TOWA PHARMACEUTICAL CO., LTD.

Revised: September 2009 (11th version, amendment in the Pharmaceutical Affairs Law (abolition of the term of "Designated drug"), change of trade name, etc.)
Revised: June 2008

Agent for hepatic disease and allergy
Prescription-only drug*

LEMIGEN® INTRAVENOUS INJECTION 20mL

Storage:
Store at room temperature.
Expiration date:
Indicated on the package and ampoule.

Standard Commodity Classification No. of Japan	873919 87449
Approval No.	22100AMX01202
Date of listing in the NHI reimbursement price	September 2009
Date of initial marketing in Japan	June 1990

* Caution - Use only pursuant to the prescription of a physician, etc.

CONTRAINDICATIONS (LEMIGEN is contraindicated in the following patients.)

1) Patients with a history of hypersensitivity to any of the ingredients of this product.
2) Patients with aldosteronism, myopathy or hypokalemia [This product may aggravate hypokalemia, hypertension, etc.]

DESCRIPTION

Volume of ampoule	20 mL
Active ingredients per ampoule	Monoammonium Glycyrrhizinate (As Glycyrrhizin ····· 40 mg) Glycine (JP) ····· 400 mg L-Cysteine (JP) (As L-Cysteine Hydrochloride ····· 20 mg)
Inactive ingredients	Dried Sodium Sulfite ····· 20 mg Sodium Chloride, pH adjusting agents (Hydrochloric Acid, Sodium Hydroxide)
Product description	Clear and colorless injection
pH	6.0 – 7.5
Osmotic pressure ratio	About 1.5 (ratio to isotonic sodium chloride solution)

INDICATIONS

Infant strophulus, eczema or dermatitis, urticaria, pruritus, stomatitis, phlycten, drug eruption or toxic eruption
Improvement of abnormal hepatic function in chronic hepatic disease

DOSAGE AND ADMINISTRATION

The usual adult dosage for intravenous injection is 5 – 20 mL once daily.
The dosage may be adjusted according to the patient's age and symptoms.
For chronic hepatic disease, the usual adult dosage for intravenous injection or drip infusion is 40 – 60 mL once daily.
The dosage may be adjusted according to the patient's age and symptoms. Dosage may be increased up to 100 mL per day.

PRECAUTIONS

1. Careful Administration (LEMIGEN should be administered with care in the following patients.)

Elderly patients [The incidence of hypokalemia, etc. is high.] (See "Use in the Elderly")

2. Important Precautions

1) To predict development of shock, etc., the patients should be carefully examined.
2) Emergency facilities should surely be prepared beforehand for development of shock, etc.
3) After administration of this product, patients should be kept at rest and under adequate supervision.
4) Caution should be exercised in coadministering preparations containing glycyrrhizae radix because overlap with glycyrrhizin of this product may cause pseudoaldosteronism.

3. Drug Interactions

Precautions for coadministration (LEMIGEN should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms and Treatment	Mechanism and Risk Factors
Loop diuretics Etacrynic acid Furosemide, etc. Thiazide and thiazide-like hypotensive diuretics Trichlormethiazide Chlortalidone, etc.	Hypokalemia (weakness, muscle weakness, etc.) may occur. Caution should be exercised including observation (such as monitoring serum potassium level).	These diuretic actions enhance potassium excretion of glycyrrhizin, a component of this product, and decrease of serum potassium level is likely to occur.
Moxifloxacin hydrochloride	Ventricular tachycardia (including Torsades de pointes) and QT prolongation may develop.	Decrease in serum potassium level due to potassium excretion effect of this product may induce ventricular tachycardia (including Torsades de pointes) and QT prolongation by moxifloxacin hydrochloride.

4. Adverse Reactions

No investigation such as a drug use investigation clearly showing the incidence of adverse reactions has been conducted.

1) **Clinically significant adverse reactions (incidence unknown)**
   (1) **Shock, anaphylactic shock**: Shock or anaphylactic shock (decreased blood pressure, loss of consciousness, dyspnea, cardio-respiratory arrest, flushing, facial edema, etc.) may occur. Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be immediately discontinued and appropriate measures should be taken.
   (2) **Anaphylactoid reaction**: Anaphylactoid reaction (dyspnea, flushing, facial edema, etc.) may occur.

Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be immediately discontinued and appropriate measures should be taken.

(3) **Pseudoaldosteronism**: Dose increase or long-term continuous use may cause pseudoaldosteronism such as increase in incidence of severe hypokalemia and hypokalemia, elevated blood pressure, retention of sodium and body fluid, edema, and weight increase. Caution should be exercised including observation (such as monitoring serum potassium level), and if any abnormalities are observed, administration of this product should be discontinued.
As a result of hypokalemia, weakness, muscle weakness, etc. may occur.

