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

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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 recommendations1,2 and used in French practices.
- The high cost of defibrotide remains a major problem for hospital budgets.

Chronology of Market Authorization (MA)

<table>
<thead>
<tr>
<th>Status (indication)</th>
<th>Named patient</th>
<th>Post-ATU</th>
<th>MA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conditions for drug rembursement</td>
<td>Preventive and curative treatment of VOD as part of ATU</td>
<td>Only in curative treatment of severe VOD</td>
<td>Drug cost included in DRG tariff</td>
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<tr>
<td>Preventive and curative treatment of VOD as part of ATU</td>
<td>European Commission approved MA for curative treatment of severe VOD</td>
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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

PMSI data (2014) :
Diagnostic Related Group (DRG) » hematopoietic stem cell transplantation », classified in function of severity degree in levels 1 to 4

<table>
<thead>
<tr>
<th>DRG</th>
<th>Tariff DRG cost</th>
<th>Part attributed to drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematopoietic stem cell transplantation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 3</td>
<td>51,725.20€</td>
<td>3,544€</td>
</tr>
<tr>
<td>Level 4</td>
<td>71,948.73€</td>
<td>4,084€</td>
</tr>
</tbody>
</table>

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).

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