—Original—

Y-site Injection Physical Compatibility of Remdesivir with Select Intravenous Drugs Used in Palliative Care and for Treating Coronavirus Disease 2019

Masayoshi Kondo, Mai Gempei, Kei Watanabe, Masato Yoshida,
Naoya Tagui, Shouhei Fukao, Kazutoshi Sugaya and Hisamitsu Takase

Department of Pharmacy, Nippon Medical School Tama Nagayama Hospital, Tokyo, Japan

Background: No compatibility tests are available for remdesivir other than 0.9% sodium chloride. In this study, we aimed to evaluate the physical compatibility of remdesivir with drugs used in palliative care and COVID-19 treatment.

Methods: Remdesivir was tested for compatibility with 10 different drugs (fentanyl, morphine, hydromorphone, oxycodone, heparin, furosemide, octreotide, acetated Ringer's injection, 2-in-1 peripheral parenteral nutrition, and 2-in-1 total parenteral nutrition). Remdesivir was formulated to a final concentration of 1 mg/mL, and the other drugs were prepared at clinical concentrations. Three test solutions were used for compatibility testing, with remdesivir and the target drugs compounded in a 1:1 ratio. Appearance measurements, including Tyndall effect, turbidity, and pH, were performed immediately after mixing and at 1 h and 4 h after mixing. Changes in appearance, including the Tyndall effect, turbidity (turbidity change of ≥ 0.5 nephelometric turbidity unit [NTU] based on control solution for each test drug), and pH (a change of ≥ 10% based on the pH immediately after mixing) were used to determine physical compatibility.

Results: All the drugs tested were compatible with remdesivir. The combination of remdesivir and furosemide produced the highest turbidity (0.23 ± 0.03 NTU) 1 h after mixing. The lowest and highest pH values were observed at 4 h after mixing for the combinations of remdesivir and morphine (3.23 ± 0.02) and remdesivir and furosemide (8.81 ± 0.06).

Conclusions: The drugs tested in this study show Y-site physical compatibility with remdesivir.

(J Nippon Med Sch 2023; 90: 381–386)

Key words: coronavirus disease 2019, remdesivir, compatibility, palliative care

Introduction

Remdesivir is a SARS-CoV-2 nucleotide analog RNA polymerase inhibitor indicated for the treatment of coronavirus disease 2019 (COVID-19)[1]. It is recommended both for patients with mild COVID-19 who do not require oxygen and for those with moderate COVID-19 who require oxygen or hospitalization[1,2]. Consequently, remdesivir can be used not only in acute care hospitals but also in outpatient and inpatient settings, including non-acute care hospitals such as palliative care facilities[3,4].

Moderate to severe pain in cancer is common, affecting 70-80% of patients with advanced stage, and most patients with cancer pain require opioids for pain management[5]. Furthermore, COVID-19 treatment or palliative care, including cancer and heart failure, may entail continuous injections of heparin, octreotide, furosemide, electrolyte infusions, or nutritional infusions[6–8]. Subcutaneous administration is the first-choice administration route in palliative care for patients who are unable to receive opioids orally or transdermally[5,9]. When subcutaneous administration is contraindicated, intravenous opioid administration is selected. This contraindication may be due to cases of peripheral edema, coagulation disorders, poor peripheral circulation, the need for high volumes and

Correspondence to Masayoshi Kondo, Department of Pharmacy, Nippon Medical School Tama Nagayama Hospital, 1–7–1 Nagayama, Tama, Tokyo 206–8512, Japan
E-mail: kondomasayoshi@nms.ac.jp
https://doi.org/10.1272/jnms.JNMS.2023_90-508
Journal Website (https://www.nms.ac.jp/sh/jnms/)

