표시자재 표준화판			20260410_03					
제 품 명	씨네졸리드주(말레이시아) 2mg 인서트			디자인 담당	RA 3팀	권성진 님 / 031-5176-4702		
규격 (장 / 폭 / 고)	230×310 (mm)	재질(카톤)	N/A	인쇄소 담당	성지종합인쇄	이창준 님 / 010-3752-3375		
인 쇄 도 수	1도 (먹)			원고 담당	로직앤매직	이현지 / 02-558-8970		
	[redacted] 먹				담당자 확인		팀장 확인	
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	3_문안 수정							
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					생산지원			
					QA책임자			
에이치케이이노엔(주)								

Rx Prescription drug

inno.N

CINEZOLID solution for infusion 2mg/mL
(Linezolid 2mg/mL)

1. NAME(S) OF THE MEDICINAL PRODUCT
CINEZOLID solution for infusion 2mg/mL
2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Solution for infusion: Each mL contains 2 mg of linezolid
3. PHARMACEUTICAL FORM
Linezolid solution for infusion is supplied as a ready-to-use sterile isotonic solution for intravenous infusion. Each mL contains 2 mg of linezolid.
Clear, colorless to yellow solution contained in a plastic bag.
4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Linezolid formulations are indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms. Linezolid is active against Gram-positive bacteria only. Linezolid has no clinical activity against Gram-negative pathogens. Specific Gram-negative therapy is required if a concomitant Gram-negative pathogen is documented or suspected (See sections *Special warnings and precautions for use and Pharmacodynamic properties*).
Vancomycin-Resistant *Enterococcus faecium* infections, including cases with concurrent bacteremia.
Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and- resistant strains), or *Streptococcus pneumonia* penicillin-susceptible strains).
Combination therapy may be clinically indicated if the documented or presumptive pathogens include Gram-negative organisms.
Complicated skin and skin structure infections including diabetic foot infections, without concomitant osteomyelitis caused by *Staphylococcus aureus* (methicillin- susceptible and -resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae.*
Linezolid has not been studied in the treatment of decubitus ulcers. Combination therapy may be clinically indicated if the documented or presumptive pathogens include Gram- negative organisms.
Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible only) or *Streptococcus pyogenes.*
Community-acquired pneumonia caused by *Streptococcus pneumonia* (penicillin-susceptible strains), including cases with concurrent bacteremia, or *Staphylococcus aureus* (methicillin-susceptible strains only). Due to concerns about inappropriate use of antibiotics leading to an increase in resistant organisms, prescribers should carefully consider alternatives before initiating treatment with linezolid in the outpatient setting.
Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to linezolid. Therapy may be instituted empirically while awaiting the results of these tests.
Once these results become available, antimicrobial therapy should be adjusted accordingly.
4.2 Posology and method of administration
Patients whose therapy is started with linezolid injection may be switched to linezolid tablets or linezolid for oral suspension, with no dosage adjustment.
Table 1. Dosage Guidelines for Linezolid

Infection*	Dosage and Route of Administration		Recommended Duration of Treatment (consecutive days)
	Pediatric Patients[1] (Birth through 11 Years of Age)	Adults and Adolescents (12 Years and Older)	
Complicated skin and skin structure infections Community-acquired pneumonia, including concurrent bacteremia Nosocomial pneumonia	10mg/kg IV or oral[2] q8h	600mg IV or oral[2] q12h	10 to 14
Vancomycin-resistant *Enterococcus faecium* infections, including concurrent bacteremia	10mg/kg IV or oral[2] q8h	600mg IV or oral[2] q12h	14 to 28
Uncomplicated skin and skin structure infections	<5 yrs: 10mg/kg Oral[2] q8h 5-11 yrs: 10mg/kg Oral[2] q12h	Adults: 400mg oral[2] q12h Adolescents: 600mg Oral[2] q12h	10 to 14

