Pharmaceuticals and Medical Devices Safety Information

No. 208 December 2004

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This translation of the original Japanese text is for information purpose only (in the event of inconsistency, the Japanese text shall prevail).

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Important Safety Information

This section presents contents of revisions, reference materials, and a case summary that served as the basis for these revisions to important adverse reactions included under the PRECAUTIONS section of package inserts of drugs that have been revised in accordance with the Notification after the previous bulletin (Pharmaceuticals and Medical Devices Safety Information No. 207).

1 Interferon Alfa (NAMALWA)

Brand Name (name of company)	Sumiferon 300 and 600, Sumiferon 900 for Injection, Sumiferon DS300 and DS600 (Sumitomo Pharmaceuticals Co., Ltd.)
Therapeutic Category	Biological preparations-Miscellaneous
Indications	(Sumiferon 300 and 600, Sumiferon DS300 and DS600) ○ Renal cancer,, multiple myeloma, hairy cell leukaemia ○ Chronic myeloid leukaemia ○ Improvement of viraemia in chronic active hepatitis B with positive status for HBe-antigen and DNA polymerase ○ Improvement of viraemia in chronic hepatitis C (excluding the cases with higher blood HCV-RNA load) (Sumiferon 300) ○ Suppression of progress of clinical symptoms by Sumiferon combined with Inosine Pranobex in subacute sclerosing panencephalitis (Sumiferon 300, Sumiferon DS300) ○ HTLV-I associated myelopathy (HAM) (Sumiferon 900 for Injection) ○ Improvement of viraemia in chronic hepatitis C (excluding the cases with higher blood HCV-RNA load)

<<**PRECAUTIONS** (underlined parts are additions)>>

[Adverse Reactions (clinically significant adverse reactions)]	**Severe infection such as sepsis, pneumonia etc.:** Severe infection such as sepsis, pneumonia etc. may occur in easily infectious case. The patient's general conditions should be carefully monitored. If abnormalities are observed, administration should be discontinued. **Aseptic meningitis [In case for subacute sclerosing panencephalitis by intrathecal (or intraventricular) administration]:** Pyrexia, headache, nausea and vomiting, consciousness clouding, cerebrospinal fluid cell count increased, cerebrospinal fluid protein increased, etc. may become severe and prolong. The patient should be carefully monitored and appropriate measures such as dose reduction or cessation of the drug should be taken, if abnormalities are observed.
<Reference Information>	Company report

Case Summary

No.	Patient		Daily dose/ Treatment duration	Adverse reactions	Remarks
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures	
1	Male 60s	Chronic hepatitis C (hypertension)	6000000 IU 68 days ↓ 6000000 IU (3 times/ week) 87 days	**Pneumonia** On day 1 of administration: Daily administration of this drug was started. White blood cell was 5700/mm^3. On day 69 of administration: Administration was switched to alternate-day administration of this drug. On day 144 of administration: White blood cell was 4200/mm^3. On day 153 of administration: Pyrexia of 40ºC level developed. On day 155 of administration (day of discontinuation): Body temperature had dropped, and this drug was administered. Later, pyrexia of 39.7°C developed. Pyrexia persisted thereafter. 4 days after discontinuation: The patient was emergently hospitalized. White blood cell was 17300/mm^3, CRP was 28.9 mg/dL. Pneumonia of the right upper lung was found by chest X-ray. Drip infusion of piperacillin sodium at 4g and amikacin sulfate at 400 mg was started. 5 days after discontinuation: White blood cell was 13800/mm^3, CRP was 26.1 mg/dL. 6 days after discontinuation: Pyrexia tended to be alleviated. 9 days after discontinuation: The body temperature returned to normal. 13 days after discontinuation: CRP was 0.3 mg/dL and white blood cell was 4000/mm^3, inflammatory reaction disappeared, and X-ray images improved. 22 days after discontinuation: The patient was discharged from the hospital.	Company report
	Concomitant medications: nisoldipine, gastritis and peptic ulcer drug, indometacin				

