- MUCOREGLATING drug-

MUCODYNE®DS (Dry Syrup) 50%
<L-Carbocisteine>

**CONTRAINDICATIONS (MUCODYNE®DS 50% is contraindicated in the following patients.)**
Patients with a history of hypersensitivity to the drug

**DESCRIPTION**

Product description

<table>
<thead>
<tr>
<th>Ingredient content</th>
<th>L-Carbocisteine 500 mg: The Japanese Pharmacopoeia (JP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive ingredient</td>
<td>Hydrogenated maltose starch syrup powder, D-mannitol, croscarmellose sodium, sodium carboxymethyl starch, Hydrated silicon dioxide, Aspartame (L-phenylalanine compound), hydroxypropylcellulose, flavor</td>
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<tr>
<td>Dosage form</td>
<td>Dry Syrup</td>
</tr>
<tr>
<td>Color</td>
<td>white granular powder</td>
</tr>
<tr>
<td>Identification code</td>
<td>KP-364(package)</td>
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</tbody>
</table>

**INDICATIONS**

For adults

Expectoration for the following diseases:
- Upper respiratory inflammation (pharyngitis, laryngitis), acute bronchitis, bronchial asthma, chronic bronchitis, bronchiectasis and pulmonary tuberculosis.
- Drainage in chronic sinusitis

For children

Expectoration for the following diseases:
- Upper respiratory inflammation (pharyngitis, laryngitis), acute bronchitis, bronchial asthma, chronic bronchitis, bronchiectasis and pulmonary tuberculosis.
- Drainage in chronic sinusitis.
- Drainage in otitis media with effusion.

**DOSAGE AND ADMINISTRATION**

**For adults**

For oral use, the usual dose for adults is 500 mg of L-carbocisteine (1.0g of MUCODYNE®DS 50%) three times daily. MUCODYNE®DS 50% should be suspended immediately before use. The dose may be adjusted according to age and symptoms.

**For children**

For oral use, the usual dose for children is 10 mg/kg of L-carbocisteine (0.02g/kg of MUCODYNE®DS 50%) three times daily. MUCODYNE®DS 50% should be suspended immediately before use. The dose may be adjusted according to age and symptoms.

**PRECAUTIONS**

1. **Careful Administration (These products should be administered with care in the following patients.)**
   1) Patients with hepatic dysfunction
   [Hepatic dysfunction may be exacerbated.]
   2) Patients with heart failure
   [It has been reported that analogous drugs affected the symptoms with heart failure.]

2. **Adverse Reactions**

   Adverse reactions to these products were reported in 101 of 11,066 patients treated (0.91%). The most frequently observed adverse reactions were anorexia in 27 patients (0.24%), diarrhea in 19 patients (0.17%), abdominal pain in 15 patients (0.14%), and rash in 11 patients (0.10%). (at the approval of MUCODYNE®DS 50% as adding dosage form). Above incidence have been collected from the reports of Mucodyne® Tablets 250mg, Tablets 500 mg, Fine granules 50%, K10, Syrup 2%, Syrup 5%, DS 33.3% and DS 50%.

   (1) **Clinically significant adverse reactions**
1) Oculomucocutaneous syndrome (Stevens-Johnson syndrome), toxic epidermal necrolysis (Lyell syndrome)

Oculomucocutaneous syndrome (Stevens-Johnson syndrome) and toxic epidermal necrolysis (Lyell syndrome) may occur. Patients should be carefully monitored. If any abnormal findings are observed, administration should be discontinued and appropriate measures must be taken.

2) Hepatic dysfunction, Jaundice

Hepatic dysfunction with increased AST (GOT), ALT (GPT), Al-P, LDH and/or jaundice may occur. Patients should be carefully monitored. If any symptoms are observed, administration should be discontinued and appropriate therapeutic measures must be taken.

3) Shock, anaphylactoid symptoms

Patients should be observed carefully because shock and anaphylactoid symptoms (such as dyspnoea, edema, urticaria, etc.) may occur. If any of abnormal findings are observed, administration should be discontinued and appropriate therapeutic measures must be taken.

(2) Other adverse reactions

<table>
<thead>
<tr>
<th>(%)</th>
<th>Incidence unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% &gt; 0.1%</td>
<td>&lt;0.1%</td>
</tr>
</tbody>
</table>

Gastro-intestinal
Anorexia, diarrhea, abdominal pain
Nausea, vomiting, abdominal distension, thirst etc.

Hypersensitivity
Rash
Eczema, erythema etc.

Edema, fever, dyspnea

Others
Itching

#: If any hypersensitive reactions are observed, administration of the drug should be discontinued.

3. Use in the Elderly

Since elderly patients have often reduced physiological function, careful supervision and measurement, such as reducing the dose are recommended.