2) Other adverse reactions
The following symptoms may occur, and there is a tendency toward increase in incidence of decrease of serum potassium level and elevated blood pressure due to dose increase.

	Incidence unknown
Hypersensitivity	Rash, urticaria, pruritus
Body fluid and Electrolytes	Decrease of serum potassium level, edema
Cardiovascular	Elevated blood pressure
Gastrointestinal	Upper abdominal discomfort, nausea or vomiting
Respiratory	Cough
Ophthalmic	Transient paraesthesia (blear eyes, irritated eyes, etc.)
Others	General malaise, myalgia, dysesthesia (numbness, tingling sensation, etc.), fever, hyperpnea (burning sensation of shoulders, coldness of limbs, cold sweat, thirst, palpitations), urine sugar positive, headache, feeling of warmth, feeling poorly

5. Use in the Elderly

Since there is a tendency toward increase in incidence of adverse reactions such as hypokalemia in elderly patients in clinical experiences, this product should be carefully administered with close monitoring of the patient's conditions.

6. Use during Pregnancy, Delivery or Lactation

The safety of this product in pregnant women, etc has not been established. This product should be used in these patients only if the expected therapeutic benefits outweigh the possible risks associated with treatment. [Animal studies (in rats) have shown that administration of monoammonium glycyrrhizinate in large doses results in kidney malformation, etc.]

7. Precautions Concerning Use

1) Rate of injection: The rate of intravenous administration should be slow to the extent possible, with monitoring of the patient's conditions.

2) Precautions when opening the ampoule: A "one-point-cut ampoule" is used for this product." To avoid contamination with foreign substances, it is recommended to wipe the tip off with an alcohol swab before opening the ampoule and break off the tip.

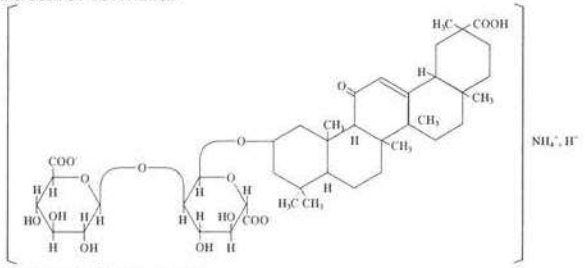
8. Other precautions

Rhabdomyolysis has been reported by oral administration of preparations of glycyrrhizin or glycyrrhizae radix.

PHYSICOCHEMISTRY

1. Monoammonium Glycyrrhizinate

Structural formula:



Nonproprietary name:
Monoammonium Glycyrrhizinate

Chemical name:
Monoammonium of 20β-carboxy-11-oxo-30-norolean-12-en-3β-yl-2-O-β-D-glucopyranuronosyl-β-D-glucopyranosiduronic acid

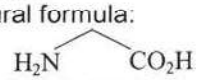
Molecular formula:
$C_{42}H_{65}NO_{16}$

Molecular weight:
839.96

Description:
Monoammonium glycyrrhizinate occurs as white fine crystals or crystalline powder. It is odorless and has a characteristic sweet taste.

2. Glycine

Structural formula:



Nonproprietary name:
Glycine

Chemical name:
Aminoacetic acid

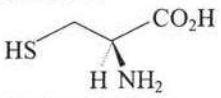
Molecular formula:
$C_2H_5NO_2$

Molecular weight:
75.07

Description:
Glycine occurs as white crystals or crystalline powder. It is odorless. It has a sweet taste.
It is freely soluble in water and in formic acid, and practically insoluble in ethanol (95).
Dissolve 1.0 g of Glycine in 20 mL of water: the pH of the solution is between 5.6 and 6.6.

3. L-Cysteine

Structural formula:



Nonproprietary name:
L-Cysteine

Chemical name:
(2*R*)-2-Amino-3-sulfanylpropanoic acid

Molecular formula:
$C_3H_7NO_2S$

Molecular weight:
121.16

Description:

L-Cysteine occurs as white crystals or white crystalline powder. It has a characteristic odor and a pungent taste.
It is freely soluble in water, and practically insoluble in ethanol (99.5).
It dissolves in 1 mol/L hydrochloric acid TS.

PRECAUTIONS FOR HANDLING

1. Precautions
A "one-point-cut ampoule" is used for this product. Break off the tip of the ampoule by pressing it in the direction opposite to that of the round mark.

2. Stability test
In an accelerated test using final packaged products (at 40°C for 6 months), LEMIGEN INTRAVENOUS INJECTION 20mL was estimated to be stable for 3 years under normal distribution conditions[1)].

PACKAGING

LEMIGEN INTRAVENOUS INJECTION 20mL:
Boxes of 20 mL x 50 ampoules

REFERENCES

1) Internal data of Towa Pharmaceutical Co., Ltd.: Stability test

Manufacturer and Distributor
TOWA PHARMACEUTICAL CO., LTD.
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