

PMDA

Medical Safety Information

Pharmaceuticals and Medical Devices Agency



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Precautions for Route of Administration of Total Parenteral Nutrition

1 Administration of total parenteral nutrition through incorrect route of administration

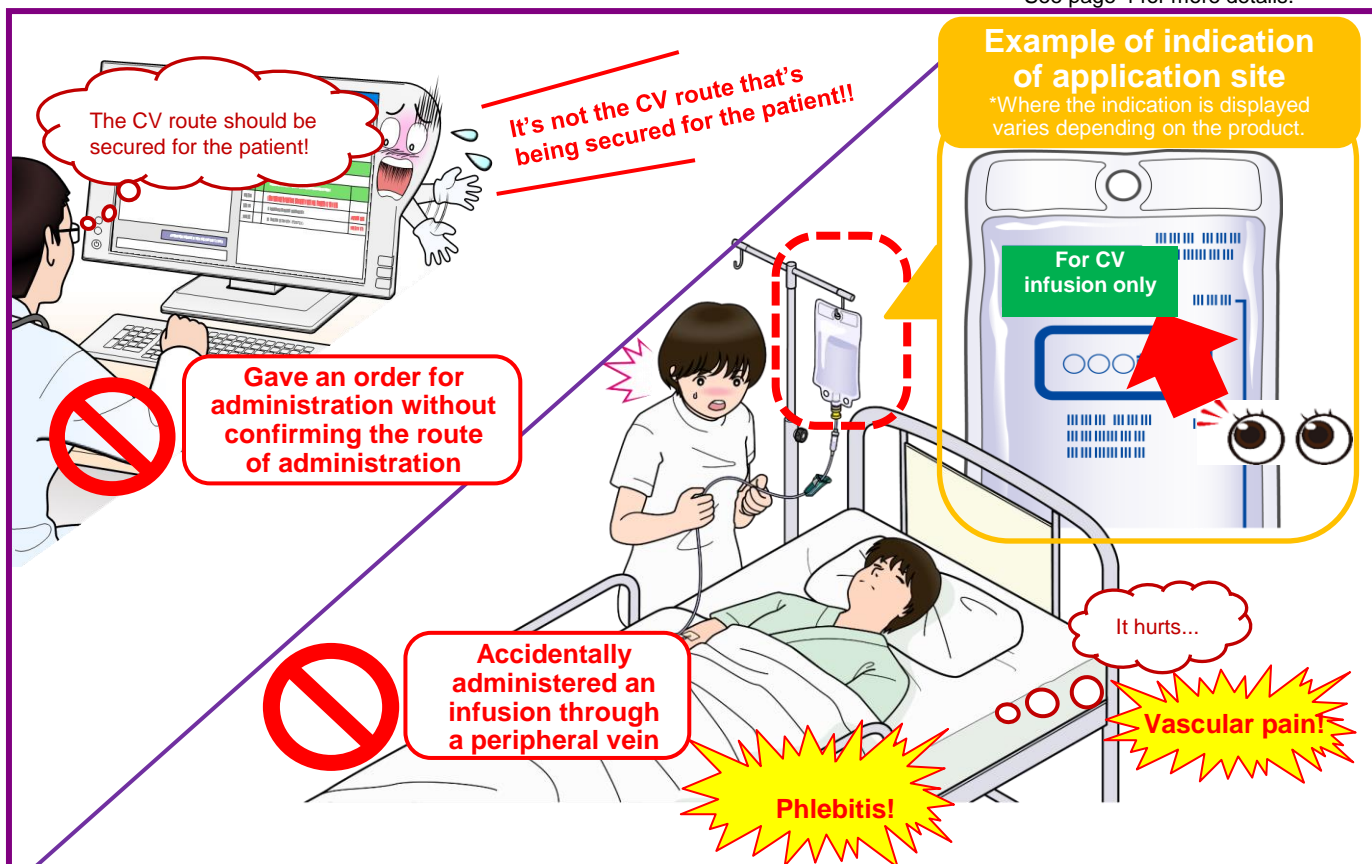
(Case 1) A nutritional infusion was administered through a peripheral vein, but the attending doctor assumed that the central venous (CV) route had been secured, and ordered a change to total parenteral nutrition. The nurse started the administration through a peripheral vein without confirming the correct route of administration.

POINT

Key points for safe use

- Please be sure to check the indication of the application site on the infusion container, such as “For CV infusion only.”
- Each line of healthcare professionals is requested to check the 6Rs* including the validity at the time of prescription, dispensing and auditing, administration or replacement of infusions, etc.

*See page 4 for more details.