4. Use during Pregnancy, Delivery or Lactation

Use of these products is not recommended in pregnant women or in women who may possibly be pregnant. [The safety of these drugs in pregnant women has not been established.]

5. Precautions concerning use

At the time of compounding
Don’t dispense drug as suspension.

Precautions regarding dispensing
Instruct the patient to take drug promptly after suspension of it.

PHARMACOKINETICS

Blood concentrations

Plasma concentrations and pharmacokinetic parameters for L-carbocisteine after single oral dose of 1.0g Mucodyne DS 50% which contains 500 mg of L-carbocisteine to the healthy adults are shown below.

![Fig. Plasma concentrations (Healthy adults)](image)

PHARMACOLOGY

1. Effect on respiratory tract

1) Normalizing effect on mucous components

L-Carbocisteine normalizes the ratio of sialic acid and fucose in spumum in patients with chronic airway deseases. L-Carbocisteine normalizes sulfur dioxide exposure-induced changes in activity of sialic acid/fucose-splitting enzyme and sialic acid/fucose synthase. At the same time, L-Carbocisteine inhibits the increase of mucin (Muc-5ac protein) production, which is the primary component of mucus secreted in rats.
Kyorin Pharmaceutical Co., Ltd.

2) Inhibitory effect on hyperplasia of goblet cells
L-Carbocisteine inhibits goblet cell hyperplasia of airway mucosa on histologic examination of patients with chronic airway diseases.4) L-Carbocisteine inhibits hyperplasia of goblet cells in the airways of rats exposed to sulfur dioxide.5)

3) Inhibitory effect on airway inflammation
L-Carbocisteine inhibits sulfur dioxide exposure-induced inflammatory cell infiltration, superoxide and elastase activity in rat airways .5(6) L-Carbocisteine inhibits human neutrophil activation mediated by fMLP.7)

4) Repairing effect on mucosa
L-Carbocisteine helps ciliated cells to be repaired in bronchiolar mucosal epithelium of patients with chronic bronchitis.8)

2. Effect on sinus
1) Improving effect on mucociliary transport
L-Carbocisteine improves the nasal mucociliary clearance which have been reduced in patients with chronic sinusitis.9)

2) Repairing effect on mucosa
L-Carbocisteine relieves the damages on sinusal mucosa induced by endotoxin or sulfur dioxide and promotes mucosal repairing in rabbits.10(11)

3. Effect on middle ear
1) Improving effect on mucociliary transport
L-Carbocisteine improves the salpingo-mucociliary clearance in patients with otitis media with effusion.12)

2) Repairing effect on mucosa
L-Carbocisteine relieves the damages on middle ear mucosa induced by sulfur dioxide (rabbits)13) or nitrogen dioxide (guinea pigs)14) and promotes mucosal repairing.

3) Excretion promoting effect on middle ear
L-Carbocisteine promotes excretion of the effusion on middle ear induced by sulfur dioxide (rabbits)13) or nitrogen dioxide (guinea pigs)14) in the animal models of otitis media with effusion.

4) Inhibitory effect on inflammation
L-Carbocisteine suppress superoxide production of neutrophil in the models of otitis media with effusion (guinea pigs).15)

PHYSICOCHEMISTRY
Nonproprietary name: L-Carbocisteine [JAN]
Chemical name:
(2R)-2-Amino-3-carboxymethylsulfanylpropanoic acid
Molecular formula: C₉H₁₄N₂O₄S
Molecular weight: 179.19
Structural formula:

\[
\text{HO}_2\text{C} \quad \text{S} \quad \text{CO}_2\text{H} \\
\text{N}_\text{H}_2
\]

Melting point: Approx. 186 °C (Decomposition)
Description:

White crystalline powder, odorless and slightly acidic in taste.
Very slightly soluble in water and practically insoluble in ethanol (95).
Dissolve in dilute hydrochloric acid solution and sodium hydroxide solution.
Partition coefficient:
0.0 (1-octanol/water system, pH 2.3 - 8.0, 20°C).

PACKAGING
MUCODYNE DS 50%
Boxes of 120 packets (1.0 g×120 packets).
Bottles of 100 g, and bottles of 500 g.

REFERENCES
1) Fujita M.: Bioequivalence study of L-Carbocisteine DS 50% (In-house Data)
10) Macyama T. et al.: OTO-RHINO-LARYNGOLOGY TOKYO, 29 (Suppl. 6), 447, 1986

REQUEST FOR LITERATURE SHOULD BE MADE TO:
A request for in-house data mentioned in the References can also be made to the following.
Kyorin Pharmaceutical Co., Ltd. Drug Information Center
6, Kanda surugadai 4-chome, Chiyoda-ku, Tokyo 101-8311, Japan
Tel. 0120-409-341 (Toll-free)
9:00 to 17:30 (Monday through Friday exclusive of national holidays)

Manufactured and marketed by:
Kyorin Pharmaceutical Co., Ltd.
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