Date	2022.02.08-(3)
Size	518X222 mm
Colors used	■ Black

PAXUS PM 30 mg and 100 mg
Paclitaxel

powder for injection

Antineoplastic

[Active Ingredient]
Each vial of Paclitaxel (Paxus-PM) for injection 30 mg or 100 mg contains
Paclitaxel (USP)..... 30 mg or 100 mg

[Description]
Paclitaxel (Paxus-PM) is supplied in a vial as a white to slightly yellowish, lyophilized cake, which requires reconstitution before administration.

[Dosage Form]
Powder for injection

[Indications]
• Breast Cancer
First-line treatment of metastatic or recurrent breast cancer

[Pharmacological Properties]
a. Pharmacodynamic properties
• Pharmacotherapeutic group: Antineoplastic agent
• Mechanism of action: Paclitaxel promotes the polymerization of tubulin into microtubules and inhibits depolymerization. That is, Paclitaxel acts by disrupting the microtubular network in cells that is essential for mitotic and interphase cellular functions

b. Pharmacokinetic properties
In non-clinical studies, Paclitaxel (Paxus-PM) showed faster blood clearance and higher volume of distribution in rodent studies and beagle dog study. Clinical pharmacological studies were conducted as a part of phase I trials. Two pharmacokinetic studies of Paclitaxel (Paxus-PM) were conducted in Korea (Study No. GXLPM) and the US (Study No. SAY0010IUS), respectively. Pharmacokinetic parameters of Paclitaxel following a 3-hour infusion of Paclitaxel (Paxus-PM) were estimated for dose levels of 135, 175, 230, 300, and 390 mg/m^2 in GXLPM study and 85, 175, 290, and 435 mg/m^2 in SAY0101IUS.

In general, the results of two studies were consistent with each other and the pharmacokinetics of Paclitaxel (Paxus-PM) displayed increased dose proportionally over the dose ranges of 85 - 435 mg/m^2 indicating predictable linear pharmacokinetics, unlike conventional Paclitaxel.

In both studies, the AUC_{inf} and C_{max} of Paclitaxel (Paxus-PM) revealed lower values than equivalent doses of Taxol (data not shown). The $T_{1/2}$ of Paclitaxel (Paxus-PM) is relatively short, compared with the 20.1 hours of Taxol. The systemic total body clearance was found to be higher than the systemic total body clearance published in the literature for Taxol (12.2 to 17.7 L/hr/m^2). The mean apparent volume of distribution of paclitaxel in the terminal elimination phase (V_d) following infusions of Paclitaxel (Paxus-PM) is greater than the V_d of Taxol. The increase in the clearance and the apparent volume of distribution estimates of Paclitaxel when administered as Paclitaxel (Paxus-PM) may be due to pronounced binding to peripheral tissues and possibly more into the tumor beds, leading to the faster removal of Paclitaxel from systemic circulation and a longer transit time in the tissues.

[Dosage and Administration]
Breast Cancer
First-line treatment of metastatic or recurrent breast cancer
•The recommended regimen for Paxus-PM is 260 mg/m^2 administered by intravenous infusion over 3 hours every 3 weeks. Premedication may be given approximately 30 minutes prior to Paxus-PM administration in order to minimize the possibility of severe hypersensitivity reactions. Such premedication may consist of hydrocortisone 100 mg IV (or its equivalent), pheniramine maleate 45.5 mg IV (or its equivalent), cimetidine 300 mg or ranitidine 50 mg IV (or its equivalent).
•If the below toxicities* occur during Paxus-PM therapy, the administration should be delayed until the toxicity is recovered. Dose reduction of Paxus-PM should be considered according to the following table.
• Dosage can be adjusted to Level-2. If patients are not tolerant to the adjusted dose at Level-2, discontinue treatment.
•If Grade 2 or higher non-hematological toxicities do not occur in the first cycle, increase the dose to 300 mg/m^2 in the second cycle. For patients with dose increase (300 mg/m^2) in the second cycle, dose can be reduced to the Level 0 (Initial dose), -1, and -2 based upon the severity of toxicities.

