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Funding breakthrough therapies: A systematic review and recommendation

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ABSTRACT

Background: Advanced therapy medicinal products (ATMPs) are innovative therapies likely associated with high prices. Payers need guidance to create a balance between ensuring patient access to breakthrough therapies and maintaining the financial sustainability of the healthcare system.
Objective: The aims of this study were to identify, define, classify and compare the approaches to funding high-cost medicines proposed in the literature, to analyze their appropriateness for ATMP funding and to suggest an optimal funding model for ATMPs.
Results: Forty-eight articles suggesting new funding models for innovative high-cost therapies were identified. The models were classified into 3 groups: financial agreement, health outcomes-based agreement and healthcoin. Financial agreement encompassed: discounts, rebates, price and volume caps, price-volume agreements, loans, cost-plus price, intellectual-based payment and fund-based payment. Health outcomes-based agreements were defined as agreements between manufacturers and payers based on drug performance, and were divided into performance-based payment and coverage with evidence development. Healthcoin described a new suggested tradeable currency used to assign monetary value to incremental outcomes.
Conclusion: With a large number of ATMPs in development, it is time for stakeholders to start thinking about new pathways and funding strategies for these innovative high-cost therapies. An "ATMP-specific fund" may constitute a reasonable solution to ensure rapid patient access to innovation without threatening the sustainability of the health care system.

1. Introduction

In the 21st century, scientific advances have led to a better understanding of numerous diseases and a fast pace of innovation [1]; innovative breakthrough therapies have emerged to treat conditions and diseases that were previously considered incurable. Among innovative therapies, there is a class of biopharmaceuticals, called Advanced Therapy Medicinal Products (ATMPs) in Europe, that include somatic cell therapies, gene therapies and tissue-engineered products [2]. This class encompasses very promising therapies in development or already approved for the treatment of conditions in a variety of therapeutic areas, including oncology, cardiology, neurology and others [3,4]. Those promising therapies will likely be associated with a high price. Paying for innovative expensive therapies constitutes a major challenge for payers worldwide and impedes the adoption of these therapies. While the pressure on governments to fund more expensive therapies is increasing, existing traditional funding and pricing models may be insufficient to ensure the sustainability of the healthcare system. Payers and policymakers need guidance to create a balance between ensuring patient access to innovation and maintaining financial sustainability. Many studies have suggested new financing models for high-cost therapies in order to mitigate the high upfront cost.

The aims of this study were to identify, define, classify and compare the approaches to funding innovative high-cost medicines

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proposed in the literature, to analyze their appropriateness for ATMP funding and to suggest an optimal funding model for ATMPs.

2. Methods

A systematic literature review was conducted in Ovid Medline, Embase and grey literature to identify studies published between 2010 and February 2017. The following keywords were used: funding, financing mechanism, pay and innovation, cost control, high cost, gene therapy, cell or tissue therapy. Where relevant, references from articles identified through the search were also reviewed.

Duplicate records were removed using Endnote X7.7.1. The titles and abstracts identified through the search were screened using the following inclusion criteria: 1) French or English language, 2) Publication date between January 2010 and February 2017, 3) Focus on financing high-cost drugs. For abstracts that met these criteria, full-text articles were retrieved and screened.

The following data was extracted from included articles: title, authors, journal, year of publication, suggested funding model, its definition, benefits and limitations. Funding models were classified into groups and subgroups based on the nature of funding agreements. For each identified model, the feasibility, acceptability, burden, financial attractiveness, appeal to payers, and appeal to manufacturer were assessed during a consensus meeting set up to compare the models (Supplementary materials). The participants of the consensus meeting were: two academic experts, one hospital pharmacist, one former payer, one pharmaceutical industry director responsible for pricing and two consultants working in the area of pricing and market access.