Table 1 Composition of Bfluid® and Elneopa®-NF No.2

Bfluid® 1,000 mL (2-in-1 peripheral parenteral nutrition)					
Glucose	75 g	SO_4^{2-}	5 mEq	Zn	5 μmol
Free amino acids	30 g	$Acetate^-$	16 mEq		
Na^+	35 mEq	L-$Lactate^-$	20 mEq		
K^+	20 mEq	$Citrate^{3-}$	6 mEq		
Mg^{2+}	5 mEq	P	10 mmol		
Ca^{2+}	5 mEq	Thiamine chloride hydrochloride	1.92 mg		
Cl^-	35 mEq				
Elneopa®-NF No. 2 1,000 mL (2-in-1 total parenteral nutrition)					
Glucose	175 g	Thiamine chloride hydrochloride	3.84 mg	Fe	10 μmol
Free amino acids	30 g	Riboflavin phosphate sodium	2.3 mg	Mn	0.5 μmol
Na^+	50 mEq	Pyridoxine hydrochloride	3.68 mg	Zn	30 μmol
K^+	27 mEq	Cyanocobalamin	2.5 μg	Cu	2.5 μmol
Mg^{2+}	5 mEq	Nicotinamide	20 mg	I	0.5 μmol
Ca^{2+}	5 mEq	Panthenol	7 mg		
Cl^-	50 mEq	Folic acid	0.3 mg		
SO_4^{2-}	5 mEq	Biotin	30 μg		
$Acetate^-$	48 mEq	Ascorbic acid	100 mg		
L-$Lactate^-$	14 mEq	Vitamin A Oil	1,650 IU		
$Citrate^{3-}$	12 mEq	Cholecalciferol	2.5 μg		
P	6 mmol	Tocopherol acetate	5 mg		
		Phytonadione	0.075 mg		

(IU, International Unit)

doses, or when rapid pain control is needed[5]. If intravenous administration rather than subcutaneous administration is chosen for palliative care patients, continuous injections containing opioids may be combined and administered intravenously via the same route as that of remdesivir. However, remdesivir compatibility tests have only been carried out with 0.9% sodium chloride; remdesivir compatibility tests with drugs used in palliative care or COVID-19 treatment have not been conducted[1].

Because of a lack of compatibility data for remdesivir with these drugs, multiple separate injectable drug administration access sites are currently required to deliver potentially incompatible drugs simultaneously. It may be difficult to obtain new injectable drug administration access sites for palliative care patients, and therefore remdesivir may be withheld due to a lack of administration access. To gather insights on this topic, in this study, we evaluated the physical compatibility of remdesivir with opioid analgesics, heparin, furosemide, octreotide, and electrolytes and nutrition infusion during simulated Y-site administration, assuming a palliative care patient.

Materials and Methods

Test materials: Remdesivir was mixed with fentanyl citrate, morphine hydrochloride hydrate, hydromorphone hydrochloride, oxycodone hydrochloride hydrate, heparin sodium, furosemide, octreotide acetate, Solyugen® F, Bfluid®, or Elneopa®-NF No.2. Solyugen® F is acetated Ringer's injection, and its composition is as follows: Na^+ 130 mEq/L, K^+ 4 mEq/L, Ca^{2+} 3 mEq/L, Cl^- 109 mEq/L, and CH_3COO^- 28 mEq/L[10]. Bfluid® is a 2-in-1 peripheral parenteral nutrition (PPN), and Elneopa®-NF No. 2 is a 2-in-1 total parenteral nutrition (TPN), and their respective compositions are shown in **Table 1**[11,12].

Target drugs containing remdesivir were prepared at the upper range of the concentrations used in clinical settings. Remdesivir (Lot AS1641CA and AR7050CA; Gilead Sciences, Inc.) was dissolved in 19 mL of water for injection (Lot 11104C; Otsuka Pharmaceutical Factory, Inc.), then diluted with 0.9% sodium chloride (Lot 2E95P and 2H89P; Otsuka Pharmaceutical Factory, Inc.) to a final concentration of 1 mg/mL. Hydromorphone hydrochloride (Lot UTA0029; Daiichi Sankyo Co., Ltd.) and octreotide acetate (Lot R108A; Aska Pharmaceutical Co., Ltd.) were diluted in 0.9% sodium chloride (Lot 2H89P; Otsuka Pharmaceutical Factory, Inc.) to prepare solutions with concentrations of 1 mg/mL and 30 μg/mL, respectively. Fentanyl citrate (Lot F2019; Terumo, Corp.), morphine hydrochloride hydrate (Lot W5696; Shionogi Pharma Co., Ltd.), oxycodone hydrochloride hydrate (Lot SQA0027; Daiichi Sankyo Co., Ltd.), heparin sodium (Lot C756; Mochida Pharmaceutical Co., Ltd.), and furosemide