No.	Patient		Daily dose/ Treatment duration	Adverse reactions	Remarks
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures	
2	Male 20s	Subacute sclerosing panencephalitis (osteoporosis)	3000000 IU (2 times/week~ once/3 weeks) 7 years 11 months ↓ (drug cessation for 53 days) ↓ 600000 IU 1 day ↓ 3000000 IU 1 day	**Meningitis aseptic** The patient's academic ability was started to decline from around 8 years and 8 months before administration. Convulsive seizures developed 8 years and 1 month before administration and the patient was hospitalized. He was diagnosed with subacute sclerosing panencephalitis (SSPE). On day 1 of administration: Intraspinal administration of this drug was started. On day 38 of administration: Route of administration was switched to intraventricular administration. In the 2nd month of administration: Until this time, symptoms rapidly progressed and the patient became bedridden. There was no progression of symptoms thereafter. In the 7 years and 11th month of administration (day of discontinuation): After administration of 3000000 UI of this drug, pyrexia of 38°C level developed. Normally pyrexia would decline after 1-2 days, but did not decline. Administration of this drug was suspended. 4 days after discontinuation: The patient visited this hospital for pyrexia of 40°C. Although blood tests were conducted, no abnormalities were confirmed. Mild redness of pharynx was confirmed. Quick inspection for influenza was negative. The patient was prescribed antibiotics (clarithromycin) for 5 days. 7 days after discontinuation: Pyrexia of 39°C level continued. Although blood tests were reconducted, there were no other abnormality other than hepatic function abnormal [AST (GOT) 103 IU/L, ALT (GPT) 78 IU/L]. 10 days after discontinuation: Pyrexia of 39°C level continued. Myoclonus of the left lower limb started to become conspicuous. Liver disorder [AST (GOT) 90 IU/L, ALT (GPT) 97 IU/L] was observed. The patient was diagnosed with meningitis aseptic based on cerebrospinal fluid examination [cerebrospinal fluid cell count 209/3/mm^3 (CSF monocyte count 204/3/mm^3, CSF polymorphonuclear cell count 5/3/mm^3) cerebrospinal fluid protein 12 mg/dL, cerebrospinal fluid glucose 52 mg/dL, cerebrospinal fluid Cl 122 mEq/L]. Intraventricular injection of hydrocortisone sodium succinate at 50 mg was conducted. Later, pyrexia dropped to around 38°C for 3-4 days, then rose to 39°C 16 days after discontinuation. After the 17 and 18 days after discontinuation, tendency toward slight reduction was indicated in pyrexia.	Company report

				18 days after discontinuation: Pyrexia of 37°C level developed. Improving tendency was confirmed in both liver disorder [AST (GOT) 57 IU/L, ALT (GPT) 79 IU/L] and spinal fluid findings. Meningitis aseptic improved. 40 days after discontinuation: Spinal fluid findings normalized. 54 days after discontinuation (on day 1 of readministration): Intracerebroventricular administration of 600000 IU of this drug was conducted. On day 22 of readministration (day of discontinuation of readministration): Intracerebroventricular administration of 3000000 IU of this drug was conducted. Pyrexia of 38°C level developed during the night and meningitis aseptic recurred (symptoms: cerebrospinal fluid cell count increased, pyrexia). Administration of this drug was discontinued. 70 days after discontinuation: Cerebrospinal fluid cell count was decreased and meningitis aseptic improved.	
	Concomitant medications: phenytoin, inosine pranobex, sodium valproate, clonazepam				

Clinical Laboratory Values

	In the 7 years and 11th month of administration (day of discontinuation)	10 days after discontinuation	18 days after discontinuation	40 days after discontinuation	6 days after discontinuation of readministration	23 days after discontinuation of readministration	35 days after discontinuation of readministration	49 days after discontinuation of readministration	70 days after discontinuation of readministration
Cerebrospinal fluid cell count (/mm^3)	4/3	209/3	80/3	10/3	54/3	118/3	54/3	13/3	7/3
Cerebrospinal fluid monocyte count (/mm^3)	4/3	204/3	67/3	9/3	52/3	90/3	52/3	12/3	6/3
Cerebrospinal fluid polymorphonuclear cell count (/mm^3)	0/3	5/3	13/3	1/3	2/3	28/3	2/3	1/3	1/3
Cerebrospinal fluid protein (mg/dL)	11	12	4	7	6	9	9	7	5
Cerebrospinal fluid glucose (mg/dL)	74	52	48	62	54	56	56	60	60

