FINAL STUDY REPORT FOR PROTOCOL HC-O-H-1408
POST-AUTHORISATION SAFETY STUDY

PASS information

Title	Retrospective drug utilisation study to investigate the routine use of hydroxyethyl starch (HES)-containing infusion solutions of B. Braun Melsungen AG in hospitals
Version identifier of the final study report	Version 1.0, September 22, 2017
Date of last version of the final study report	Not applicable
EU PAS register number	ENCEPP/SDPP/12540
Active substance	Poly(O-2-hydroxyethyl)starch Sodium chloride Sodium acetate trihydrate (for Tetraspan) Potassium chloride (for Tetraspan) Magnesium chloride hexahydrate (for Tetraspan) Calcium chloride dehydrate (for Tetraspan) Malic acid (for Tetraspan) **ATC code:** Blood substitutes and plasma protein fractions B05AA07 hydroxyethylstarch
Medicinal product	The registered product name for the individual products of B. Braun Melsungen AG concerned in the European countries in which the drug utilisation study (DUS) is conducted is provided in Annex 1.
Product reference	Not applicable
Procedure number	SE/H/414/001/MR; SE/H/0609/001-002/MR
Marketing authorisation holder(s)	B. Braun Melsungen AG Carl-Braun-Straße 1, 34212 Melsungen, Germany.
Joint PASS	No
Research question and objectives	The objective of the DUS was to assess the adherence of hospital physicians to the revised European Product Information (PI) [Summary of Product Characteristics; Package Leaflet] for HES-containing medicinal products of B. Braun Melsungen AG concerning indication, posology (dosage) and contraindications (as listed in Annex III of the European Commission [EC] decision).
Country(-ies) of study	Belgium, Czech Republic, France, Germany, Italy, Netherlands, Poland, Spain and Sweden.
Author	[redacted]

Marketing authorisation holder(s)

Marketing authorisation holder(s)	B. Braun Melsungen AG Carl-Braun-Straße 1, 34212 Melsungen, Germany.
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Abstract

Title

Retrospective drug utilisation study to investigate the routine use of hydroxyethyl starch (HES)-containing infusion solutions of B. Braun Melsungen AG in hospitals

Keywords

Retrospective; Drug Utilisation Study; Hydroxyethyl; Starch; Infusion

Rationale and Background

The European Medicines Agency Pharmacovigilance Risk Assessment Committee (PRAC) recommended in the Article 107i procedure according to Directive 2001/83/EC for HES-containing medicinal products (EMEA/H/A-107i/1376) in October 2013 that HES solutions must no longer be used to treat patients with sepsis, burn injuries or critically ill patients because of an increased risk of kidney injury and mortality while the benefit-risk ratio for HES-containing medicinal products remains favourable in the treatment of hypovolaemia due to acute blood loss when crystalloids alone are not considered sufficient.

The final implementing decision, issued by the European Commission on December 19, 2013, implicates new contraindications, special warnings, precautions for use and other changes to the European Product Information (PI) for risk minimisation measures.

To "evaluate the effectiveness of the risk minimisation measures taken", all Marketing Authorisation Holders (MAHs) of HES products subject to the PRAC procedure were requested to conduct a joint Drug Utilisation Study (DUS) with HES-containing medicinal products in several European Union (EU) Member States. However, after endorsement of the protocol contract negotiations between the MAHs failed and therefore B. Braun Melsungen AG and Fresenius Kabi Deutschland GmbH conducted the DUS separately.

Research Question and Objectives

The objective was to assess the adherence of hospital physicians to the revised European PI for HES-containing medicinal products of B. Braun Melsungen AG concerning indication, posology and contraindications.

Study Design

Retrospective, non-interventional, multinational, multi-centre European DUS of HES-containing medicinal products of B. Braun Melsungen AG in hospitals.

Setting

Any hospital in Belgium, Czech Republic, France, Germany, Italy, Netherlands, Poland, Spain and Sweden using any HES products of B. Braun Melsungen AG.

Subjects and study size, including dropouts

Twenty-nine sites from nine countries participated. Full Analysis Population = 3058 patients, Per Protocol Population = 3055 patients.

Variables and data Sources

This DUS documents patient data describing the medical status at initiation of treatment, posology and contraindications of B. Braun HES to identify deviations from the revised European PI.

Data were collected retrospectively from patient charts of patients previously treated with HES within a defined timeframe (January 2015 – May 2015).

Results

- Compliance with posology was very high (>99%).
- Relevant co-morbidities that would preclude HES administration (i.e. contraindications) were absent in approximately three-quarters (78%) of the patients.
- 44% of the patients received HES according to the indication of the updated European PI (''treatment of hypovolaemia due to acute blood loss'').
- Nearly one-third (30%) of patients had been treated with HES fully compliant with the updated European PI.

Discussion

- The revised European PI which was implemented to reduce the risks for the patients was not followed completely across all nine countries. Current literature reveals that a similar high frequency of non-compliance is common in clinical practice.