Dose Adjustment method

Dose Level	Level+1 increase	0 Initial dose	Level-1 reduction	Level-2 reduction
Recommended Dose	300 mg/m^2	260 mg/m^2	220 mg/m^2	180 mg/m^2

- If the dose is reduced based upon the below toxicities*, dose should not be increased in the subsequent cycles.
- The patient should not be rechallenged with subsequent cycle until neutrophils counts reach a level of at least 1.5×10^9/L, and platelet counts exceed 100×10^9/L.
-The administration could be delayed up to 3 weeks until recovery from toxicities. If toxicity is not recovered within 3 weeks, discontinue treatment.
- The dose is adjusted based upon the most severe toxicity when various toxicities occur and any possible conservative treatment for toxicities should be performed.
- The severity of each toxicity is graded according to the NCI CTCAE V3.0. If the severity of a toxicity could not be graded using CTCAE V3.0, the severity is classified as 1. Mild, 2. Moderate, 3. Severe, 4. Life-threatening and 5. Death.
-If symptoms related to cancer are reduced and patients show the clinical benefit (tumor response), treatment may be continued according to the physician's judgment and patient's consent even though toxicity continues to occur after the Level-2 dose reduction.

• Dose Adjustment
Dose to be injected in the subsequent cycle is dependent on hematologic or non-hematologic toxicities based on the chart below.

Dose Reduction*	The dose should be reduced by one level when a physician determines that dose reduction is required. If patients are not tolerant to the adjusted dose at Level-2 or meet the following conditions, discontinue treatment. - ANC < 0.5 ×10^9/L lasts for 1 week - Platelets < 25 ×10^9/L lasts for 1 week - Febrile neutropenia (≥38.5°C) or neutropenia with infection lasts for 1 week - Non-hematologic toxicities > Grade 3 (except nausea, vomiting and alopecia)

• After treatment is discontinued in patients with no premedication due to hypersensitivity reactions, the therapy can be resumed by the decision of physicians. At resumption, patients should receive premedication and the dosage should remain the same as the previous dose before discontinuation (the reduced dose in case of a dose reduction due to toxicities). When this resumption shows a tolerable result, premedication can be given afterwards.

• Carefully monitor a patient for the first 10 minutes and check blood pressure/heart rate as possible as one can during the 1st and 2nd infusion of the solution in order to immediately take appropriate actions when adverse events occur. Discontinue treatment when severe hypersensitivity reactions as below occur:
- Hypotension requiring treatment (pressor therapy)
- Dyspnea requiring bronchodilators
- Vascular edema
- Whole body urticaria
Hypersensitivity reactions other than mentioned above may require discontinuation of infusion based on the physician's judgment.

• Preparation for Solution for Infusion
1) Preparation of Pre-Mix Solution (Paclitaxel 6mg/mL)
- Paclitaxel (Paxus-PM) should be reconstituted by injecting 5ml of distilled water for injection (30mg) or 16.7ml of distilled water for injection (100mg) to the vial of the product, using an aseptic syringe and a needle and swirling gently to dissolve.
- The reconstituted solution is a colorless to bluish solution. If bubbles are visible on the top of the solution due to solubilizer, it is recommended to wait for 5 minutes until the bubbles disappear and then immediately use it for IV, but not necessarily wait until the bubbles are completely disappeared.

2) Preparation of Solution for Infusion
- Use calibrated syringe to take appropriate amount of Pre-Mix solution. Dilute the solution with 0.9% sodium chloride injection or 5% dextrose injection to the concentration of 0.6 ~ 3.0 mg/mL and swirl gently for complete mixing.
It should be inspected visually prior to administration. If particular matters are observed, discard the solution.
- The physical and chemical stability of the solution for infusion is as follows:

Diluting solvent	Storage condition (°C)	Concentration (mg/ml)	Stability of i.v. infusion solution (hour)
0.9% sodium chloride injection	below 20°C	0.6 ~ 3.0	24
	20~25°C	0.6 ~ 3.0	24
	25~30°C	0.6 ~ 3.0	12
5% dextrose injection	below 20°C	0.6 ~ 3.0†	24
	20~25°C	0.6 ~ 3.0†	12
	25~30°C	0.6 ~ 3.0†	6