Table 2 Control solutions for each drug

	Control solution [a]		
	Turbidity (NTU)	Tyndall effect	Visual
Remdesivir	0.19 ± 0.04	None	Colorless, clear
Fentanyl	0.04 ± 0.03[b]	None	Colorless, clear
Morphine	0.09 ± 0.02	None	Colorless, clear
Hydromorphone	0.04 ± 0.02	None	Colorless, clear
Oxycodone	0.04 ± 0.04[b]	None	Colorless, clear
Heparin	0.08 ± 0.03	None	Colorless, clear
Furosemide	0.03 ± 0.03[b]	None	Colorless, clear
Octreotide	0.03 ± 0.03	None	Colorless, clear
Solyugen® F[c]	0.02 ± 0.03[b]	None	Colorless, clear
Bfluid®[d]	0.04 ± 0.03[b]	None	Colorless, clear
Elneopa®-NF No. 2[e]	0.01 ± 0.00[b]	None	Yellow, clear

(NTU, Nephelometric turbidity unit)
a) 6 mL of the target drug and 6 mL of 0.9% sodium chloride were combined
b) Including less than the quantification limit
c) Acetated Ringer's injection
d) 2-in-1 peripheral parenteral nutrition
e) 2-in-1 total parenteral nutrition

(Lot D0142; Towa Pharmaceutical Co., Ltd.) were prepared as solutions with concentrations of 0.05 mg/mL, 10 mg/mL, 10 mg/mL, 1,000 U/mL, and 10 mg/mL without dilution. Solyugen® F (Lot 22M42D; Hikari Pharmaceutical Co., Ltd.), Bfluid® (Lot M2F86N; Otsuka Pharmaceutical Factory, Inc.), and Elneopa®-NF No. 2 (Lot K2 G82; Otsuka Pharmaceutical Factory, Inc.) were prepared as is. Before being mixed as test or control solutions, each of the prepared test materials was passed through a 0.22 μm filter (Millex-GV PVDF filter unit, Lot R1JB14225; Merck Millipore, Ltd.). Furthermore, during each test, 1 mL of each target drug, including remdesivir, was prepared for pH measurement.

Test solutions: In a turbidity measuring vial, the test solutions were prepared by mixing remdesivir and the target drugs at an equal volume ratio (1:1) to a total volume of 12 mL. The compatibility tests were conducted by preparing three test solutions. pH, turbidity, visual inspection, and the Tyndall effect were evaluated immediately after mixing, and at 1 h and 4 h post-mixing. The pH and turbidity were measured by inverting the test solutions 10 times immediately before measurement.

Control solutions: Control solutions were prepared for all target drugs to evaluate their visual appearances, including turbidity. The control solutions were prepared with 0.9% sodium chloride to a concentration corresponding to the test solution.

Physical compatibility tests: pH was measured using a pH meter (LAQUA act D72, Horiba, Ltd.) and a pH electrode (9618S-10D, Horiba., Ltd.) according to the 18th edition of the Japanese Pharmacopeia[13]. The pH meter was calibrated before each experiment using pH 4, pH 7, and pH 9 standards. Turbidity was measured using a turbidimeter (TurbiDirect TB300IR, Tintometer., GmbH.) based on the scattered light measurement method. Three consecutive measurements of turbidity were performed for each test solution in each period. The turbidimeter was calibrated before each experiment using the standard turbidity of <0.1, 20, 200, and 800 nephelometric turbidity units (NTU) according to the manufacturer's recommendations. The dynamic range of the turbidimeter used was 0.01-1,100 NTU. If an individual measurement result surpassed the dynamic range, the sample was recorded as 0.01 NTU or 1,100 NTU, and it was specified that the limit of quantification was exceeded.

Visual inspection was performed against both a white and black background with the naked eyes at a position of light intensity of 2,000 to 3,750 lx under a white LED light source (DS-LS24DSM-W, illumination; 3,000 lx under the condition of 30 cm straight down, OHM Electric., INC.) according to the 18th edition of the Japanese Pharmacopeia[13]. The presence of the Tyndall effect was observed by shining a red laser pointer (PR500-RC, 635 nm, maximum output 1 mW or less, Canon Marketing Japan Co., Ltd.) from the bottom of each test solution in the dark.