2 Telithromycin

Brand Name (name of company)	Ketek Tablets 300 mg (Aventis Pharma Limited)
Therapeutic Category	Acting mainly on gram-positive bacteria and mycoplasma
Indications	<Susceptible strains> Bacterial strains susceptible to this drug include *staphylococcus*, *streptococcus*, *pneumococcus*, *moraxella* (*branhamella*) *catarrhalis*, *haemophilus influenza*, *legionella*, *peptostreptococcus*, *prevotella*, *hlamydia pneumoniae*, and *mycoplasma pneumoniae* <Indications> Laryngopharyngitis, tonsillitis, acute bronchitis, pneumonia, secondary infection of chronic respiratory lesion, sinusitis, periodontitis, pericoronitis, jaw inflammation

<<**PRECAUTIONS** (underlined parts are additions)>>

[Important Precautions] As loss of consciousness, optical accommodation disorder, vision blurred, etc. may occur. Patients should be cautioned against operating machines with hazardous activities such as driving a car.

[Adverse Reactions (clinically significant adverse reactions)]

Loss of consciousness: Loss of consciousness may occur. Discontinue administration and take appropriate measures in such a case.

Hepatic function disorder, jaundice: Hepatic function disorder with such as significant elevation of AST (GOT), ALT (GPT), Al-P levels and jaundice may occur. Patients should be carefully monitored and if abnormalities are observed, discontinue administration and take appropriate measures.

<Reference Information> Company report

Case Summary

No.	Patient		Daily dose/ Treatment duration	Adverse reactions	Remarks
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures	
1	Male 70s	Acute laryngopharyngitis (cervical lymphadenitis)	600 mg 2 days	**Fainting with loss of consciousness** Patients with allergic constitution (rhinitis allergic). On day 1 of administration: The patient was examined in the morning and 600 mg of this drug was prescribed for acute laryngopharyngitis. Administration of this drug was conducted after lunch. Approx. 4 hours later, fainting with loss of consciousness (fall) occurred. The patient was recovered the same day. Although the patient's head was bruised, he does not remember the fact of fall. On day 2 of administration (day of discontinuation): The patient was examined in the morning. He did not report the previous day's fainting with loss of consciousness because he did not believe the oral dosing of this drug as the cause of the incident. Administration of this drug was conducted after lunch. Approx. 4 hours later, the patient suffered seizure and fell down at the foyer of his home. The patient was transported to another hospital by ambulance. Although the patient's head was examined in detail, no abnormalities were found. The patient recovered the same day. Administration of this drug was discontinued.	Company report
	Concomitant medications: none				

No.	Patient		Daily dose/ Treatment duration	Adverse reactions	Remarks
	Sex/ Age	Reason for use (complications)		Clinical course and therapeutic measures	
2	Male 20s	Bronchitis (none)	600 mg 5 days	**Hepatic function disorder** On day 1 of administration: The patient was examined for cough and sputum. He was diagnosed with acute bronchitis and administration of this drug, carbocisteine, dextromethorphan hydrobromide was started. On day 5 of administration (day of completion of administration): Administration of this drug was completed in 5 days. Administration of the other drugs was continued. 12 days after completion: Increase in AST (GOT) and ALT (GPT) was confirmed by blood test, and pyrexia was noted. 13 days after completion: Although no abnormalities were confirmed through ultrasound and CT scan, AST (GOT) and ALT (GPT) values further increased to 398 IU/L and 574 IU/L, respectively in blood test. The patient was hospitalized. The patient was treated with bed rest, drip infusion, and liver supporting therapy. As cough was persistent, administration of carbocisteine and dextromethorphan hydrobromide was continued. 19 days after completion: The patient was gradually improved from hepatic function disorder and was discharged. Liver supporting therapy was continued as out-patient. 32 days after completion: The patient recovered. Drinking history: none OTC drugs: none Hepatitis viral test (13 days after completion): HBsAg (–), HCV-Ab (–) Autoantibody test (14 days after completion): antinuclear antibody (–), antimitochondrial antibody (–)	Company report
	Concomitant medications: carbocisteine, dextromethorphan hydrobromide				