[Cautions and Contraindications]
1. Warnings
1) Paclitaxel (Paxus-PM) should be administered under the supervision of a physician with experiences of the use of chemotherapeutic agents.
2) Paclitaxel (Paxus-PM) should be administered intravenously as a diluted solution.
3) Clinical study has shown that severe hypersensitivity reactions characterized by anaphylaxis, dyspnea, hypotension requiring treatment, angioedema, and generalized urticaria were observed in 4.9% of breast cancer patients administered the drug. If severe hypersensitivity reactions occur, the discontinuation of drug and the following treatment should be given;
- IV infusion of pheniramine maleate 45.5mg (or its equivalent)
- Administration of epinephrine or its equivalent until the resolution of hypersensitivity reactions or total 6 doses. Administration of IV when hypotension which does not respond to epinephrine or its equivalent occurs.
- Spray of albuterol or its equivalent at stridor which does not respond to adrenaline or its equivalent occurs.
- Infusion of methylprednisolone 125mg or its equivalent to prevent recurrent or advanced allergy.
4) When premedication is determined to be necessary to minimize the risk of severe hypersensitivity reactions in breast cancer, premedication may be given approximately 30 minutes prior to therapy, including hydrocortisone 100 mg IV (or its equivalent), pheniramine maleate 45.5mg IV (or its equivalent), and cimetidine 300 mg or ranitidine 50 mg IV (or its equivalent).
5) Paclitaxel (Paxus-PM) should not be administered to patients with baseline neutrophil counts of less than 1,500 cells/mm^3. Bone marrow suppression (primarily neutropenia) is a dose-dependent and a dose-limiting toxicity. Frequent monitoring of blood counts should be instituted during Paclitaxel (Paxus-PM) treatment. Patients should not be re-treated with subsequent cycles of Paclitaxel (Paxus-PM) until neutrophil counts recover to a level >1,500 cells/mm^3 and platelet counts recover to a level > 100,000 cells/mm^3.

2. Do not administer to the following patients
1) Paclitaxel (Paxus-PM) should not be administered to patients who have a history of severe hypersensitivity reactions to paclitaxel.
2) Paclitaxel (Paxus-PM) should not be used in patients with severe myelosuppression with baseline neutrophil counts < 1,500 cells/mm^3. (Myelosuppression is a dose-limiting toxicity and may accompany infection and become severe.)
3) Paclitaxel (Paxus-PM) should not be used in patients who accompany infection.
(Infection may be worsened by myelosuppression.)
4) Paclitaxel (Paxus-PM) should not be used in pregnant women or women of child-bearing potential.
5) Because Paclitaxel (Paxus-PM) contains lactose, this drug should not be administered to the patients who have genetic abnormalities such as galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption.

3. Administer with care to the following patients
1) Patients with myelosuppression (Myelosuppression may be worsened.)
2) Patients with liver dysfunction (As metabolism function may be decreased, severe adverse events may occur.)
3) Patients with renal dysfunction (As renal function may be decreased, severe adverse events may occur.)
4) Geriatric patients (Please note "8. Use in Geriatric patients")
5) Patients with interstitial pneumonia or pulmonary fibrosis (Symptoms may be worsened.)

4. Adverse events
Adverse events occurred in the first-line treatment of metastatic breast cancer

Adverse events of a Phase III clinical trial for metastatic or recurrent breast cancer

Adverse events in the following table are based on 212 patients whose safety can be evaluated in a Phase III clinical trial for metastatic or recurrent breast cancer

Summary of Adverse events in a Phase III clinical trial for metastatic or recurrent breast cancer

		Patient with adverse events No. (=104) Incidence (%)
Bone Marrow		
Neutropenia	<1,500/mm^3	72.12
	<500/mm^3	38.46
Leukopenia	< 3,000/mm^3	8.65
	< 1,000/mm^3	0.96
Thrombocytopenia	< 75,000/mm^3	0.0
	<25,000/mm^3	0.0
Anemia	< 10.0g/dL	0.96
Hypersensitivity reactions		
Any symptoms		16.35
Severe symptoms		3.85
Peripheral Neuropathy		
Any symptoms		35.58
Severe symptoms		7.69
Myalgia		
Any symptoms		60.58
Severe symptoms		8.65
Arthralgia		
Any symptoms		23.08
Severe symptoms		0.96
Gastrointestinal system		
Nausea		40.38
Severe symptoms		2.88
Vomiting		21.15
Severe symptoms		3.85
Diarrhea		11.54
Severe symptoms		0.96
Constipation		37.50
Severe symptoms		0.0
Alopecia		
Any symptoms		49.04
Severe symptoms		0.96
Hepatic		
ALT elevations		4.81
AST elevations		3.85

