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Challenge of the cure

Examining the P&MA challenges of disruptive therapies in Europe

To help understand the pricing and access challenges facing disruptive therapies such as gene and cell therapy (GCT), we recently enlisted the help of payers from EU5 countries. In our discussions—held in Zurich, London, Munich and Paris—we asked our experts to provide both their personal and country-specific perspectives.

Can healthcare systems afford GCTs?

Whether healthcare systems can afford GCTs is a question being asked by industry, payers and policymakers as the affordability of disruptive therapies poses a range of new challenges. For our payer panellists, these challenges do not focus exclusively on pricing but instead on budget impact. Budget impact concerns are heightened when immediate access needs to be provided to large patient cohorts at launch, as was the case for Sovaldi. Bridging the gap between the time when the saving is realised (benefit) and when the treatment is paid for (cost) is therefore critical.

In preparation, some countries have set up innovation funds, separate from their standard payer budgets, to support the uptake of disruptive therapies. In Italy, for example, these special funds are reserved for innovative drugs. In Germany, innovative funds are available for treatments that have the potential to drive down overall healthcare spending.

Mostly, payers expect to release budget from cost-savings within today's funding system. To help finance innovation, there could be a stronger focus on the interchangeability of biosimilars as higher uptake would help shift funds to innovations like GCTs. In this context, for example, Germany may consider mandatory biosimilar substitution or funding from alternative sources.

Affordability of GCTs may not become an issue if expenditure on ineffective treatments is also limited. According to one of the payers, reallocating resources and confirming patient benefits may help reduce the 20% of healthcare expenditures currently estimated to bring no patient benefits.[1] With two-thirds of cancer drugs thought to be leading to limited outcomes or a decrease in quality of

[1] OECD report "Tackling Wasteful Spending on Health," 10 January 2017, available at: https://www.oecd.org/health/tackling- wasteful-spending-on-health-9789264266414-en.htm.

life, and the majority of the cost of cancer occurring in the last few weeks of life,[2] cost savings are possible.

A further option, mentioned by an Italian panellist, is to make additional budget available by increasing the proportion of pharmaceutical spending within the wider healthcare budget—it currently averages around 17%.[3] Increasing the percentage of gross domestic product (GDP) allocated to healthcare, is another way to support the potential budget impact of disruptive therapies.

Payers also expect price erosion over time, driven by technology evolution. Despite the high number of GCTs in development, payers do not anticipate the new wave of innovation to hit budgets any time soon, due to a high attrition rate. By the time the new wave of GCTs hits the market, new technologies including artificial intelligence (AI) are likely to have brought about cost savings, and current prices will have dropped as GCTs become more widely used. Competitive pressures inherent in the GCT space will also help contain costs, even if this takes some time to realise.

But all these solutions for affording GCTs rely on the ability of healthcare systems to negotiate a 'fair' price for efficacy and select the 'best' patients for treatment. While France always wants to be a front-runner and there is competition among the G7 countries, none of the individual countries are racing to be the first country to reimburse GCTs at any cost. A hardening of the Commission de la Transparence (CT) stance in France is expected to reduce the number of positive recommendations to be more in line with neighbouring countries. It is expected that the CT will use safety versus standard of care, magnitude and homogeneity of effect or robustness of evidence as anchors for refusing or delaying reimbursement. For GCTs specifically, this implies that their likely limited duration of evidence and demonstration of size of effect is expected to face major stumbling blocks to reimbursement—at least initially. GCTs will have to be successful in the rest of the EU to become a commercial success in France.

It all comes down to managing affordability.

How can payers deal with uncertainty through cost?

Beyond affordability, our panellists agreed that uncertainty surrounding effectiveness is a key stumbling block. Payers are willing to accept some level of uncertainty, but not at any cost. For example, UK payers suggested a managed access arrangement for Spinraza (nusinersen) to limit the exposure to incremental cost-effectiveness ratio (ICER) estimates of GBP400-600k per quality-adjusted life year (QALY). One note of caution from payers, however: if a market access decision depends on the inclusion of a managed entry agreement (MEA) as part of the business case, then the offered package must be better than a straight discount and manufacturers must be ready to explain why it has benefits for payers.

Financial schemes may focus on limiting the initial cost impact by spreading payments. This may lead to a disadvantage for manufacturers if they bind themselves to a price or payment scheme over 10 years, for example. A strategy such as leasing is harder to implement for a GCT because, once a therapy is supplied to the patient, it cannot be returned to the manufacturer.

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[2] Courtney Davis, et al., "Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13," *The BMJ*, 4 October 2017, available at https://www.bmj.com/content/359/bmj.j4530.

[3] OECD, 2019, "Pharmaceutical spending" (indicator), https://doi.org/10.1787/998febf6-en, accessed on 7 February 2019.

In countries like Germany with several national health insurers or countries like Italy or Spain where budgets are regional, the implementation of such schemes would be complicated by patients switching insurers or moving regions.

