

Storage: Store at room temperature

Shelf Life: 3 years

|                                    |                  |
|------------------------------------|------------------|
| Approval No.                       | 16100AMZ04038000 |
| Date of Initial Marketing in Japan | October 1986     |

Kampo product

N12

## Kotaro Saikokaryukotsuboreito Extract Fine Granules

### 3. COMPOSITION AND PRODUCT DESCRIPTION

#### 3.1 Composition

|                              |  |
|------------------------------|--|
| Brand name                   | Kotaro Saikokaryukotsuboreito Extract Fine Granules  |
| Active ingredient            | 7.5g of Kotaro Saikokaryukotsuboreito Extract Fine Granules contains 5.0g of the dried extract of the following mixed crude drugs. |
|                              | JP Bupleurum Root.....5.0g   |
|                              | JP Pinellia Tuber.....4.0g   |
|                              | JP Poria Sclerotium.....3.0g   |
|                              | JP Cinnamon Bark .....3.0g   |
|                              | JP Scutellaria Root .....2.5g  |
|                              | JP Jujube.....2.5g   |
|                              | JP Ginger.....0.7g   |
|                              | JP Ginseng .....2.5g   |
|                              | JP Longgu .....2.5g  |
|                              | JP Oyster Shell.....2.5g   |
|                              | JP Rhubarb .....1.0g   |
| (JP: Japanese Pharmacopoeia) |  |
| Excipients                   | Magnesium Stearate, Corn Starch, Lactose Hydrate, Pullulan, Magnesium Aluminometasilicate  |

#### 3.2 Product Description

|             |                     |
|-------------|---------------------|
| Dosage form | Fine granules       |
| Color       | Dark brown to brown |
| Taste       | Slightly bitter     |
| Odor        | Characteristic odor |
| ID code     | N12                 |

### 4. INDICATIONS

In patients with the conditions below, symptoms include mental anxiety and being easily startled, accompanied by heart acceleration, chest discomfort, dizziness, hot flushes, insomnia, etc., or awareness of palpitations around the umbilicus, with constipation due to congestion in the pit of the stomach, and decreased urine output.

Arteriosclerosis, hypertension, kidney diseases, insomnia, nervous cardiac palpitation, heart failure, seizures, sleep terror disorder in children, climacteric neurosis, impotence, neurotic disorder.

### 6. DOSAGE AND ADMINISTRATION

The usual adult dosage for oral use is 7.5g daily in 2 or 3 divided doses before or between meals.

The dosage may be adjusted according to the patient's age, body weight, and symptoms.

### 8. IMPORTANT PRECAUTIONS

#### 8.1 When this product is used, the patient's "SHO"

(constitution/symptoms) should be taken into consideration. The patient's progress should be carefully monitored, and if no improvement in symptoms or findings is observed, continuous administration should be avoided.

8.2 When this product is used in combination with other Kampo products, etc., attention should be paid to the duplication of the contained crude drugs. Special attention should be paid to concomitant use with preparations containing Rhubarb.

8.3 Since there are individual differences in the cathartic action of Rhubarb, caution should be exercised with respect to dosage and administration.

### 9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with complication or history of diseases, etc.

9.1.1 Patients with diarrhea, loose stools

These symptoms may be aggravated.

9.1.2 Patients with an extremely weak gastrointestinal tract

Anorexia, epigastric distress, abdominal pain, diarrhea, etc. may occur.

9.1.3 Patients with extremely weakened constitution

Adverse reactions are likely to occur, and the symptoms may be aggravated.

9.5 Pregnant Women

It is not recommended to administer this product to pregnant women or women who may possibly be pregnant. There is a risk of premature birth or miscarriage due to the uterotonic action and hyperemic action of the pelvic organs of Rhubarb contained in this product.

9.6 Breast-feeding Women

Considering the therapeutic benefits and the benefits of breastfeeding, continuation or discontinuation of breastfeeding should be considered. Anthraquinone derivatives in Rhubarb contained in this product are excreted in breast milk and may cause diarrhea in infants.

9.7 Pediatric Use

No clinical studies have been conducted in children.

9.8 Geriatric Use

Since the physiological functions are generally decrease in elderly patients, careful supervision is recommended; measures such as reducing the dose may be considered.

### 11. ADVERSE REACTIONS

The following adverse reactions may occur. Patients should be carefully monitored, and if any abnormalities are observed, appropriate measures such as discontinuation of administration should be taken.

#### 11.1 Clinically Significant Adverse Reactions

##### 11.1.1 Interstitial pneumonia (frequency unknown)

If cough, dyspnea, pyrexia, abnormal lung sound, etc. are observed, administration of this product should be discontinued, and examinations such as chest X-ray and chest CT scan should be performed immediately, and appropriate measures such as administration of corticosteroid should be taken. In addition, patients should be advised to discontinue administration of this product and contact the physician immediately if cough, dyspnea, or pyrexia, etc. occur.

##### 11.1.2 Hepatic impairment, jaundice (frequency unknown)

Hepatic impairment and/or jaundice with marked elevations of AST, ALT, Al-P,  $\gamma$ -GTP, etc. may occur.

##### 11.2 Other Adverse Reactions

|                  | Frequency unknown   |
|------------------|---|
| Hypersensitivity | Rash, Redness, Pruritus, Urticaria, etc.                      |
| Gastrointestinal | Anorexia, Epigastric distress, Abdominal pain, Diarrhea, etc. |

## 15. OTHER PRECAUTIONS

### 15.1 Information Based on Clinical Use

According to the results of 199 placebo-controlled clinical studies of multiple antiepileptic drugs conducted overseas in patients with epilepsy, psychiatric disorders, etc., the risk of suicidal ideation or suicide attempt was approximately twice as high in the antiepileptic drug group as in the placebo group (antiepileptic drug group: 0.43%, placebo group: 0.24%), and was higher in 1.9 per 1000 patients in the antiepileptic drug group than in the placebo group (95% CI: 0.6-3.9). In addition, in the subgroup of epilepsy patients, the incidence was calculated to be 2.4 more patients per 1,000 than in the placebo group.

## 20. PRECAUTIONS FOR HANDLING

- 20.1 To maintain the quality of the product, avoid moisture as much as possible and store in a cool place, away from direct sunlight.
- 20.2 Avoid moisture, especially after opening, and handle with care.
- 20.3 Since this product is made from crude drugs, the color of the product may vary.

## 22. PACKAGING

- 500g [bottle, loose]  
2.5g×42 packets [sachets]  
2.5g×189 packets [sachets]

## 24. REFERENCE REQUEST AND CONTACT INFORMATION

Pharmaceutical Division, Kotaro Pharmaceutical Co., Ltd.  
5-23, Nakatsu 2-chome, Kita-ku, Osaka 531-0071, Japan

## 26. MARKETING AUTHORIZATION HOLDER, etc.

- 26.1 Marketing Authorization Holder  
Kotaro Pharmaceutical Co., Ltd.  
5-23, Nakatsu 2-chome, Kita-ku, Osaka 531-0071, Japan