CONTRAINDICATIONS (KALIMATE is contraindicated in the following patients.)

Patients with intestinal obstruction [Intestinal perforation may occur.]

(1) Patients susceptible to constipation [Intestinal obstruction or intestinal perforation may occur.]

(2) Patients with intestinal stenosis [Intestinal obstruction or intestinal perforation may occur.]

(3) Patients with gastrointestinal ulcers [Symptoms may be exacerbated.]

(4) Patients with hyperparathyroidism [Blood concentration of calcium may be increased by ion exchange.]

(5) Patients with multiple myeloma [Blood concentration of calcium may be increased by ion exchange.]

DESCRIPTION

Composition  Calcium polystyrene sulfonate

Dosage form  Powder

Color  Pale yellowish white to light yellow

Odor  Nearly odorless

Taste  Nearly tasteless

INDICATIONS

Hyperpotassemia resulting from acute or chronic renal failure.

DOSEAGE AND ADMINISTRATION

1. Oral administration
   The usual adult dosage is 15 - 30 g daily in two or three divided doses. Each dose should be suspended in 30 - 50 mL of water and administered orally. The dosage may be adjusted according to the patient’s condition.

2. Rectal route
   A single dose of 30 g should be suspended in 100 mL of water or a 2% methylcellulose solution and administered via the rectal route after warming to body temperature. It should be left in the intestinal tract for 30 minutes to 1 hour after administration. In case the suspension leaks out, the hip should be lifted up by placing a pillow underneath or the patient should be sit on the knee-chest position. 5% glucose solution may be substituted for the water or 2% methylcellulose solution.

PRECAUTIONS1-8)

1. Careful Administration (KALIMATE should be administered with care in the following patients.)
   (1) Patients susceptible to constipation [Intestinal obstruction or intestinal perforation may occur.]

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   (4) Patients with hyperparathyroidism [Blood concentration of calcium may be increased by ion exchange.]

   (5) Patients with multiple myeloma [Blood concentration of calcium may be increased by ion exchange.]

2. Important Precautions
   (1) Intestinal perforation or intestinal obstruction may occur. If any abnormal findings such as severe constipation, prolonged abdominal pain, or vomiting, etc. are observed, administration of the drug should be discontinued and appropriate measures taken.

   (2) Patients should be instructed to pay attention to their feces and consult with their physicians if constipation is followed by significant symptoms such as abdominal pain, abdominal distention, or vomiting, etc.

   (3) This product should be administered while measuring the serum potassium and serum calcium levels regularly to prevent the overdose. If any abnormal findings are observed, appropriate measures such as reducing the dose or withdrawing of the drug should be taken.

3. Drug Interactions
   Precautions for coadministration (KALIMATE should be administered with care when coadministered with the following drugs.)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Signs, Symptoms, and Treatment</th>
<th>Mechanism and Risk Factors</th>
</tr>
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<tbody>
<tr>
<td>Digitalis preparation</td>
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4. Adverse Reactions

169 cases of adverse reactions to this drug were reported in 151 (12.8%) of 1,182 patients with oral administration in clinical studies before and after drug approval. The major adverse reactions were constipation in 109 patients (9.2%), anorexia in 18 patients (1.5%), nausea in 16 patients (1.4%), etc. Changes in laboratory data were observed in 13 patients (1.1%). These changes were hypopotassemia, which can be normalized by adjustment of the dosage. (At the end of the investigation of adverse reaction incidences)

(1) Clinically significant adverse reactions

Since intestinal perforation and intestinal obstruction may occur (incidence unknown), the patient should be carefully observed. If any abnormalities suggestive of these conditions such as clinically significant constipation, prolonged abdominal pain, or vomiting, etc. are observed, administration of the drug should be discontinued and appropriate measures including auscultation, palpation, and diagnostic imaging taken.

(2) Other adverse reactions

<table>
<thead>
<tr>
<th>Incidence unknown</th>
<th>Incidence ≥5%</th>
<th>Incidence 5% &gt; ≥0.1%</th>
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<tr>
<td>Gastrointestinal</td>
<td>Constipation</td>
<td>Nausea, anorexia, stomach discomfort</td>
</tr>
<tr>
<td>Electrolytic</td>
<td>Hypopotassemia (Oral administration)</td>
<td>Hypopotassemia (Rectal route)</td>
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</tbody>
</table>

Note) See “Important Precautions” (1)

8. Other Precautions

It has been reported that cases of colon stenosis and colon ulcer, etc. occurred after oral administration of sorbitol suspension of KALIMATE.

PHARMACOKINETICS

(For reference)

It is thought that this product is not absorbed (rabbit). However, it has been reported from the result of the experiment with calf that fine particles less than 5 µm in size have been absorbed through mucous membrane and deposited in the reticuloendothelial system tissue. KALIMATE is controlled in order that such fine particles are less than 0.1% in rate.

CLINICAL STUDIES

The serum potassium level lowering effect was estimated to be equal to sodium polystyrene sulfonate, the control drug, in a double-blind comparative study in 59 patients with oral administration. Open clinical studies with 119 patients are summarized below.

PHARMACOLOGY

1. Pharmacological action

(1) KALIMATE contains 7.0 - 9.0% calcium, 1 g of which is exchanged for 53 - 71 mg (1.36 - 1.82 mEq/g) of potassium in vitro (KCl solution).

(2) By administering 15 - 30 g/day of KALIMATE to renal failure patients (adults), the serum potassium level is reduced about 1 mEq/L (humans).

(3) Unlike sodium-typed resin, KALIMATE does not cause the increase in serum sodium and phosphate levels and the decrease in serum calcium level when it is used for the renal failure (humans).
(4) Since KALIMATE is calcium-typed resin, it is used even for the patients who restricted ingestion of sodium. Moreover, it can be used without fear of appearance and aggravation of edema, hypertension or cardiac insufficiency induced by sodium (humans).14, 15)

2. Mechanism of action
After administration of KALIMATE via oral or rectal route, calcium ion of KALIMATE is exchanged for potassium ion in the intestinal tract, particularly around the colon, and the drug is excreted as unchanged polystyrene sulfonate resin into the feces without digestion and absorption. In consequence, potassium in the intestinal tracts excreted outside the body.

PHYSICOCHEMISTRY
Nonproprietary name: Calcium polystyrene sulfonate (JAN)
Structural formula:
It has an irregularly intricate sterical structure. A part of it is shown as follows.

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CH2-CH2-CH2-CH2-CH2-
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Description:
It occurs as a pale yellowish white to light yellow powder with odorless and tasteless. It is practically insoluble in water, ethanol and ether.

PACKAGING
Powder: 5 g × 105 sachets, 500 g

REFERENCES
5) Safety Division, Pharmaceutical Affairs Bureau, Ministry of Health and Welfare, Japan: Iyakuhin Fukusayo Joho (Information on adverse drug reaction), No. 40, 9, 1979
13) Hirasawa Y.: Shinryo to Shin-yaku (Medical Consultation & New Remedies), 10, 1021, 1973

REQUEST FOR LITERATURE SHOULD BE MADE TO:
Product Marketing Department
Fax: 03-3544-0989
Nikken Chemicals Co., Ltd.
12-6, Tsukiji 1-chome, Chuo-ku, Tokyo, 104-0045

Manufactured by:
Nikken Chemicals Co., Ltd.
12-6, Tsukiji 1-chome, Chuo-ku, Tokyo, 104-0045

BRAND NAMES IN OTHER COUNTRIES
KALIMATE (Taiwan, Thailand, Malaysia)
KALIMATE, KALITAKER (Korea)
KALITAKE (Indonesia)