Clinical Laboratory Values

	12 days after completion	13 days after completion	14 days after completion	17 days after completion	32 days after completion
AST (GOT) (IU/L)	166	398	325	110	38
ALT (GPT) (IU/L)	220	574	597	348	71
Al-P (IU/L)	322	298	264	277	450
LDH (IU/L)	280	591	405	202	142
γ-GTP (IU/L)	20	20	28	37	39
Total bilirubin (mg/dL)	--	0.5	0.8	0.5	0.3

AST: Asparate Aminotransferase
ALT: Alanine Aminotransferase
Al-P: Alkaline Phosphatase
LDH: Lactate Dehydrogenase
γ-GTP: γ-Glutamyltranspeptidase

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Revision of PRECAUTIONS

(No. 161)

This section presents details of revisions to the PRECAUTIONS section of package inserts and brand names of drugs that have been revised according to the Notifications after the previous bulletin (Pharmaceuticals and Medical Devices Safety Information No. 207) (excluding those presented in "1. Important Safety Information" of this Bulletin), together with reference materials.

1 <Psychotropics> Amitriptyline Hydrochloride

[Brand Name]	Tryptanol Tablets-10 and 25 (Banyu Pharmaceutical Co., Ltd.), and others
[Contraindications]	Patients with urinary retention (prostate disease etc.)
[Important Precautions]	Withdrawal symptoms such as queasy, headache, malaise, irritability, emotional instability, and sleep disorder may occur due to a dramatic decrease in dosage or discontinuation of administration. Discontinuation of administration should be carefully carried out by tapering off, etc.
[Adverse Reactions (clinically significant adverse reactions)]	**Serotonin syndrome:** Serotonin syndrome with major symptoms of anxiety, irritation, delirium, excitement, pyrexia, sweaty, tachycardia, tremor, myoclonus, hyperreflexia, and diarrhoea etc. may occur. If such symptoms occur, discontinue administration, implement whole body control such as fluid intake, and take appropriate measures. **Hallucination, delirium, mental confusion, convulsion:** If such symptoms occur, take appropriate measures such as tapering off or suspending administration.
<Reference Information>	Company report

2 <Cardiovascular agents-Miscellaneous> Sevelamer Hydrochloride

[Brand Name]	Phosblock Tablets 250 mg (Kirin Brewery Company, Limited), Renagel Tablet 250 mg (Chugai Pharmaceutical Co., Ltd.)
[Careful Administration]	Patients with intestinal diverticulum. Patients with a history of abdominal surgery.
[Important Precautions]	Since intestinal perforation or bowel obstruction may occur, pay careful attention to the following points. 1) Prior to the use of this drug, the patient's daily bowel movement should be confirmed. 2) If any symptoms such as aggravated constipation or feeling of abdominal distention etc. are observed after the administration of this drug, appropriate measures such as reduction in dosage or withdrawal of this drug should be taken as needed. Especially, if any abnormalities including severe constipation, sustaining abdominal pain or vomiting, etc. are observed, the administration should be discontinued as soon as possible, and examination of abdomen or diagnostic imaging (plain radiography, echography, CT scan, etc.) should be made, and appropriate measures should be taken.

3) Instruct the patient to confirm the daily bowel movement and consult with a physician if any symptoms such as aggravated constipation or feeling of abdominal distention etc. are observed.

[Adverse Reactions (clinically significant adverse reactions)]

Diverticulitis, ischemic enterocolitis: Since diverticulitis and/or ischemic enterocolitis may occur, patients should be carefully monitored. If any abnormalities are observed, this drug should be discontinued and appropriate measures should be taken to prevent progression of these pathologic conditions and leading severe condition including intestinal perforation.

Gastrointestinal haemorrhages, gastrointestinal ulcers: Since hematemesis, melena, and gastric, duodenal, colon, rectum ulcers etc. may occur, patients should be carefully monitored. If any of these pathologic conditions are suspected, appropriate measures such as discontinuation of administration should be taken.

Hepatic dysfunction: Hepatic dysfunction with marked elevations of AST(GOT), ALT (GPT), and γ-GTP may occur.Patients should be carefully monitored. If any abnormalities are observed, appropriate measures such as discontinuation of administration should be taken.