When total parenteral nutrition is administered through a peripheral vein, patients may experience adverse events, including **vascular pain** and **phlebitis**.

The reasons for administering total parenteral nutrition through a central vein are ...

- (1) An **osmotic pressure ratio** of approximately 3 is considered to be the limit for the administration of infusions through a peripheral vein.
 A higher glucose concentration in a glucose-electrolyte solution leads to increased osmotic pressure and more frequent phlebitis.
- (2) **pH and other factors** also have some impacts.
 When delivering peripheral venous nutrition, please choose one with a pH close to neutral.

Source) Guideline for parenteral and enteral nutrition Version 3 Partially revised from p.34 (Japanese Society for Parenteral and Enteral Nutrition (Current Japanese Society for Clinical Nutrition and Metabolism))



As central veins are thick and have abundant blood flow, infusions are quickly diluted with blood and total parenteral nutrition can be administered.

Source) Page 283, excerpted and reprinted with permission from Eiji Yamanaka, "Route of Administration (including PICC)" issued in 2021, Japanese Society for Clinical Nutrition and Metabolism, JSPEN Textbook, published by Nankodo

**List of infusions that should be administered through a central vein
 (in Japanese syllabary order)**

*Note) Osmotic pressure ratios after mixing are shown for bag-type kit preparations.

Brand name	Therapeutic category (or non-proprietary name, etc.)	Osmotic pressure ratio ^{*Note)} (ratio to saline solution)
ELNEOPA-NF Injection	Amino acid/glucose/electrolytes/multivitamin/trace element solution for total parenteral nutrition	About 4 to 6
OTSUKA GLUCOSE INJECTION 70%	Glucose Injection, the Japanese Pharmacopoeia	About 15
OTSUKA GLUCOSE INJECTION 50% (200 mL , 500 mL)	Glucose Injection, the Japanese Pharmacopoeia	About 12
50w/v% Glucose Injection (200 mL , 500 mL)	Glucose Injection, the Japanese Pharmacopoeia	About 12
NEOPAREN Injection	Amino acid/glucose/electrolytes/multivitamin solution for total parenteral nutrition	About 4 to 6
HICALIQ RF Infusion	Basic solution for total parenteral nutrition	About 11
HICALIQ Infusion	Basic solution for total parenteral nutrition	About 4 to 8
PNTWIN Injection	Glucose/electrolytes/amino acid solution for total parenteral nutrition	About 4 to 7
FULCALIQ Infusion	Multivitamin/glucose/amino acid/electrolyte solution for total parenteral nutrition	About 4 to 6
MIXID Injection	Amino acid/glucose/fat/electrolyte solution for total parenteral nutrition	About 4 to 5
Rehabix Injection	Basic solution for total parenteral nutrition, for pediatric use	About 4 to 5
ONEPAL Injection	Glucose/electrolytes/amino acid/vitamin/trace element solution for total parenteral nutrition	About 4.8 to 6.7

The tables on this page and the next page are as of December 2023.

Multiple preparations are listed together. For more information, please refer to the latest package insert for each product.

To search package insert, visit the URL or scan the QR code <https://www.pmda.go.jp/PmdaSearch/iyakuSearch/>



2 Infusions that can be used through both peripheral and central venous routes, but require attention

(Case 2) Although a 70% glucose solution and amino acid infusion were administered through a CV route, they were removed due to signs of infection. The doctor assumed that the 70% glucose solution could be administered through a peripheral vein and ordered to administer it through a peripheral vein. No pharmacists checked it because it was only a change in the route of administration. Phlebitis was observed after administration through a peripheral vein, revealing that the 70% glucose solution should not have been administered through a peripheral vein.

POINT Points to be noted for safe use

- There are infusions with different doses, etc. for peripheral and CV administration. Please be sure to check the latest package insert.
- Bag preparations of a highly concentrated (hyperosmotic) glucose solution of **50% or more** (200 mL or more) are used as **total parenteral nutrition** and must be administered through a central vein.