Physical incompatibilities were determined by visual, turbidity, and pH assessments. Visual and turbidity-based physical incompatibilities were defined as gross precipitation, change in the Tyndall effect, cloudiness, or

Table 3 Physical compatibility of remdesivir with test drugs

Combination of the test drugs				Immediately	1 h	4 h
	Remdesivir	Fentanyl	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	0.05 mg/mL	Tyndall	None	None	None
Mfr	Gilead Sciences	Terumo	pH	3.91 ± 0.01	3.87 ± 0.05	3.80 ± 0.01
pH	3.60	4.08	Turbidity (NTU)	0.14 ± 0.03	0.15 ± 0.04	0.19 ± 0.05
	Remdesivir	Morphine	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	10 mg/mL	Tyndall	None	None	None
Mfr	Gilead Sciences	Shionogi Pharma	pH	3.27 ± 0.01	3.23 ± 0.03	3.23 ± 0.02
pH	3.61	2.79	Turbidity (NTU)	0.13 ± 0.04	0.15 ± 0.05	0.19 ± 0.05
	Remdesivir	Hydromorphone	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	1 mg/mL[b)]	Tyndall	None	None	None
Mfr	Gilead Sciences	Daiichi Sankyo	pH	3.87 ± 0.01	3.86 ± 0.02	3.93 ± 0.03
pH	3.60	3.93	Turbidity (NTU)	0.12 ± 0.04	0.11 ± 0.03	0.15 ± 0.03
	Remdesivir	Oxycodone	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	10 mg/mL	Tyndall	None	None	None
Mfr	Gilead Sciences	Daiichi Sankyo	pH	4.40 ± 0.03	4.38 ± 0.02	4.49 ± 0.02
pH	3.60	4.55	Turbidity (NTU)	0.16 ± 0.04	0.18 ± 0.05	0.18 ± 0.06
	Remdesivir	Heparin	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	1,000 U/mL	Tyndall	None	None	None
Mfr	Gilead Sciences	Mochida	pH	4.78 ± 0.01	4.78 ± 0.01	4.76 ± 0.04
pH	3.76	5.60	Turbidity (NTU)	0.12 ± 0.02	0.15 ± 0.06	0.20 ± 0.05
	Remdesivir	Furosemide	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	10 mg/mL	Tyndall	None	None	None
Mfr	Gilead Sciences	Towa	pH	8.65 ± 0.07	8.65 ± 0.04	8.81 ± 0.06
pH	3.67	9.07	Turbidity (NTU)	0.19 ± 0.07	0.23 ± 0.03	0.22 ± 0.07
	Remdesivir	Octreotide	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	30 μg/mL[b)]	Tyndall	None	None	None
Mfr	Gilead Sciences	Aska	pH	4.05 ± 0.01	4.03 ± 0.03	4.02 ± 0.01
pH	3.74	4.07	Turbidity (NTU)	0.07 ± 0.05	0.13 ± 0.06	0.07 ± 0.05
	Remdesivir	Solyugen® F[c)]	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	Undiluted solution	Tyndall	None	None	None
Mfr	Gilead Sciences	Hikari	pH	5.90 ± 0.06	5.90 ± 0.06	5.90 ± 0.07
pH	3.74	6.55	Turbidity (NTU)	0.06 ± 0.03	0.05 ± 0.02	0.06 ± 0.04
	Remdesivir	Bfluid®[d)]	Visual	Colorless, clear	Colorless, clear	Colorless, clear
Conc	1 mg/ mL[a)]	Undiluted solution	Tyndall	None	None	None
Mfr	Gilead Sciences	Otsuka	pH	6.64 ± 0.02	6.65 ± 0.04	6.64 ± 0.01
pH	3.76	6.75	Turbidity (NTU)	0.06 ± 0.05	0.07 ± 0.01	0.02 ± 0.02
	Remdesivir	Elneopa®-NF No.2[e)]	Visual	Yellow, clear	Yellow, clear	Yellow, clear
Conc	1 mg/ mL[a)]	Undiluted solution	Tyndall	None	None	None
Mfr	Gilead Sciences	Otsuka	pH	5.34 ± 0.01	5.33 ± 0.02	5.36 ± 0.01
pH	3.76	5.32	Turbidity (NTU)	0.04 ± 0.03[f)]	0.05 ± 0.04	0.04 ± 0.03

(Conc, Concentration of the tested drug; Mfr, Manufacturer of the test drug; NTU, Nephelometric turbidity unit)

a) Dissolved in 19 mL of water for injection and then diluted with 0.9% sodium chloride

b) Prepared in 0.9% sodium chloride injection

c) Acetated Ringer's injection

d) 2-in-1 peripheral parenteral nutrition

e) 2-in-1 total parenteral nutrition

f) Including less than the quantification limit

a turbidity change of ≥ 0.5 NTU, based on the highest turbidity in the control solutions[14–16]. A pH change of ≥ 10% relative to the pH immediately after mixing was defined to be indicative of physical incompatibility[17].