<Reference Information> Company report

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3 <Antidiabetic agents> Mitiglinide Calcium Hydrate

[Brand Name] Glufast Tab. 5 mg and 10 mg (Kissei Pharmaceutical Co., Ltd.)

[Adverse Reactions (clinically significant adverse reactions)]

Hepatic dysfunction: Hepatic dysfunction with marked elevations of AST (GOT), ALT (GPT), or γ-GTP may occur. Patients should be carefully monitored. If abnormalities are observed, administration should be immediately discontinued, and appropriate measures should be taken

<Reference Information> Company report

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4 <Miscellaneous metabolism agents> Gabexate Mesilate

[Brand Name] FOY for Injection, FOY for Injection 500 (Ono Pharmaceutical Co., Ltd.), and others

[Adverse Reactions (clinically significant adverse reactions)]

White blood cell decrease, platelets decreased: White blood cell decreased and platelets decreased may occur. If abnormalities are observed, administration should be discontinued.

Hyperkalaemia: Hyperkalaemia may occur. If any abnormalities are observed, administration should be discontinued immediately and appropriate measures be taken.

<Reference Information> Company report

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5 <Antineoplastics-Miscellaneous> Rituximab (Genetical recombination)

[Brand Name] Rituxan Injection 10 mg (Zenyaku Kogyo Co., Ltd.)

[Important Precautions] Re-inflammation of hepatitis may occur when hepatitis B virus carrier patients are treated with this drug, especially in patients with concomitant use of chemotherapy for cancer. When administering this drug in patients infected with or suspected to be infected with the hepatitis B virus, patients should be carefully monitored during or after the treatment period by monitoring hepatic function tests values and hepatitis virus markers. If abnormalities are observed, appropriate measures such as administrating antiviral drugs should be taken.

[Adverse Reactions (clinically significant adverse reactions)]

Pancytopaenia, white blood cell decreased, neutropaenia, platelets decreased: Serious haematocytopenia may occur, and as there have been reports of neutropaenia occurred 4 weeks and more after the final administration of this drug, patients should be carefully monitored during and after the treatment period of this drug such as conducting periodic blood tests. If abnormalities are observed, appropriate measures such as suspending administration etc. should be taken. Caution should be exercised as serious haematocytopenia may be complicated with infection (sepsis, pneumonia, etc.).

Hepatic function disorder, jaundice: Hepatic function disorder with elevation of values of liver function test such as AST (GOT), ALT (GPT), Al-P, and total bilirubin and jaundice may occur. Patients should be carefully monitored through liver function tests etc. If abnormalities are observed, appropriate measures should be taken. Caution should be exercised as there have been reports of patients infected with hepatitis B virus causing re-inflammation of hepatitis after the administration of this drug and resulting in death due to hepatic failure.

<Reference Information>

Company report

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6 <Acting mainly on gram-positive bacteria> Vancomycin Hydrochloride (injectable dosage form)

(not having effect on preparation for sepsis, pneumonia, purulent meningitis due to penicillin-resistant streptococcus pneumoniae (PRSP) sensitive to vancomycin)

[Brand Name]

Vancomycin for Intravenous Infusion 0.5 g "Merck" (Merck Hoei Ltd.), Storacin for Intravenous Injection 0.5 g (Mercian Corporation), Solrein for Intravenous Infusion 0.5 g (Towa Pharmaceutical Co., Ltd.), Vancomycin for I.V. Infusion 0.5 "MEEK" (Kobayashi Kako Co., Ltd.), Vanmycin for Intravenous Infusion 0.5 g (Nichi-iko Pharmaceutical Co., Ltd.)

[Warning]

WARNING

To prevent bacterial resistance to this drug, make efforts toward the proper use of this drug after carefully reading the section "Precautions of Dosage and Administration".

[PRECAUTIONS of Indications]

Eight clinical nerve neuropathy such as hypoacusis and deafness etc., as well as sequela from purulent meningitis such as hearing impaired may occur as adverse reactions of this drug. Caution should be exercised in the selection of applicable patients, particularly for children etc., and administer the drug with care.

[Precautions of Dosage and Administration]

Caution should be exercised for the following points to prevent bacterial resistance in the use of this drug.