*Due to the designated pathogens
[1] **Neonates <7 days:** Most pre-term neonates <7 days of age (gestational age <34 weeks) have lower systemic linezolid clearance values and larger AUC values than many full-term neonates and older infants. These neonates should be initiated on a dosing regimen of 10 mg/kg every 12 hours (q12h).
Consideration may be given to the use of 10 mg/kg q8h regimen in neonates with a sub-optimal clinical response. All neonatal patients should receive 10 mg/kg q8h by 7 days of life.
[2] Oral dosing using either Linezolid Tablets or Linezolid for Oral Suspension.
Elderly patients: No dose adjustment is required.
Patients with renal insufficiency: No dose adjustment is required (see section *Pharmacokinetic properties*).
Patients with severe renal insufficiency (i.e., CLcr <30ml/min): No dose adjustment is required. Due to the unknown clinical significance of higher exposure (up to 10 fold) to the two primary metabolites of linezolid in patients with severe renal insufficiency, linezolid should be used with special caution in these patients and only when the anticipated benefit is considered to outweigh the theoretical risk.
As approximately 30% of a linezolid dose is removed during 3 hours of hemodialysis, linezolid should be given after dialysis in patients receiving such treatment. The primary metabolites of linezolid are removed to some extent by hemodialysis, but the concentrations of these metabolites are still very considerably higher following dialysis than those observed in patients with normal renal function or mild to moderate renal insufficiency.
Therefore, linezolid should be used with special caution in patients with severe renal insufficiency who are undergoing dialysis and only when the anticipated benefit is considered to outweigh the theoretical risk.
To date, there is no experience of linezolid administration to patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or alternative treatments for renal failure (other than hemodialysis).
Patients with hepatic insufficiency: No dose adjustment is required. However, there are limited clinical data and it is recommended that linezolid should be used in such patients only when the anticipated benefit is considered to outweigh the theoretical risk (see section *Pharmacokinetic properties*).
Linezolid Solution for infusion
Administer linezolid solution for infusion by intravenous infusion over a period of 30 to 120 minutes. **Do not use this intravenous infusion bag in series connections.** Do not introduce additives into the intravenous solution. If linezolid solution for infusion is to be given concomitantly with another drug, each drug should be given separately, in accordance with the recommended dosage and route of administration for each product.
Linezolid solution for infusion was physically incompatible with the following drugs when combined in simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isethionate, phenytoin sodium, erythromycin lactobionate, and trimethoprim -sulfamethoxazole.
Linezolid solution for infusion was chemically incompatible when combined with ceftriaxone sodium.
Compatible Intravenous Solutions
5% Dextrose Injection,
0.9% Sodium Chloride Injection,
Lactated Ringer's Injection,
4.3 Contraindications
Linezolid is contraindicated in patients who have previously demonstrated hypersensitivity to linezolid or any of the other product components.
Monoamine Oxidase Inhibitors
Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, iso carboxazid) or within two weeks of taking any such medicinal product.
Potential Interactions Producing Elevation of Blood Pressure
Unless patients are monitored for potential increases in blood pressure, linezolid should not be administered to patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following types of medications: directly and indirectly acting sympathomimetic agents (e.g., pseudoephedrine, phenylpropanolamine), vasopressive agents (e.g., epinephrine, norepinephrine), dopaminergic agents (e.g., dopamine, dobutamine) (see section *Interactions with other medicinal products and other forms of interaction*).
Potential Serotonergic Interactions
Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, linezolid should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), meperidine or buspirone (see section *Interactions with other medicinal products and other forms of interaction*).
4.4 Special warnings and precautions for use
Reversible myelosuppression (anemia, thrombocytopenia, leukopenia, and pancytopenia) that may be dependent on duration of therapy has been reported in some patients receiving linezolid. Monitoring of complete blood counts should be considered for patients who are at increased risk for bleeding, who have pre-existing myelosuppression, who receive concomitant medications that may decrease hemoglobin levels or platelet count or function, or who receive linezolid for more than 2 weeks.