In addition, the applicability of the models to different disease types was evaluated: chronic progressive disease (e.g. Parkinson, Alzheimer), chronic disease with exacerbations (e.g. asthma), acute disease (e.g. acute leukemia) and organ defects (e.g. cartilage defect).

The appropriateness of each model to fund ATMPs was then evaluated based on all the information collected through the literature review, and an optimal sustainable funding model for ATMPs was recommended by the consensus meeting panel.

3. Results

3.1. Identification, definition and classification of funding models

Overall, 6995 papers were extracted from the keyword search in Ovid Medline; Embase and grey literature; among which 268 articles were eligible for full text screening. Forty-eight articles proposing methods of paying for high-cost therapies were identified (Fig. 1). The funding models identified were classified into 3 categories: financial agreements; health outcomes-based agreements; and healthcoin (Fig. 2).

3.1.1. Financial agreements

Several financial agreements were proposed in 30 articles. These agreements between payers and manufacturers were based only on financial aspects, independently of health outcomes of the novel therapy (Table 1). The financial agreements identified were grouped as follows:

- Bundle payment, episode of care [5–13].

An episode of care (EOC) is a single payment for the whole care a patient needs over the course of a defined medical condition. It is characterized by events defining the start and end dates [7,9]. A bundle payment is an integrated single payment that covers all healthcare services related to a specific treatment or procedure [5–11,13]. The aim is to incentivize healthcare providers (HCP) to control drug expenditure, while maintaining the quality of care monitored through predefined quality metrics. This is also the principle of an integrated health system, where HCP create a joint organization to deliver comprehensive care for patients with a given condition. In the United States (US), integrated systems were promoted by Obamacare (the Patient Protection and Affordable Care Act) and are called Affordable Care Organizations (ACO). For cancer care, a new model of ACO – the Oncology Care Model (OCM) – was developed by Centers for Medicare & Medicaid Services (CMS). In addition to the fee-for-service payment for each episode of oncology care, the model includes two further payments [12]: per-beneficiary per-month (PBPM) fee for each episode of chemotherapy, and performance-based payment, the latter dependent on satisfactory quality metrics and spending per chemotherapy episode falling below a predefined target.

- Rebates [14,15].

Payments refunded by the manufacturer to the payer after the transaction has occurred. This commercial agreement, usually confidential, is becoming increasingly popular in several countries. It may be driven by incremental cost-effectiveness ratio (ICER) or result simply from negotiations, with no objective economic evidence to support the affordability or willingness-to-pay subjectively defined by the payer.

- Discounts [16–18]

Price reductions granted to payers, usually confidentially, under specific conditions without affecting the drug list price.

- Price cap/volume cap [14,15,19].

Price caps and volume caps are methods used to control and limit pharmaceutical prices and manufacturer revenues. At patient level, they aim, respectively, at capping the yearly price, or the number of yearly treatment courses reimbursed. If additional courses are needed, these have to be provided by the manufacturer free of charge. At population level, these strategies aim at capping the yearly expenditure or volume the manufacturer allowed to be sold. Beyond the cap, manufacturer may have to reimburse the full retail price, the full ex-factory price, or a proportion of the price, depending on the agreement. Levy et al. [19] suggested a model that provides a theoretical foundation for price caps to face the monopolistic power of pharmaceutical companies. A mild price regulation (a 20% decrease) was considered the “golden path” to improving patient health without stifling the incentive for innovation [19].

- Price-volume agreements [15,20–22].

Agreements where drug prices are reduced based on sales volume (e.g. after every 10,000 vials sold, the price is reduced by 20% for the next vials). Alternatively, depending on the total sales volume, the price will be discounted for all vials sold, according to a predefined scheme.

- Cost-plus price [23,24].

This model has been proposed for orphan drugs that are generally not considered cost-effective due to their high costs. Price is set based on the development and production costs; it produces total revenues equal to a fixed and pre-determined amount. The “rate of return” method helps to determine a “just and reasonable price” for the orphan drug [23].

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