Results

The control solutions for each drug are listed in **Table 2**. The turbidity of remdesivir's control solution was 0.19 ± 0.04 NTU, the highest turbidity value among control solutions. The Tyndall effect was not observed in any of the control solutions.

The results of all compatibility tests and the pH of each drug before the tests are listed in **Table 3**. The pH of remdesivir (mean value ± standard deviation) was 3.68 ± 0.07 (n =10). Morphine had the lowest pH of 2.79, and furosemide had the highest pH, at 9.07. The combination of remdesivir and morphine (3.23 ± 0.02) 4 h after mixing, and the combination of remdesivir and furosemide (8.81 ± 0.06) 4 h after mixing, had the lowest and highest pH, respectively. The combination of remdesivir and furosemide produced the highest turbidity and change of turbidity than the remdesivir control solution (0.23 ± 0.03 NTU; change of turbidity, 0.04 NTU) 1 h after mixing. Therefore, remdesivir was compatible with all the drugs and drug combinations up to 4 h after mixing.

Discussion

Our results revealed that during simulated Y-site administration, remdesivir had no physical incompatibilities with fentanyl, morphine, hydromorphone, oxycodone, heparin, furosemide, octreotide, acetated Ringer's injection, 2-in-1 PPN, or 2-in-1 TPN. These findings may be useful in deciding whether to administer a combination of these drugs through the same infusion route.

The mixing of injection drugs carries the risk of potential physicochemical incompatibility and should be avoided as much as possible. Mixing of injectable drugs, including continuous infusions, is considered based on the results of physicochemical compatibility tests while mixing of intermittent drugs can be avoided by scheduling. Therefore, in this study, a continuous infusion drug was selected as the target drug for the compatibility test with remdesivir. Octreotide was investigated as a target drug in this study in combination with remdesivir; although continuous intravenous infusion of octreotide for treatment of malignant bowel obstruction is not recommended in Japan[18], in practice, octreotide is sometimes administered by continuous intravenous infusion during off-label use[8].

The pH of remdesivir compounded with the target drugs ranged from 3.23 (remdesivir and morphine) to 8.81 (remdesivir and furosemide), whereas the pH of remdesivir without the target drugs was 3.68 ± 0.07. However, no combinations were found to be incompatible in this study. Furosemide has been reported to be incompatible with other drugs due to pH fluctuations and furosemide (10 mg/mL) has a cloudy appearance below pH 6.27[19]. Remdesivir has a lower buffering capacity than furosemide, and thus furosemide and remdesivir could be combined, as the buffering capacity of remdesivir was lower than that of furosemide, and the combination of remdesivir and furosemide did not have a pH below 6.27. In this study, remdesivir did not show any relationship between pH fluctuation and drug incompatibility.

This study has some limitations. Primarily, chemical compatibility evaluations, encompassing stability assessments, were not undertaken. Hence, when administering remdesivir in conjunction with the drugs examined in this research, including opioids, heparin, furosemide, and octreotide, considering the potential instability of these medications and tracking their therapeutic impacts are essential. Additionally, due to the short-term nature of the investigation, we did not determine whether the formulations of the drugs left for more than 4 h were incompatible.

Conclusions

This study found no physical incompatibilities in the combination of remdesivir with fentanyl, morphine, hydromorphone, oxycodone, heparin, furosemide, octreotide, acetated Ringer's injection, 2-in-1 PPN, or 2-in-1 TPN up to 4 h after mixing. This study provides useful data to prove that remdesivir can be administered through the existing infusion route for patients who have difficulty securing an infusion route.

Acknowledgements: Masayoshi Kondo received funding from JSPS KAKENHI (Grant Number 22K09104) for this research. The funders had no role in the execution of this study or in the interpretation of the results.