1) Administration should be conducted under supervision of a physician with sufficient knowledge and experience for treatment of infections or under the direction of such physician.
2) As a general rule, patient's sensitivity to this drug and other antibacterial drugs should be confirmed.
3) Treatment period should be limited to the minimum required to treat the disease, after considering the infection site, severity, patient symptoms etc., and determine whether continuous administration of this drug is necessary at an appropriate time.

<Reference Information>

Company report

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7 <Acting mainly on gram-positive bacteria> Vancomycin Hydrochloride (oral dosage form)

[Brand Name]

Vancomycin Hydrochloride Powder (Eli Lilly Japan K.K.)

[Warning]

WARNING

To prevent bacterial resistance to this drug, make efforts toward the proper use of this drug after carefully reading the section "Precautions of Dosage and Administration".

[Precautions of Dosage and Administration]

Caution should be exercised for the following points to prevent bacterial resistance in the use of this drug.

1) Administration should be conducted under supervision of a physician with sufficient knowledge and experience for treatment of infections or under the direction of such physician.
2) As a general rule, patient's sensitivity to this drug and other antibacterial drugs should be confirmed.
3) Treatment period should be limited to the minimum required to treat the disease, after considering the infection site, severity, patient symptoms etc., and determine whether continuous administration of this drug is necessary at an appropriate time.

<Reference Information> Company report

<X-ray contrast media>

8 Magnesium Citrate (hypertonic/isotonic solution dosage form)

[Brand Name] Magcorol, Magcorol P (Horii Pharmaceutical Ind., Ltd.)

[Precautions of Dosage and Administration]

This drug should be carefully administered while confirming for bowel movements and abdominal pain etc. for every 200 mL dosing. If digestive symptoms such as abdominal pain are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and carefully consider whether to continue administration.

If there are no bowel movements after administration of 1.8 L, discontinue administration, confirm absence of abdominal pain or vomiting etc., conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and carefully consider whether to continue administration.

[Careful Administration]

Patients with intestinal diverticulum

The elderly

[Important Precautions]

If abdominal pain and vomiting continues even after patient has had bowel movements from the administration of this drug, conduct abdominal examinations and imaging tests (plain X-ray, ultrasound, CT etc.), and check that no intestinal perforations etc. have occurred.

[Adverse Reactions (clinically significant adverse reactions)]

Intestinal perforation and intestinal obstruction may occur. Patients should be carefully monitored. If abnormalities such as abdominal pain are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.). If intestinal perforation or intestinal obstruction is suspected, appropriate measures should be taken.

[Use in the Elderly]

Intestinal perforation and intestinal obstruction in the elderly may lead to more serious outcomes. An isotonic solution should be administrated over a long period of time and patients should be carefully monitored during the administration. If abnormalities such as abdominal pain are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and take appropriate measures.

There is often a decline in physiological functions (renal function etc.) in the elderly and electrolyte abnormalities such as blood magnesium increased etc. may occur more easily. Caution should be exercised by decreasing the dosage, etc. If abnormalities such as dizziness, wooziness, blood pressure decreased etc. are observed, administration should be discontinued and appropriate measures should be taken.

<Reference Information> Company report

<X-ray contrast media>

9 Magnesium Citrate (hypertonic solution dosage form)

[Brand Name] Tectlol Powder (Taiyo Yakuhin Co., Ltd.), and others

[Important Precautions] If abdominal pain and vomiting continues even after patient has had bowel movements from the administration of this drug, conduct abdominal examinations and imaging tests (plain X-ray, ultrasound, CT etc.), and check that no intestinal perforations etc. have occurred.

[Adverse Reactions (clinically significant adverse reactions)] Intestinal perforation and intestinal obstruction may occur. Patients should be carefully monitored. If abnormalities such as abdominal pain are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.). If intestinal perforation or intestinal obstruction is suspected, appropriate measures should be taken.