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including linezolid, and may range in severity from mild to life-threatening.
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including linezolid, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*
C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.
Peripheral and optic neuropathy have been reported in patients treated with linezolid, primarily those patients treated for longer than the maximum recommended duration of 28 days. In cases of optic neuropathy that progressed to loss of vision, patients were treated for extended periods beyond the maximum recommended duration.
If symptoms of visual impairment appear, such as changes in visual acuity, changes in color vision, blurred vision, or visual field defect, prompt ophthalmic evaluation is recommended. Visual function should be monitored in all patients taking linezolid for extended periods (greater than or equal to 3 months) and in all patients reporting new visual symptoms regardless of length of therapy with linezolid. If peripheral or optic neuropathy occurs, the continued use of linezolid in these patients should be weighed against the potential risks.
Lactic acidosis has been reported with the use of linezolid. Patients who develop recurrent nausea or vomiting, unexplained acidosis, or a low bicarbonate level while receiving linezolid should receive immediate medical attention.
Convulsions have been reported to occur rarely in patients when treated with linezolid. In most of these cases, a history of seizures or risk factors for seizures were reported.
Spontaneous reports of serotonin syndrome associated with the co-administration of linezolid and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs) have been reported.
Where administration of linezolid and concomitant serotonergic agents is clinically appropriate, patients should be closely observed for signs and symptoms of serotonin syndrome such as cognitive dysfunction, hyperpyrexia, hyperreflexia and incoordination. If signs or symptoms occur physicians should consider discontinuation of either one or both agents. If the concomitant serotonergic agent is withdrawn, discontinuation symptoms can be observed.
Linezolid has no clinical activity against Gram-negative pathogens and is not indicated for the treatment of Gram-negative infections. Specific Gram-negative therapy is required if a concomitant Gram-negative pathogen is documented or suspected. Linezolid should be used with special caution in patients at high risk for life threatening systemic infections, such as those with infections related to central venous catheters in intensive care units. Linezolid is not approved for the treatment of patients with catheter-related bloodstream infections. Rhabdomyolysis has been reported with the use of linezolid. If signs or symptoms of rhabdomyolysis are observed, linezolid should be discontinued and appropriate therapy initiated.
4.5 Interactions with other medicinal products and other forms of interaction
Linezolid is a weak, reversible, nonselective inhibitor of monoamine oxidase. Therefore, some patients receiving linezolid may experience a mild reversible enhancement on the pressor response induced by pseudoephedrine HCl or phenylpropanolamine HCl. Initial doses of adrenergic agents, such as dopamine or dopamine agonists, should be reduced and titrated to achieve the desired response.
Very rare spontaneous reports of serotonin syndrome with co-administration of linezolid and serotonergic agents have been reported (see section *Special warnings and precautions for use*).
Antibiotics: The pharmacokinetics of linezolid were not altered when administered together with either aztreonam or gentamicin.
The mechanism of interaction between rifampicin and linezolid and its clinical significance are unknown.
4.6 Fertility, pregnancy and lactation
There are no adequate and well-controlled studies in pregnant women.
Therefore linezolid should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
It is not known whether linezolid is excreted in human milk. Therefore, caution should be exercised when linezolid is administered to a nursing woman.
4.7 Effects on ability to drive and use machines
Patients should be warned about the potential for dizziness or symptoms of visual impairment whilst receiving linezolid and should be advised not to drive or operate machinery if any of these symptoms occurs
4.8 Undesirable effects
Adverse Drug Reaction Table