Manifestation of Adverse Events by Body System
1) Hematology: Blood/lymphatic system toxicities were observed in 74.04% (77/104) of patients in Phase III clinical trial for metastatic or recurrent breast cancer. The most commonly observed adverse event was neutropenia (75/104, 72.12%). Leukopenia (10/104, 9.62%), febrile neutropenia (4/104, 3.85%), thrombocytopenia (1/104, 0.96%), and anemia (1/104, 0.69%) were observed. Severe thrombocytopenia and severe anemia were not observed.
2) Hypersensitivity reactions: Hypersensitivity reactions occurred in 16.35% (17/104) of patients and 3.85% (4/104) were severe hypersensitivity reactions. Symptoms in all patients with hypersensitivity reactions disappeared.
3) Neurologic system: Neurological toxicities were observed in 89.42% (93/104) of patients. Among the patients, Peripheral Neuropathy were observed in 35.58% (37/104) of patients. None of them showed severe symptoms (of Grade 4 or above). 4 cases of patients discontinued the treatment due to peripheral neuropathy. Sensory symptoms generally disappeared or improved within several months after discontinuation of treatment.
4) Musculoskeletal system: Myalgia (63/104, 60.58%), arthralgia (24/104, 23.08%), back pain (17/104, 16.35%), limb pain (12/104, 11.54%), and flank pain (5/104, 4.81%) were reported. None of them showed severe symptoms (of Grade 4 or above).
5) Gastrointestinal system: Gastrointestinal system toxicities were observed in 76.92% (80/104) of patients and the symptoms were generally mild. Nausea (42/104, 40.38%), constipation (39/104, 37.50%), vomiting (22/104, 21.15%), stomachache (18/104, 17.31%), dyspepsia (14/104, 13.46%), diarrhea (12/104, 11.54%), upper stomachache (10/104, 9.62%), and dry mouth (5/104, 4.81%) were reported. None of them showed severe symptoms (of Grade 4 or above).
6) Dermatological/Skin: Dermatological toxicities were observed in 67.31% (70/104) of patients. The most commonly observed adverse event was alopecia (51/104, 49.04%). Rash (29/104, 27.88%), pruritus (22/104, 21.15%), changes in the nail (7/104, 6.73%), and urticaria (5/104, 4.81%) were reported. None of them showed severe symptoms (of Grade 4 or above).
7) General disorders and injection site reaction: Fatigue (20/104, 19.23%), asthenia (16/104, 15.38%), fever (13/104, 12.50%), pain (9/104, 8.65%), edema (9/104, 8.65%), and localized edema (7/104, 6.73%) were reported. None of them showed severe symptoms (of Grade 4 or above).
8) Other toxicities: Hemoglobin reduction (10/104, 9.62%), AST elevations (4/104, 3.85%), ALT elevations (5/104, 4.81%), neutropenia (3/104, 2.88%), thrombocytopenia (1/104, 0.96%), and weight loss (4/104, 3.85%) were reported.
9) Metabolism and nutrient: Loss of appetite (29/104, 27.88%), hypercholesterolemia (4/104, 3.85%), hypophosphatasia (3/104, 2.88%), and hypocalcemia (2/104, 1.92%) were reported. None of them showed severe symptoms (of Grade 4 or above).
10) Infection/other infection: Rhinopharyngitis (19/104, 18.27%), upper respiratory infection (10/104, 9.62%), and cystitis (7/104, 6.73%) were reported.
11) The respiratory system: Cough (12/104, 11.54%), difficulty in breathing (12/104, 11.54%), sore throat (17/104, 16.35%), wet cough (5/104, 4.81%), and nose drippings (3/104, 2.88%) were reported.
12) Urinary system: The most commonly observed adverse event was dysuria (3/104, 2.88%). No severe adverse event was reported.
13) Vascular system: The most commonly observed adverse event was flushing (4/104, 3.85%). No severe adverse event was reported.
14) Mental disorder: The most commonly observed adverse event was insomnia (21/104, 20.19%).None of them showed severe symptoms (of Grade 4 or above).
15) Eye: The most commonly observed adverse event was blurred vision (15/104, 14.42%). None of them showed severe symptoms (of Grade 4 or above).
16) Ear: Dizziness(3/104, 2.88%) and tinnitus(1/104, 0.96%) were reported. No severe adverse event was reported.

