CSL Behring

Safety of a Pasteurized Plasma-Derived Factor VIII and von Willebrand Factor Concentrate: Analysis of 33 Years of Pharmacovigilance Data

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HIGHLIGHTS

From 1982 to 2015, a total of 670 postmarketing cases had been reported via pharmacovigilance

343

Out of a total of 670 postmarketing cases being reported from 1982 to 2015, 343 of these reported cases involved ADRs also considered clinically relevant risks

Thromboembolic complications, inhibitor formation, hypersensitivity or allergic reactions, or suspected virus transmissions were among the clinically relevant risks reported

INTRODUCTION

Humate-P
is a pasteurized human plasma-derived concentrate containing **FVIII and a near-normal spectrum of VWF multimers**

Global cumulative distribution of Humate-P between 1990 and 2015 was >5.2 billion IU, equivalent to about 2.6 million standard doses and 25,000 patient-year exposure

Humate-P safety profile was reviewed based on **33 years (1982 to 2015) of spontaneous postmarketing reports** of potential adverse drug reactions (ADRs) and the medical literature

This review provides clinicians with **essential safety data** to inform the choice between Humate-P and newer recombinant factor products

STUDY CHARACTERISTICS

33

Objective
Humate-P safety assessments based on >33 years of postmarketing pharmacovigilance data

Study design
Literature review and pharmacovigilance database assessment

Patient population
Humate-P recipients

RESULTS

33 years

Over a 33-year period, 670 postmarketing ADR cases were reported

Overall ADR reporting rate was 1 per 3900 administered standard doses

13 non-treatment-related fatalities were reported (see Table)

Table. Fatal reports

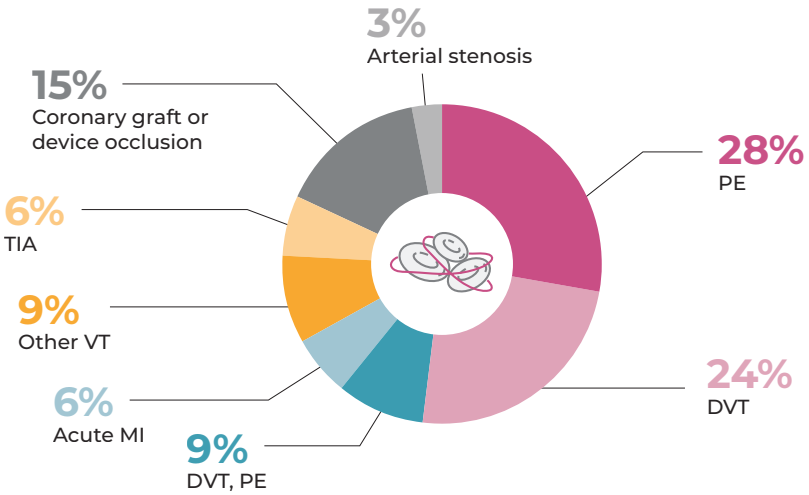
Fatal reports Humate-P				
Case	**Diagnosis**	**Cause of death**	**Age**	**Sex**
1	Hemophilia A	HIV/AIDS	24	M
2	Hemophilia A	HIV/AIDS	21	M
3	Hemophilia A	HIV/AIDS	9	M
4	Acquired FVIII inhibitor	Hepatitis B	unknown	F
5	Angiodysplasia, acquired VWD, MGUS	Gastrointestinal bleeding	76	F
6	VWD	Sepsis	37	F
7	Hemophilia A	HIV/AIDS, hepatitis C	48	M
8	Sepsis, multiorgan failure, DIC	Multiorgan failure, TRALI, shock	14	M
9	Hemophilia A, ITI for inhibitor	Dyspnea, hemoptysis, cardiac failure, PE	5	M
10	Aortic dissection	Postsurgery, had been treated with dabigatran, died of hemorrhagic shock	76	M
11	Hemophilia A	Hemorrhagic shock, ARDS	53	M
12	VWD Type 3	Hypoglycemia, unexpected sudden death	52	F
13	Unknown	HIV/AIDS, hepatitis C	32	M

RESULTS

Figure 1. Thrombotic complications

33 cases of thrombotic complications were reported over the 33-year period; approximately 1 case per 78,787 standard doses

Reported thromboembolic complications included mainly DVT, PE, TIA, and stroke, and most occurred in patients undergoing surgery or with other known risk factors



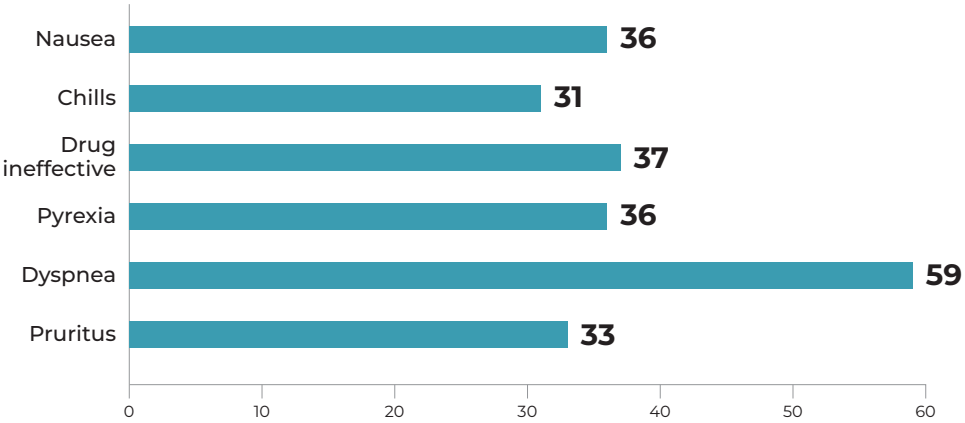
FVIII/VWF inhibitor formation among cases with known Humate-P use in the United States

1 case of inhibitor formation was reported per 26,804 doses

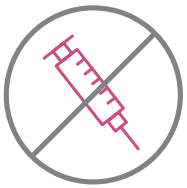
97 cases of inhibitor formation (69 cases for FVIII, 28 cases for VWF)

It was unknown if Humate-P was given in 33 cases

Figure 2. Other most common (≥30 events) reported events, according to MedDRA-PT



1 case of hypersensitivity or allergic reactions was reported per 23,636 standard doses



No confirmed cases of viral or prion transmission have been associated with Humate-P

HUMATE-P is indicated for the treatment and prevention of bleeding in adult patients with hemophilia A and in adult and pediatric patients with VWD. The dosage is individualized based on the patient's weight, type and severity of hemorrhage, FVIII level, and the presence of inhibitors.

Abbreviations
ADR: adverse drug reactions; ARDS: acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; DVT: deep vein thrombosis; FVIII: factor VIII; IU: international unit; ITI: immune tolerance induction; MedDRA: Medical Dictionary for Regulatory Activities; MGUS: monoclonal gammopathy of undetermined significance; MI: myocardial infarction; PE: pulmonary embolism; PT: preferred terms; TIA: transient ischemic attack; TRALI: transfusion-related acute lung injury; VT: vein thrombosis; VWD: von Willebrand disease; VWF: von Willebrand factor.

Reference
Kouides P, Wawra-Hehenberger K, Sajan A, et al. *Transfusion*. 2017;57(10):2390-2403.

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