<Reference Information> Company report

<Non-main therapeutic purpose agents-Miscellaneous>

10 Sodium Chloride/Potassium Chloride/Sodium Bicarbonate/Anhydrous Sodium Sulfate

[Brand Name] Niflec (Ajinomoto Pharma Co., Ltd.), and others

[Warning]

WARNING

Intestinal perforation due to increased intestinal pressure may occur from the administration of this drug. Administration should be carefully conducted while confirming bowel movements and abdominal pain etc. If digestive symptoms such as abdominal pain are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and carefully consider whether to continue administration. In particular, administration should be conducted after confirming the absence of intestinal obstruction through medical examination by interview, palpation, rectal examination, and imaging test etc. in patients with suspected intestinal obstruction. Caution should be exercised for patients with intestinal stenosis, severe constipation, intestinal diverticulum.

[Precautions of Dosage and Administration] If there are no bowel movements after administration of 2 L, discontinue administration, confirm absence of abdominal pain or vomiting etc., conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and carefully consider whether to continue administration.

[Careful Administration] The elderly
Patients with a history of abdominal surgery

[Important Precautions] If abdominal pain and vomiting continues even after patient has had bowel movements from the administration of this drug, conduct abdominal examinations and imaging tests (plain X-ray, ultrasound, CT etc.), and check that no intestinal perforations etc. have occurred.

[Adverse Reactions (clinically significant adverse reactions)] **Intestinal perforation, intestinal obstruction:** Intestinal perforation and intestinal obstruction may occur. Patients should be carefully monitored and if abnormalities are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and take appropriate measures. If administering this drug at home, refer to the section "Important Precautions" and instruct the patient accordingly.

Colitis ischaemic: Colitis ischaemic may occur. Patients should be carefully monitored. If abnormalities are observed, appropriate measures should be taken. If administering this drug at home, refer to the section "Important Precautions" and instruct the patient accordingly.

Mallory-Weiss syndrome: Mallory-Weiss syndrome associated with vomiting and queasy may occur. Patients should be carefully monitored. If haematemesis or

	bloody stools etc., are observed, appropriate measures should be taken. If administering this drug at home, refer to the section "Important Precautions" and instruct the patient accordingly.
[Use in the Elderly]	Physiological functions are generally decline in the elderly. This drug should be administrated slowly and patient should be carefully monitored during administration. Intestinal perforation and intestinal obstruction particularly in the elderly may lead to more serious outcomes. Patients should be carefully monitored during administration and if abnormalities are observed, discontinue administration, conduct abdominal examination and imaging tests (plain X-ray, ultrasound, CT etc.), and appropriate measures should be taken.
<Reference Information>	Company report

Over the counter drugs

11 Dichlorvos Vapour (those which are used with insecticide sprayer)

[Brand Name]	Vaporsect (Kokusai Eisei Co., Ltd.), and others
[Precautions of Dosage and Administration]	After spraying this drug using a specialized device for 8 hours, leave the sprayed room idle for 1 hour, then sufficiently ventilate the room before entering.

Over the counter drugs

12 Dichlorvos Vapour (of those which do not use an insecticide sprayer, those containing 5g and more of dichlorvos in 1 sheet)

[Brand Name]	Bapona Insecticide Plate, Bapona Half Insecticide Plate (Earth Chemical Co., Ltd.), and others
[When not to use the Product]	This drug should not be used in rooms (including guest room, office room, school room, and hospital room). This drug should also not be used inside cupboards and cabinets of the rooms. This drug should not be used in rooms where people eat and drink (dining rooms etc.) and places where food and drink are exposed (kitchen, food storehouse, food processing plants etc.).

Over the counter drugs

13 Dichlorvos Vapour (of those which do not use an insecticide sprayer, those containing less than 5g of dichlorvos in 1 sheet)

[Brand Name]	Bapona Mini Insecticide Plate (Earth Chemical Co., Ltd.), and others
[When not to use the Product]	This drug should not be used in rooms (including guest room, office room, school room, and hospital room). This drug should also not be used inside cupboards and cabinets of the rooms. This drug should not be used in rooms where people eat and drink and places where food and drink are exposed (food storehouse, etc.).

Over the counter drugs

14 Dichlorvos Vapour (of those which do not use an insecticide sprayer, those containing less than 5g of dichlorvos in 1 can)

[Brand Name]	Paranon (ARECO Corporation), and others
[When not to use the Product]	This product should only be used in designated locations and should not be used in rooms (including guest room, office room, school room, and hospital room). This product should not be used in rooms where people eat and drink and places where food and drink are exposed (food storehouse, etc.).