System Organ Class	Adverse Drug Reactions
Infections and infestations	Moniliasis
Blood and lymphatic system disorders	Pancytopenia*, leucopenia*, thrombocytopenia*, Reversible anaemia*, sideroblastic anaemia*#
Immune system disorders	Anaphylaxis*
Metabolism and nutrition disorders	Lactic acidosis*^
Nervous system disorders	Convulsion*, peripheral neuropathy*, headache, taste alteration
Eye disorders	Optic neuropathy*^a
Gastrointestinal disorders	Vomiting, diarrhoea, nausea, abdominal pain abdominal cramps, abdominal distension, tongue discoloration*^b, Superficial tooth discoloration*b
Skin and subcutaneous tissue Disorders	Bullous skin disorders including severe cutaneous adverse reactions (such as toxic epidermal necrolysis* and Stevens-Johnson syndrome), angioedema*, rash*
Investigations	Abnormal haematology tests, abnormal liver function Tests
Musculoskeletal and connective tissue disorders	Rhabdomyolysis*c

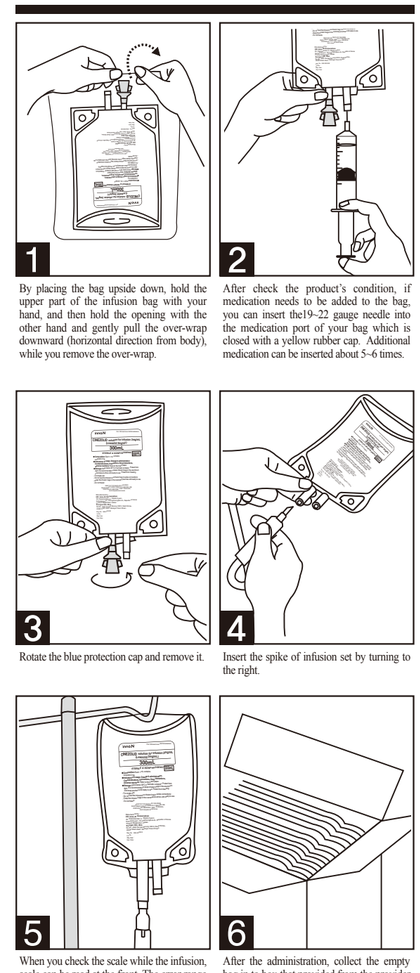
*ADR identified post-marketing
Primarily reported in patients receiving linezolid for more than the maximum recommended duration of 28 days
^ See section 4.4 Special Warnings and Precautions for Use
[a] Sometimes progressing to loss of vision, have been reported in patients treated with linezolid.
These reports have primarily been in patients treated for longer than the maximum recommended durations of 28 days
[b] discoloration was removable with professional dental cleaning (manual descaling) in cases with known outcome
[c] frequency : rare
4.9 Overdose
In the event of overdosage, supportive care is advised, with maintenance of glomerular filtration. Hemodialysis removes approximately 30% of a dose of linezolid.
5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
General Properties
Linezolid is a synthetic antibacterial agent that belongs to a new class of antimicrobials, the oxazolidinones. It has in *vitro* activity against aerobic Gram-positive bacteria, some Gram-negative bacteria and anaerobic micro-organisms. Linezolid selectively inhibits bacterial protein synthesis via a unique mechanism of action. Specifically, it binds to a site on the bacterial ribosome (23S of the 50S subunit) and prevents the formation of a functional 70S initiation complex which is an essential component of the translation process.
Susceptibility
Only micro-organisms relevant to the given clinical indications are presented here.

Category
Susceptible organisms
Gram positive aerobes:
Enterococcus faecalis
Enterococcus faecium
Staphylococcus aureus
Coagulase negative staphylococci
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes
Group C streptococci
Group G streptococci
Gram positive anaerobes:
Clostridium perfringens
Peptostreptococcus anaerobius
Peptostreptococcus species
Resistant organisms
Haemophilus influenzae
Moraxella catarrhalis
Neisseria species
Enterobacteriaceae
Pseudomonas species