Conflict of Interest: The authors declare that there are no conflicts of interest.

References

1. Veklury (Remdesivir) [package insert]. Foster City, CA: Gilead Sciences, Inc.; 2020.
2. Yamakawa K, Yamamoto R, Terayama T, et al. Japanese rapid/living recommendations on drug management for COVID-19: updated guidelines (July 2022). Acute Med Surg. 2022 Oct;9(1):e789.
3. Takahashi Y, Wakita H, Ishihara T, et al. Short-course remdesivir for healthcare-associated COVID-19: case series from a non-acute care hospital. J Infect Chemother.

2023 Jan;29(1):95–7.
4. Panagopoulos P, Petrakis V, Trypsianis G, Papazoglou D. Early 3-day course of remdesivir in vaccinated outpatients with SARS-CoV-2 infection. A success story. J Chemother. 2022 Dec;34(8):550–3.
5. Caraceni A, Hanks G, Kaasa S, et al. Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC. Lancet Oncol. 2012 Feb;13 (2):e58–68.
6. Pilia E, Belletti A, Fresilli S, Finco G, Landoni G. Efficacy and safety of heparin full-dose anticoagulation in hospitalized non-critically ill COVID-19 patients: a meta-analysis of multicenter randomized controlled trials. J Thromb Thrombolysis. 2022;54(3):420–30.
7. Brown A, Westley K, Robson J, et al. Furosemide in end-stage heart failure: community subcutaneous infusions. BMJ Support Palliat Care. 2022 Dec;12(e6):e763–6.
8. Hisanaga T, Shinjo T, Morita T, et al. Multicenter prospective study on efficacy and safety of octreotide for inoperable malignant bowel obstruction. Jpn J Clin Oncol. 2010 Aug;40(8):739–45.
9. Parsons HA, Shukkoor A, Quan H, et al. Intermittent subcutaneous opioids for the management of cancer pain. J Palliat Med. 2008 Dec;11(10):1319–24.
10. Solyugen F. Injection [package insert]. Tokyo: Hikari Pharmaceutical Co., Ltd.; 2022. Japanese.
11. Bfluid Injection [package insert]. Tokushima: Otsuka Pharmaceutical Factory, Inc.; 2022. Japanese.
12. Elneopa-NF No.2 Injection [package insert]. Tokyo: Otsuka Pharmaceutical Factory, Inc.; 2022. Japanese.
13. Ministry of Health, Labour and Welfare. The Japanese Pharmacopeia, Eighteenth Edition [Internet]. Tokyo: Ministry of Health, Labour and Welfare; 2021. [cited 2023 Apr 21]. Available from: https://www.pmda.go.jp/rs-std-jp/standards-development/jp/0192.html
14. Kondo M, Nagano M, Yoshida M, et al. Physical Compatibility of Nafamostat with Analgesics, Sedatives, and Muscle Relaxants for Treatment of Coronavirus Disease 2019. J Nippon Med Sch. 2021 Dec 29;88(6):533–9. Epub 2021 Mar 9.
15. Ghazi IM Dr, El Nekidy WS Dr, Sood AMr, et al. Y-site Administration of Imipenem/Cilastatin/Relebactam With Common Intravenous Medications. Clin Ther. 2020 Mar; 42(3):475–85. Epub 2020 Mar 2.
16. Housman ST, Tessier PR, Nicolau DP, Kuti JL. Physical compatibility of telavancin hydrochloride with select i.v. drugs during simulated Y-site administration. Am J Health Syst Pharm. 2011 Dec 1;68(23):2265–70.
17. Kondo M, Yoshida N, Yoshida M, et al. Physical compatibility of remimazolam with opioid analgesics, sedatives, and muscle relaxants during simulated Y-site administration. Am J Health Syst Pharm. 2023 Jan 1;80(1):e53–8.
18. Octreotide for s.c. injection [package insert]. Tokyo: Aska Pharmaceutical Co., Ltd.; 2021. Japanese.
19. Furosemide Injection 20 mg "TOWA" [Pharmaceutical interview form]. Osaka: Towa Pharmaceutical Co., Ltd.; 2019. Japanese.

(Received, February 2, 2023)
(Accepted, May 1, 2023)
(J-STAGE Advance Publication, June 2, 2023)