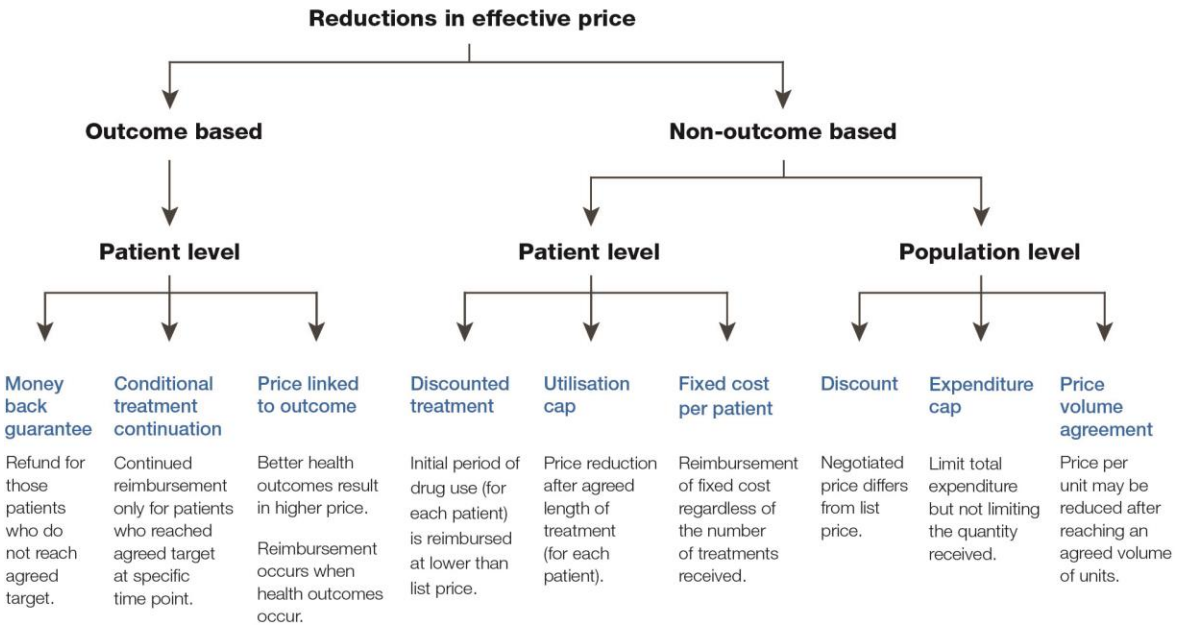
While distributing payment over an extended period is a less preferred option, an upfront payment that incorporates the uncertainty is often easier to implement. In effect, this is as simple as lowering costs to account for the expected share of non-responders.

Other innovative contracts have also been explored. Spanish regions may consider risk-pooling across regions to limit the impact of uncertainty. There also could be a solution where a third party manages the financial aspect, like a bank manages the loan on a house or car.

Beyond traditional funding models

Government officials in European countries are also thinking outside of traditional funding models. For example, the new Italian government recently proposed that medicines could be funded using state bonds. Authorities in the UK have considered similar proposals, plus ideas such as leasing and financing, before eventually arriving at a staged approach to encourage more flexible solutions. The first stage has been the introduction of managed entry agreements whereby six different payer management tools can be used to measure efficacy (see Figure 1). The Cancer Drug Fund and the Highly Specialized Technology (HST) processes are proof that approaches are evolving, though to date budget impact and affordability still underpin thinking and decision-making.

Figure 1: MEA options: reductions in effective price[4]



Funding is a complex challenge that requires complex solutions. Reaching a consensus on future solutions will require ongoing cooperation between payers, policymakers and industry.

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[4] Adapted from Walker et al., Garrison et al. and Bruegger, *see* Sabine Grimm et al., "Framework for Analysing Risk in Health Technology Assessments and its Application to Managed Entry Agreements Report by the Decision Support Unit," School of Health and Related Research, University of Sheffield, January 2016, available at http://nicedsu.org.uk/wp-content/uploads/2018/05/DSU-Managed-Access-report-FINAL.pdf.

Is there a way to deal with risk beyond cost?

Beyond cost, there are two ways to tackle uncertainty around effectiveness. First, by providing more evidence and, second, by analysing the clinical data in a way that meets payers' expectations.

Ultimately, decisions always include a level of uncertainty. While GCTs bring a higher level of uncertainty than traditional drugs, financial risk is often mitigated, albeit in the short-term, by their launch in rare diseases. Measures to manage the impact of decisions taken based on limited clinical data may therefore include temporary approval, such as a re-evaluation every two years.

Registries may also be used to reduce the level of uncertainty over time and to evaluate whether the benefit/risk profile achieved in clinical trials can be seen in the real world. One expert called for establishing a European Medicines Agency (EMA) patient registry to increase the level of treatment evidence and facilitate discussions with payers. In Italy, registries are used extensively to make sure that real world data is collected.

Another issue for payers will be the capacity of healthcare systems to deal with the new wave of GCTs from a value-assessment perspective. Health Technology Assessment agencies (HTAs), especially in the UK, value information analysis and are open to additional new metrics that help inform the decision-making process. Our payers thought that to be helpful, uncertainty at different levels needs to be explicitly quantified in order to mitigate it through appropriate measures.

Our panellists believe current HTAs will be able to deal with the new wave of disruptive therapies. In the UK, for example, the QALY is still considered an appropriate tool, suggesting that the more challenging part is survival, as that is harder to gauge based on a relatively short trial. German payers also believe that the benefit assessment is built to manage uncertainty in price negotiations and in allowing for reassessment.

Conclusion

While uncertainty is, and will continue to be, a known factor in decision-making for GCTs, the challenges of risk and affordability may be areas where healthcare systems can find workable solutions that will allow payers to contain costs while encouraging innovation.

Opportunities for cost-savings can be identified in most healthcare systems and in payment methods that alleviate the additional cost burdens of GCTs. As for the task of encouraging pharmaceutical industry innovation, this is a much broader topic that must be addressed at the macro policy and political level.

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