Results of postmarketing surveillance
186 subjects were investigated for postmarketing surveillance for 4 years to treat metastatic and recurrent breast cancer as first-line treatment, and metastatic breast cancer after failure of standard chemotherapy as second-line treatment. The incidence of adverse events was 77.96% (145/186, 710 cases) of patients regardless of causal relationship. Among those adverse events, the incidence of adverse drug reactions which could not exclude the relationship with drug was 75.27% (140/186, 620 cases) of patients. Adverse drug reactions were neutropenia in 23.12% (43/186, 110 cases) of patients, peripheral neuropathy in 18.28% (34/186, 41 cases), nausea in 15.59% (29/186, 37 cases), myalgia in 13.44% (25/186, 27 cases), leukopenia in 12.90% (24/186, 56 cases), and peripheral sensory neuropathy in 10.22% (19/186, 24 cases). Adverse drug reactions of less than 10% were categorized by body system as follows.
- Neurologic system: neuropathy, tingling, headache, dizziness, neuralgia, anesthesia, tremor, fainting, polyneuropathy, peripheral motor neuropathy, bell's palsy, ataxia.
- Musculoskeletal system: arthralgia, osteocope, pantalgia, neck stiffness, limb weakness.
- Gastrointestinal system: loss of appetite, vomiting, constipation, diarrhea, stomatitis, dyspepsia, stomachache, mucositis, gastritis, abdominal discomfort, gingivitis.
- Dermatological/Skin: alopecia, rash, pruritis, urticaria, papule rash, exfoliation, erythema, local skin reactions, sweat, acne.
- Hematologic system: febrile neutropenia, decreased hemoglobin level, erythropenia, anemia, thrombocytopenia.
- General disorders: fatigue, general weakness, fever, chest discomfort, pain, edema, lower limb pain, asthenia, chest wall pain, anaphylaxis, arm swelling, chest tension, pelvic pain, anaphylactic shock, chill.
- Respiratory system: dyspnea, cough, runny nose, upper respiratory tract infection, cold, decreases in oxygen saturation, stridor.
- Hepatobiliary system: elevated SGOT level, elevated SGPT level, liver function abnormality, bilirubin elevations.
- Urinary system: urinary tract infection.
- Cardiovascular system: tachycardia, arrhythmia, cardiac standstill, hypotension.
- Other: otalgia.
The incidence of serious adverse events was 11.29% (21/186, 34 cases) of patients regardless of causal relationship to the study drug. Among those serious adverse events, the incidence of adverse drug reactions which could not exclude the relationship with drug was 5.91% (11/186, 15 cases) of patients. 15 cases were neutropenia in 1.61% (3/186, 3 cases) of patients, each of fever and febrile neutropenia in 1.08% (2/186, 2 cases), and each of headache, fainting, rash, arm swelling, anaphylactic shock, dyspnea, pneumonia and cardiac standstill in 0.54% (1/186, 1 case). The incidence of unexpected adverse events were 4.84% (9/186, 11 cases) of patients regardless of causal relationship to the study drug. Among those unexpected adverse events, the incidence of adverse drug reactions which could not exclude the relationship with drug was 3.23% (6/186, 7 cases) of patients. 7 cases were ataxia in 0.54% (1/186, 2 cases) of patients, each of fainting, acne, stridor, arrhythmia, and cardiac standstill in 0.54% (1/186, 1 case).

5. General Precautions
1) As adverse events may occur even low-dose administration or at the beginning, patients should be fully aware of precautions.
2) Hematology: Paclitaxel (Paxus-PM) therapy should not be administered to patients with baseline neutrophil counts less than 1,500 cells/mm^3. All patients receiving Paclitaxel (Paxus-PM) should check frequent peripheral blood cell counts to monitor the occurrence of myelotoxicity. Patients should not be rechallenged with subsequent cycles of Paclitaxel (Paxus-PM) before the neutrophils counts reach above 1,500 cells/mm^3 and platelets counts reach above 100,000 cells/mm^3. When severe neutropenia (< 500 cells/mm^3) occurs during Paclitaxel (Paxus-PM) therapy, reduce dose by 20% in subsequent cycle.
3) Hypersensitivity reactions: Minor symptoms such as flushing, skin reactions, dyspnea, hypotension, or tachycardia do not require interruption of therapy. However, severe reactions including hypotension requiring treatment, dyspnea requiring bronchodilators, angioedema, or generalized urticaria require immediate discontinuation of Paclitaxel (Paxus-PM) and aggressive symptomatic therapy. Patients who have developed severe hypersensitivity reactions should not be rechallenged with drug.
4) Nervous system: Peripheral neuropathy was frequently observed, but was hardly developed to severe condition. For moderate or severe condition, reduce dose by 20% in all subsequent cycles.
5) Hepatic system: Caution should be taken and dose reduction should be considered to patients with moderate or severe hepatic dysfunction.
6) Injection site reaction: Injection site reactions including extravasation were usually mild and they include edema, abnormal sensitiveness of pain sense to pressure or touch, skin discoloration, or swelling at the injected site. These reactions have been observed more frequently in those with 24-hour infusion than with the 3-hour infusion. Recurrence of skin reactions at a site of previous extravasation following Paclitaxel (Paxus-PM) administration injected at a different site has rarely been reported. It is advisable to closely monitor the infusion site during drug administration.