5.2 Pharmacokinetic properties
Absorption
Linezolid is rapidly and extensively absorbed after oral dosing. Maximum plasma concentrations are reached within 2 hours of dosing. Absolute oral bioavailability of linezolid (oral and intravenous dosing) is complete (approximately 100%). Absorption is not significantly affected by food and absorption from the oral suspension is similar to that achieved with the film-coated tablets. Plasma linezolid Cmax and Cmin (mean and [SD]) at steady-state following twice daily intravenous dosing of 600mg have been determined to be 15.1 [2.5]mg/l and 3.68 [2.68]mg/l, respectively.
Distribution
Volume of distribution at steady-state averages at about 40-50 litres in healthy adults and approximates to total body water. Plasma protein binding is about 31% and is not concentration dependent.
Pharmacokinetic information generated in pediatric patients with ventriculoperitoneal shunts showed variable cerebrospinal fluid (CSF) linezolid concentrations following single and multiple dosing of linezolid; therapeutic concentrations were not consistently achieved or maintained in the CSF. Therefore, the use of linezolid for the empiric treatment of pediatric patients with central nervous system infections is not recommended.
Metabolism
Linezolid is primarily metabolized by oxidation of the morpholine ring resulting mainly in the formation of two inactive open-ring carboxylic acid derivatives: the aminoethoxyacetic acid metabolite (PNU-142300) and the hydroxyethyl glycine metabolite (PNU-142586). The hydroxyethyl glycine metabolite (PNU-142586) is the predominant human metabolite and is believed to be formed by a non-enzymatic process. The aminoethoxyacetic acid metabolite (PNU-142300) is less abundant. Other minor, inactive metabolites have been characterised.
Elimination
In patients with normal renal function or mild to moderate renal insufficiency, linezolid is primarily excreted under steady-state conditions in the urine as PNU-142586 (40%), parent drug (30%) and PNU-142300 (10%). Virtually no parent drug is found in the feces while approximately 6% and 3% of each dose appears as PNU-142586 and PNU-142300, respectively. The elimination half-life of linezolid averages at about 5-7 hours.
Non-renal clearance accounts for approximately 65% of the total clearance of linezolid. A small degree of non-linearity in clearance is observed with increasing doses of linezolid. This appears to be due to lower renal and non-renal clearance at higher linezolid concentrations. However, the difference in clearance is small and is not reflected in the apparent elimination half-life.
Special Populations
Patients with renal insufficiency: After single doses of 600 mg, there was a 7-8 fold increase in exposure to the two primary metabolites of linezolid in the plasma of patients with severe renal insufficiency (i.e. creatinine clearance <30 ml/min). However, there was no increase in AUC of parent drug. Although there is some removal of the major metabolites of linezolid by hemodialysis, metabolite plasma levels after single 600 mg doses were still considerably higher following dialysis than those observed in patients with normal renal function or mild to moderate renal insufficiency.
Patients with hepatic insufficiency: Limited data indicate that the pharmacokinetics of linezolid, PNU-142300 and PNU-142586 are not altered in patients with mild to moderate hepatic insufficiency (i.e. Child-Pugh class A or B). The pharmacokinetics of linezolid in patients with severe hepatic insufficiency (i.e. Child-Pugh class C) have not been evaluated. However, as linezolid is metabolized by a non-enzymatic process, impairment of hepatic function would not be expected to significantly alter its metabolism (see section *Posology and method of administration*).
Children and adolescents (<18 years old): In adolescents (12 to 17 years old), linezolid pharmacokinetics were similar to that in adults following a 600 mg dose. Therefore, adolescents administered 600 mg every 12 hours daily will have similar exposure to that observed in adults receiving the same dosage.
In children 1 week to 12 years old, administration of 10 mg/kg every 8 hours daily gave exposure approximating to that achieved with 600 mg twice daily in adults.
In neonates up to 1 week of age, the systemic clearance of linezolid (based on kg body weight) increases rapidly in the first week of life. Therefore, neonates given 10 mg/kg every 8 hours daily will have the greatest systemic exposure on the first day after delivery. However, excessive accumulation is not expected with this dosage regimen during the first week of life as clearance increases rapidly over that period.
Elderly patients: The pharmacokinetics of linezolid are not significantly altered in elderly patients (65 years or older).
