**BACKGROUND**

Since December 2008 the European Union (EU) Regulation 1394/2007/EC on Advanced Therapy Medicinal Products (ATMPs) has become applicable. ATMPs are products, gene therapeutic products and tissue engineered products that have been approved by the European Medicines Agency (EMA) and one only ATMP (ChondroCelect®) is currently reimbursed within five member states (EU5).

Three directives were drafted at a time when several ATMPs seemed close to translating into clinical practice however, only ChondroCelect® has been developed and reimbursed for niche indications and the number of patients affected is small. This can be small enough to make it difficult for companies to recovery costs and make a profit at the price level required by European stakeholders.

There is a known to be a number of regulatory and reimbursement challenges (Table 1). Understanding the complex environment in Europe and the requirements of Payers and HTA bodies is essential for developers seeking pricing and reimbursement.

**OBJECTIVES**

- To assess the payer perspective on ATMPs and to underómo regulatory, financial and reimbursement challenges for ATMPs.

**METHODS**

- We used a mixed methods approach to review cases of ATMPs with market authorization and reimbursement within EU5.

- The online EMA database of medicinal products was searched to collect information on all regulatory approvals of ATMPs between January 2008 to June 2014 (EU5) and only stericile and gene therapeutic products that have been approved by the EMA and one only ATMP (ChondroCelect®) is currently reimbursed for niche indications and the number of patients affected is small.

- Findings were filtered to identify articles and online literature and interviews with regulators and payers.

- To understand the payer perspective on ATMPs and to identify the key factors on potential reimbursement decisions, we undertook 15, hour-long, structured interviews with Payers, Health Technology Assessment bodies and formulary committee members (who have been or worked in regulatory or reimbursement). All interviewees were asked to provide an overview of their recent or planned reimbursement decisions and or decline reimbursement of ATMPs from five EU member states (UK, Spain, France, Germany and Italy).

**RESULTS**

- Table 1: Development challenges for ATMPs

- Pricing and reimbursement of ATMPs – the case of ChondroCelect®

- The example of ChondroCelect® illustrates some of the unique challenges to obtaining reimbursement in Europe.

- As shown by the timeline (Figure 1), after 5 years ChondroCelect is in nationally reimbursed in only a handful of countries.

- Many ATMPs require multiple hospital procedures. For example, ChondroCelect requires two surgical implantation procedures (removal of cartilage and implantation of a repair material) and medical device (a collagen membrane), and various authorities may be involved in pricing and reimbursement decisions:
  - Hospital management authorities for the surgical procedures
  - Medical device pricing and reimbursement authorities for the collagen membrane.

- Adding to the complexity for developers to gain rapid product market access is the differences in decision making and reimbursement bodies, and the unexplained delays or price negotiations (often over many years) to demonstrate effect, including uncertainty of value and budget restrictions; numerous interactions with various stakeholders including regulatory authorities, payers, health economics experts and formulary committee members.

**CONCLUSIONS**

- The European pricing and reimbursement landscape for ATMPs is complex and presents a substantial challenge for small enterprises that comprise most of the developers.

- At the time of this study, four ATMPs had been granted marketing authorization by the EMA (Table 2), but only one of these products (ChondroCelect®) is reimbursed.

- The development and reimbursement funding will continue to face significant challenges and will require a continued effort and time (often many years) to demonstrate effect, including uncertainty of value and budget restrictions; numerous interactions with various stakeholders including regulatory authorities, payers, health economics experts and formulary committee members.

- There are numerous regulatory and reimbursement challenges (Table 1).

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- Understanding the complex environment in Europe and the requirements of Payers and HTA bodies is essential for developers seeking pricing and reimbursement.

- ATMPs symbolize a paradigm shift in the prevention, treatment and even cure of many difficult-to-treat diseases and require different evaluations to drugs, treatment and even cure of many difficult-to-treat diseases.

- ATMPs can be combinations of devices, procedures and pharmacological therapies, particularly for patients with rare diseases.

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