6. Drug Interaction
1) In a Phase I trial of Paclitaxel (Paxus-PM) (110~220 mg/m^2) and cisplatin (50 or 75 mg/m^2) given as sequential infusions, myelosuppression was more profound when cisplatin was administered ahead of Paclitaxel (Paxus-PM) than in reverse order: Administer Paclitaxel (Paxus-PM) and then cisplatin. Pharmacokinetic data from these patients demonstrated a decrease in paclitaxel clearance when cisplatin was administered ahead of Paclitaxel (Paxus-PM). In addition, peripheral neuropathy may increase because of the concurrent therapy. When the concurrent therapy is given, dose adjustment or prolonged dose interval should be considered with the observation of patients.
2) The metabolism of drug is catalyzed by cytochrome P450 isoenzymes CYP2C8 and CYP3A4. As there are no adequate clinical studies for drug interactions, caution should be taken when Paclitaxel (Paxus-PM) is administered with known substrates or inhibitors (such as ritonavir, saquinavir, indinavir, and nelfinavir) of cytochrome P450 isoenzymes CYP2C8 and CYP3A4.
3) The metabolism of paclitaxel may be suppressed by Vitamin A, azole antifungal agents (e.g. ketoconazole, miconazole), macrolide hormones (e.g. ethynyl estradiol), dihydrophyridine calcium channel inhibitor (e.g. nifedipine), terfenadine, cyclosporine, verapamil, quinidine, midazolam, phenaeetin, ritonavir, saquinavir, indinavir, and nelfinavir. At concurrent administration, dose adjustment or prolonged dosing interval should be considered with the observation of patients.
4) Radiation Therapy: At concurrent therapy with radiotherapy to the chest, severe esophagitis or lung enteritis, and increase in myelosuppression were reported. It thereby requires caution to the condition of patients.
5) Anticancer Drugs: The concurrent therapy with anticancer drugs may increase the risk of myelosuppression.

7. Use in Pregnancy and Nursing Mothers

1) Pregnancy: Paclitaxel can be fatal to an unborn child. Paclitaxel has shown to embryo- and feto-toxic in rabbits and fertility decrease in rats. No clinical study for pregnant women has been reported. Women with childbearing potential should be advised to avoid becoming pregnant.
2) Nursing mothers: Paclitaxel should not be administered to nursing mothers or nursing should be discontinued during the therapy.

8. Use in Geriatric patients
Since decreased physiologic function and frequent myelosuppression commonly occur in geriatric patients, dose and dosing interval should be considered with care and clinical laboratory test (e.g. blood test, hepatic function test, renal function test) should be frequently performed.

9. Use in Pediatric patients
The safety in a premature infant, a newborn baby, infant, toddler, or pediatric patients has not been established.

10. Treatment on Overdosage
There is no known antidote for this drug overdosage. The primary anticipated complications of overdosage include bone marrow suppression, peripheral neurotoxicity and mucositis.

11. Preparation and Administration Precautions
This drug is a cytotoxic anticancer drug, and thus should be treated carefully like other potentially toxic compounds. The use of gloves is recommended. The compounds causes tingling, burning, and redness when exposed to skin. If this drug solution contacts the skin, wash the skin immediately and thoroughly with soap and water. If the drug contacts mucous membranes, flush it thoroughly with water. Upon inhalation, dyspnea, chest pain, sore throat, nausea and burning eyes have been reported.

12. Storage and Handling
1) Keep out of reach of children.
2) The solution is recommended to be kept in an original container because the change of a container may lead to unintended accidents and damage its quality.

[Storage]
Store at room temperature (below 30°C).
Protect from light.

[Expiration duration]
24 months from manufacturing date

[Packaging Size]
• 30 mg per vial
• 100 mg per vial

Revision Date : 08 February 2022

Manufactured by:
Samyang Holdings Corporation
79, Sinildong-ro, Daedeok-gu, Daejeon, Korea

Product Registration Holder:
Kalbe Malaysia Sdn. Bhd.
Suite 2A-3-2, Block 2A, Plaza Sentral
Jalan Stesen Sentral 5, Kuala Lumpur Sentral,
50470 Kuala Lumpur

MAL No. MAL21106047ACZ
MAL No. MAL21106046ACZ

1946330A01