Female patients: Females have a slightly lower volume of distribution than males and the mean clearance is reduced by approximately 20% when corrected for body weight. Plasma concentrations are higher in females and this can partly be attributed to body weight differences. However, because the mean half-life of linezolid is not significantly different in males and females, plasma concentrations in females are not expected to substantially rise above those known to be well tolerated and, therefore, dose adjustment are not required.
6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Solution for Infusion: The intravenous formulation contains sodium citrate dihydrate, anhydrous citric acid, dextrose, sodium hydroxide, hydrochloric acid, and water for injection in an aqueous vehicle for intravenous administration. The sodium (Na^+) content is 0.38 mg/mL (5 mEq per 300-mL bag).
6.2 Incompatibilities
Solution for Infusion: Linezolid solution for infusion was physically incompatible with the following drugs when combined in simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isethionate, phenytoin sodium, erythromycin lactobionate, and trimethoprim-sulfamethoxazole.
Linezolid solution for infusion was chemically incompatible when combined with ceftriaxone sodium.
6.3 Shelf life
Solution for Infusion: 30 months
6.4 Special precautions for storage
Store below 30ºC in hermetic container. Protect from light. It is recommended to keep infusion bags in the aluminium overwrap pouches until ready to use. Protect from freezing.
6.5 Nature and contents of container
Solution for Infusion
Linezolid solution for infusion is available in single-use, clear and transparent multi-layer film Non-PVC(Polyester/Polyethylene/ Propylene Copolymer)bags connected with clear and transparent IR rubber open tubes stoppered with blue PP twist-off port. The bag is enclosed in aluminum overwrap pouches. 20 packs of pouches are packed in a carton paper box together a package insert. The infusion bags are available in the following package sizes:
300 mL bag (600 mg linezolid)
6.6 Special precautions for disposal and other handling
Solution for Infusion Administration
Linezolid solution for infusion is supplied in single-use, ready-to-use infusion bags.
Parenteral drug products should be inspected visually for particulate matter prior to administration. Check for minute leaks by firmly squeezing the bag. If leaks are detected, discard the solution, as sterility may be impaired.
Linezolid solution for infusion should be administered by intravenous infusion over a period of 30 to 120 minutes. **Do not use this intravenous infusion bag in series connections.** Additives should not be introduced into this solution. If linezolid solution for infusion is to be given concomitantly with another drug, each drug should be given separately in accordance with the recommended dosage and route of administration for each product. In particular, physical incompatibilities resulted when linezolid solution for infusion was combined with the following drugs during simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isothionate, erythromycin lactobionate, phenytoin sodium, and trimethoprim-sulfamethoxazole. Additionally, chemical incompatibility resulted when linezolid solution for infusion was combined with ceftriaxone sodium.
If the same intravenous line is used for sequential infusion of several drugs, the line should be flushed before and after infusion of linezolid solution for infusion with an infusion solution compatible with linezolid solution for infusion and with any other drug(s) administered via this common line.
Compatible Intravenous Solutions
5% Dextrose Injection,
0.9% Sodium Chloride Injection,
Lactated Ringer's Injection,
Keep the infusion bags in the overwrap until ready to use. Store at room temperature.
Protect from freezing. Linezolid solution for infusion may exhibit a yellow color that can intensify over time without adversely affecting potency.
7.0 MANUFACTURER
HK inno.N Corporation
20, Daesosandan-ro, Daeso-myeon,
Eumseong-gun, Chungcheongbuk-do, Republic of Korea.
8.0 Product Registration Holder
Eucogen Sdn. Bhd.
No 6A, Jalan Sungai Burung U32/U,
Bukit Rimau, 40460 Shah Alam,
Selangor Darul Ehsan.

Date of Revision: 04 April, 2025

[How to use infusion bag]



1 By placing the bag upside down, hold the upper part of the infusion bag with your hand, and then hold the opening with the other hand and gently pull the over-wrap downward (horizontal direction from body), while you remove the over-wrap.

2 After check the product's condition, if medication needs to be added to the bag, you can insert the19~22 gauge needle into the medication port of your bag which is closed with a yellow rubber cap. Additional medication can be inserted about 5~6 times.

3 Rotate the blue protection cap and remove it.

4 Insert the spike of infusion set by turning to the right.

5 When you check the scale while the infusion, scale can be read at the front. The error range is less than ± 5%.

6 After the administration, collect the empty bag in to box that provided from the provider or dispose them into the proper waste container.

The font size of the contents is 7. This package insert is printed appropriately and readable