Published by
Ministry of Health, Labour and Welfare

Translated by
Pharmaceuticals and Medical Devices Agency

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.

Revision of Precautions

Hydroxyethylated starch 130000

January 12, 2023

Therapeutic category

Blood substitutes

Non-proprietary name

Hydroxyethylated starch 130000

Safety measure

Precautions should be revised.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

Revision in line with the Instructions for Package Inserts of Prescription Drugs, PAB Notification No. 606 by the Director General of Pharmaceutical Affairs Bureau, MHW, dated April 25, 1997 (Old instructions): Revised language is underlined.

Current	Revision
Warning The condition of patients may be exacerbated when this drug is used in relative decreased blood volume during the management of critically ill patients <u>including patients with severe sepsis</u>. This drug should be administered only if the therapeutic benefits outweigh the risks.	Warning The condition of patients may be exacerbated when this drug is used in relative decreased blood volume during the management of critically ill patients. This drug should be administered only if the therapeutic benefits outweigh the risks.
Contraindications (N/A)	Contraindications <u>Patients with severe sepsis [The condition of patients may be exacerbated.]</u>
Careful Administration (N/A)	Careful Administration <u>Patients with sepsis (excluding patients with severe sepsis)</u> <u>[If the disease becomes severe, the condition of patients may be exacerbated.]</u>
Other Precautions In overseas clinical studies, it has been reported that the use of HES preparations in patients with severe sepsis was associated with a higher mortality risk at 90 days after administration and a higher percentage of patients requiring renal replacement therapy,	Other Precautions In overseas clinical studies, it has been reported that the use of HES preparations in patients with severe sepsis <u>(having infection, meeting the systemic inflammatory response syndrome (SIRS) criteria, and having at least one organ dysfunction [= SOFA score of</u>

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

as compared with the use of acetated Ringer's solution. It has been also reported that the use of HES preparations in patients admitted to the ICU including patients with sepsis was associated with a higher percentage of patients requiring renal replacement therapy, as compared with the use of saline, although the mortality risk up to 90 days after administration did not increase.	3 or more]) was associated with a higher mortality risk at 90 days after administration and a higher percentage of patients requiring renal replacement therapy, as compared with the use of acetated Ringer's solution. It has been also reported that the use of HES preparations in patients admitted to the ICU including patients with sepsis was associated with a higher percentage of patients requiring renal replacement therapy, as compared with the use of saline, although the mortality risk up to 90 days after administration did not increase.

N/A: Not Applicable. No corresponding language is included in the current Precautions.

Revision in line with the Instructions for Electronic Package Inserts of Prescription Drugs, etc. PSEHB Notification No. 0611-1 by the Director of Pharmaceutical Safety and Environmental Health Bureau, MHLW, dated June 11, 2021 (New instructions): Revised language is underlined.

Current	Revision
1. WARNINGS The condition of patients may be exacerbated when this drug is used in relative decreased blood volume during the management of critically ill patients including patients with severe sepsis. This drug should be administered only if the therapeutic benefits outweigh the risks. 2. CONTRAINDICATIONS (N/A)	1. WARNINGS The condition of patients may be exacerbated when this drug is used in relative decreased blood volume during the management of critically ill patients. This drug should be administered only if the therapeutic benefits outweigh the risks. 2. CONTRAINDICATIONS Patients with severe sepsis [The condition of patients may be exacerbated.]

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.1 Patients with Complication or History of Diseases, etc. (N/A)	9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS 9.1 Patients with Complication or History of Diseases, etc. Patients with sepsis (excluding patients with severe sepsis) If the disease becomes severe, the condition of patients may be exacerbated.
15. OTHER PRECAUTIONS 15.1 Information Based on Clinical Uses In overseas clinical studies, it has been reported that the use of HES preparations in patients with severe sepsis was associated with a higher mortality risk at 90 days after administration and a higher percentage of patients requiring renal replacement therapy, as compared with the use of acetated Ringer's solution. It has been also reported that the use of HES preparations in patients admitted to the ICU including patients with sepsis was associated with a higher percentage of patients requiring renal replacement therapy, as compared with the use of saline, although the mortality risk up to 90 days after administration did not increase.	15. OTHER PRECAUTIONS 15.1 Information Based on Clinical Uses In overseas clinical studies, it has been reported that the use of HES preparations in patients with severe sepsis (having infection, meeting the systemic inflammatory response syndrome (SIRS) criteria, and having at least one organ dysfunction [= SOFA score of 3 or more]) was associated with a higher mortality risk at 90 days after administration and a higher percentage of patients requiring renal replacement therapy, as compared with the use of acetated Ringer's solution. It has been also reported that the use of HES preparations in patients admitted to the ICU including patients with sepsis was associated with a higher percentage of patients requiring renal replacement therapy, as compared with the use of saline, although the mortality risk up to 90 days after administration did not increase.

N/A: Not Applicable. No corresponding language is included in the current Precautions.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp