Defibrotide in veno-occlusive disease in public hospitals of Paris: funding issues and perspectives

Steelandt J[1], Bocquet F[1,2,3], Fusier I[1], Cordonnier AL[1], Paubel P[1,2,3]

1. General Agency of Equipment and Health Products (AGEPS), Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France
2. Faculty of Pharmacy, Paris Descartes University, Sorbonne Paris Cité, Paris, France
3. Health Law Institute, Inserm, UMR S 1145, Paris Descartes University, Sorbonne Paris Cité, Paris, France

Introduction

- In hematopoietic stem cell transplantation, **veno-occlusive disease (VOD)** is a major complication associated with high mortality rates (90%) in which **defibrotide is the first line treatment**.
- In 2014, this treatment received a market authorization (MA) only in **curative treatment of severe VOD**.
- In France, a temporary authorization for use was attributed to defibrotide for **preventive treatment of VOD** (01/2009 – 06/2014) but European Commission gave a negative opinion on this indication because of the lack of clinic proofs data. Preventive use in VOD is always described in British and European recommendations[1,2] and used in french practices.
- The **high cost of defibrotide** remains a major problem for hospital budgets.

Chronology of Market Authorization (MA)

Status *(indication)*	**Named patient Temporary Authorisation for Use (ATU)** *(preventive and curative treatment of VOD)*	**Post-ATU** *(treatment of severe VOD)*	**MA** *(treatment of severe VOD)*
Conditions for drug remboursement	**Preventive and curative treatment** of VOD as part of ATU	Only in **curative treatement** of severe VOD	

- **January 2009** — Named patient Temporary Authorisation for Use (ATU)
- **March 2013** — Negative opinion for MA in **preventive and curative** VOD treatment (lack of efficiency data)
- **October 2013** — European Commission approved MA for **curative** treatment of **severe VOD**
- **June 2014** — Post-ATU
- **October 2014** — **Drug cost included in DRG tariff**

Objectives

Assessment of economic impact of defibrotide treatment and perspectives to regulate prescriptions to reduce costs were purposed for the 37 hospitals of the Public Assistance–Hospitals of Paris (AP-HP).

Method

- **Consumptions and expenditures** in defibrotide from 01/2011 to 04/2015.
- **2014 Medical information from PMSI hospital database** *(French medical information system program)*
- **Diagnostic Related Group** (DRG) **tariff** and **part of drugs cost.**
- **Opinions of experts** in hematology in preventive treatment of VOD for Paris Hospitals.

Results

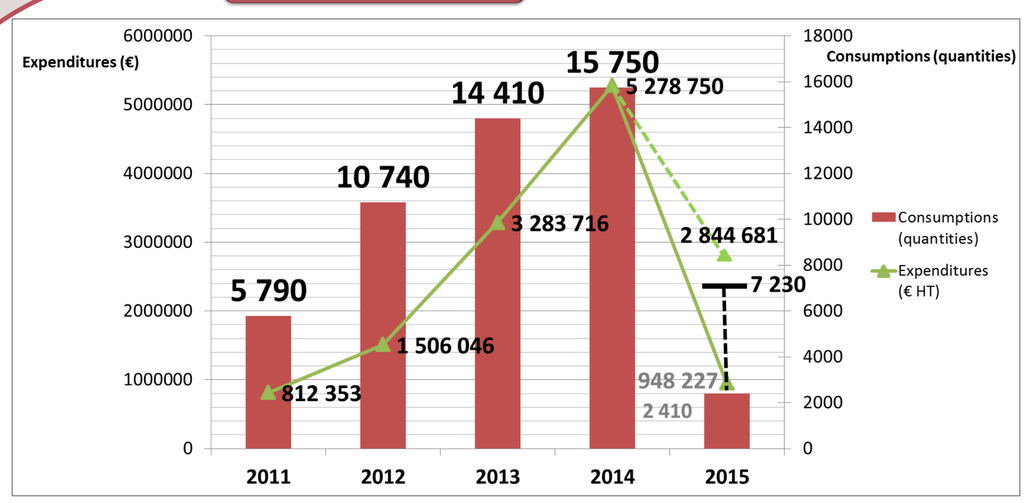

Figure 1. Consumptions and expenditures of AP-HP in defibrotide

Since 2011, consumptions increased to reach 15,750 vials for 5.2M€ in 2014. In contrast, extrapolated values in 2015 have showed decreasing amounts which could be explained by a self-regulation of prescribers in front of the economic impact and practices changes.

PMSI data (2014) : Diagnostic Related Group (DRG) « hematopoietic stem cell transplantation », classified in function of severity degree in levels 1 to 4	
Number of patients	440
Patients receiving defibrotide in 2014	80
Average age of patients	19 years
Main diagnosis associated to defibrotide treatment	Acute myeloblastic leukaemia (11 / 80)
DRG repartition	Hematopoietic stem cell transplantation, severity levels 3 (31.5%) or 4 (58.5%).

DRG		Tariff DRG cost[3]	Part attributed to drugs [4]
Hematopoietic stem cell transplantation	Level 3	**51,725.20€**	**3,544€**
	Level 4	**71,948.73€**	**4,084€**

The part attributed to drugs cover a small part of treatment cost (97,524€ for an adult).

Experts recommended defibrotide use in prevention **after considering alternatives**, only in **high risk situations defined by consensus**, an **improvement of pre-transplant cares** (reduction of the liver damage and conditioning regimen intensity), an **optimization of vials numbers per patient** (centralized preparations, limitation of treatment duration).

Conclusion

Aware of economic impact, experts have initiated a change of practice and they recommend a restrictive use of defibrotide specially limitation the off-label use in preventive (only patients with very high risk of VOD).

[1]EBMT / ESID ; http://www.ebmt.org, consulté le 20 janvier 2015.
[2]Dignan F. L, Wynn R. F, Hadzic N, Karani J, Quaglia A, Pagliuca A, et al. M. N. BCSH/BSBMT guideline: diagnosis and management of veno-occlusive disease (sinusoidal obstruction syndrome) following haematopoietic stem cell transplantation. British journal of haematology, 2013, 163(4), 444-457.
[3]JO (04/03/2015)
[4]ENC 2012 (extrapolation data)

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