Examples of infusions requiring different routes of administration depending on concentration, dose, etc. (in Japanese syllabary order)

Brand name	Therapeutic category (or non-proprietary name , etc.)	Osmotic pressure ratio (Ratio to saline solution)
AMIZET B Infusion	Comprehensive amino acid preparation	About 3
AMINIC Injection	Comprehensive amino acid preparation	About 3
AMINOLEBAN Injection	Amino acid injection for treatment of hepatic encephalopathy	About 3
AMIPAREN Injection	Comprehensive amino acid preparation	About 3
OTSUKA GLUCOSE INJECTION	Glucose Injection, the Japanese Pharmacopoeia	OTSUKA GLUCOSE INJECTION 5%: About 1 (It varies depending on the concentration)
KIDMIN Injection	Amino acid injection for renal failure	About 2
TERUFIS I.V. Infusion	Amino acid injection for treatment of hepatic encephalopathy	About 3
Glucose Injection	Glucose Injection, the Japanese Pharmacopoeia	5w/v% Glucose Injection: About 0.9 (It varies depending on the concentration)
Neoamiyu Injection	Comprehensive amino acid injection for renal failure	About 2
Hikarilevan Injection	Amino acid injection for treatment of hepatic encephalopathy	About 3
PROTEAMIN 12 Injection	Comprehensive amino acid preparation	About 5
MORIPRON-F Injection	Comprehensive amino acid preparation	About 3
MORIHEPAMIN Injection	Amino acid injection for hepatic failure	About 3

When these infusions are administered as total parenteral nutrition, they are given as a continuous intravenous infusion through a central vein!



3 Measures to prevent incorrect route of administration of total parenteral nutrition

The 6Rs to prevent medication errors are...

Six specific points where pointing and calling out, double-checking, etc. should be implemented.

At the time of prescribing (**doctors**), dispensing and auditing (**pharmacists**), preparing in advance and immediately before administration (**nurses**)

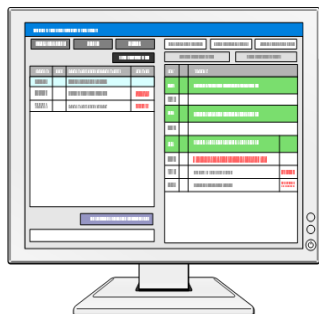
It is important for each line of healthcare professionals to check the 6Rs including the validity at their own timing!
It is a good idea to create rules about the timing and method of confirming the 6Rs for each line at your facility!

- 1 Right Patient
- 2 Right Drug
- 3 Right Purpose
- 4 Right Route
- 5 Right Dose
- 6 Right Time

• Please be sure to check if the route of administration is the CV route at the time of initial order, audit, changing the infusion or route of administration!

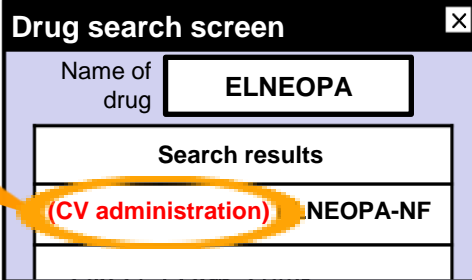
• Please trace the route of administration to the infusion site and check it at the time of changing the infusion or route of administration!

Examples of ordering system ingenuity



Display the route of administration before the name of the drug.

Example of search



The Intravenous Solutions Society has also issued a precaution related to this “PMDA Medical Safety Information No. 67.”



https://www.yueki.com/anti_malpractice/index.html

>Initiatives for prevention of medical malpractices

- Total parenteral nutrition should not be administered through a peripheral vein!
- Checkpoints for administering total parenteral nutrition

According to an independent arrangement among industry associations, the containers of injections and infusions are required to include the indication of “application site, etc.”

●September 19, 2007, Notification No. 529 issued by The Federation of Pharmaceutical Manufacturers' Associations of JAPAN

“Independent Arrangement on Indication of Application Site, etc. on Containers for Injections”

●April 21, 2008, Notification No. 3 issued by The Intravenous Solutions Society
“Indication of Application Site, etc. on Containers for Infusions, etc.”

(Reference) Addition of indication of application site, etc.
(Website page of The Intravenous Solutions Society)
<https://www.yueki.com/measure3/3/index.html>



About this information

- PMDA Medical Safety Information is issued by the Pharmaceuticals and Medical Devices Agency for the purpose of providing healthcare providers with clearer information from the perspective of promoting the safe use of pharmaceuticals and medical devices. The information presented here has been compiled, with the assistance of expert advice, from cases collected as Medical Accident Information Reports by the Japan Council for Quality Health Care, and collected as Adverse Drug Reaction and Malfunction Reports in accordance with the Law on Securing Quality, Efficacy and Safety of Pharmaceuticals and Medical Devices.
- We have tried to ensure the accuracy of this information at the time of its compilation but do not guarantee its accuracy in the future.
- This information is not intended to impose constraints on the discretion of healthcare professionals or to impose obligations and responsibility on them, but is provided as a support to promote the safe use of pharmaceuticals and medical devices by healthcare professionals.
- This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Access to the most up-to-date safety information is provided via the PMDA Medi-navi service.

