special caution should be exercised when TJ-107 is coadministered with preparations containing Aconite Tuber.

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-107 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-107 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-107 immediately and to make contact with the physician in the event of fever, cough, dyspnea, etc.

2) **Hepatic dysfunction and jaundice**: Hepatic dysfunction, with increased AST (GOT), ALT (GPT), Al-P, and γ-GTP levels, and/or jaundice may occur. The patient should be carefully monitored for abnornal 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.
Gastrointestinal	Anorexia, Epigastric distress, Nausea, Vomiting, Feeling of enlarged abdomen, Abdominal pain, Diarrhea, Constipation, etc.
Others	Palpitation, Hot flush, Numbness of the tongue, 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

Use of TJ-107 in pregnant women, women who may possibly be pregnant is not recommended. [Achyranthes Root and Moutan Bark contained in TJ-107 may cause premature birth or abortion. Besides, adverse reactions due to Powdered Processed Aconite Root contained in TJ-107 are likely to occur.]

6. Pediatric Use

TJ-107 should be administered with care in children. [TJ-107 contains Powdered Processed Aconite Root.]

PHARMACOLOGY

1. Effect on nerve

(1)Oral administration of Goshajinkigan suppressed the reduction of sciatic nerve conduction velocity in streptozotocin (STZ)-induced diabetic rats[1].

(2) Oral administration of Goshajinkigan to rats suppressed the oxaliplatin-induced cold hyperalgesia[2].

2. Antiallodynic effect and antinociceptive (analgesic) effect

(1)Oral administration of Goshajinkigan elevated the lowered antinociceptive threshold in rats with STZ-induced diabetes[3].

(2) Oral pretreatment of Goshajinkigan to tumor-bearing mice inhibited the mechanical allodynia in lower limbs induced by paclitaxel[4].

3. Blood flow-increasing actions

(1) Oral administration of TJ-107 (2.5g) to diabetes patients increased the blood flow in the forearm skin at 90 and 120 min. after the administrations. Furthermore, TJ-107 elevated the temperature of palm surface (n=17)[5].

(2)Oral administration of Goshajinkigan to rats with STZ-induced diabetes inhibited a decrease in gastrocnemial muscle blood flow[6].

4. Effect on pollakiuria

Four-week feeding of Goshajinkigan in the diet suppressed C-fiber activation-induced bladder overactivity due to intrabladder infusion of acetic acid in rats[7][8].

5. Action mechanism

Goshajinkigan shows pharmacological effects via the following actions:

(1)Antinociceptive (analgesic) effect

- The antinociceptive effect of orally administered Goshajinkigan in rats with STZ-induced diabetes was diminished by intrathecal injection of anti-dynorphin antiserum. A similar diminishment was observed after pretreatment with a κ-opioid receptor antagonist, norbinaltorphimine[3].
- The antinociceptive effect of orally administered Goshajinkigan in rats with STZ-induced diabetes was diminished by intraplantar injection with the NO synthetase inhibitor N^G-nitro-L-arginine methyl ester (L-NAME) and was abolished by concomitant treatment with anti-dynorphin antiserum[9].

(2) Increase of blood flow

The increase of peripheral blood flow by the intraduodenal administration of Goshajinkigan in rats with STZ-induced diabetes was abolished by intraperitoneal pretreatment with L-NAME[6].

(3) Effect on pollakiuria

- The decrease in the frequency of spontaneous bladder contraction by Goshajinkigan in rats was abolished by subcutaneous injection of a κ-opioid receptor antagonist, and was diminished by intrathecal injection of anti-dynorphin antibody, a serotonin receptor antagonist (methysergide), or an α_2 adrenergic receptor antagonist (yohimbine) [10].
- After a Goshajinkigan diet for four weeks, the following changes were observed in rats: decreases in plasma dopamine and serotonin levels[8]; suppression of increases in levels of neurokinin A and B, substance P, sensory receptor (TRPV1), or purine receptor and the expression of their mRNA in the bladder tissue when acetic acid was injected into the bladder[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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5) Shikano, M. et al. J. Med. Pharm. Soc. WAKAN- YAKU. 1988, 5(3), p.378.
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11)Imamura, T. et al. Neurourol. Urodyn. 2008, 27(8), p.832.

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