Patient Access to New Medicines: The Changing Landscape

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BACKGROUND

- The market access landscape has changed substantially since the introduction of the National Institute for Health and Care Excellence (NICE) in 1999 and the Pharmaceutical Price Regulation Scheme (PPRS) in 2009 (updated in 2014). Increasingly formalised pricing mechanisms were introduced in the 2009 PPRS to allow a range of options for industry, including patient access schemes (PASs).
- Traditionally, a patient's treatment is administered more than once, over a period of time, and treatment cost is managed per administration. In the case of transformative therapies, the treatment is administered once and the benefits are expected to be experienced by the patient for an extended period of time afterwards.
- The large up-front cost of treatment is a potential barrier to market access, and there is no tangible ongoing provision of product to allow for staggered payment for the benefit accrued; this situation creates a challenge for the National Health Service (NHS) and the current financial flows, particularly in demonstrating the cost-effectiveness of such therapies when assessed through the NICE Technology Appraisal process.
- Crabb and Stevens (2016)[1] explored the assessment and appraisal of regenerative medicines and cell therapy products in regards to the suitability of NICE's current process and concluded that "the NICE appraisal methods and decision framework are applicable to regenerative medicines and cell therapies."
  - However, they noted that circumstances existed in which additional factors would need to be considered, such as the discounting rate, and that "innovative payment methodologies need to be developed to manage and share risk to facilitate timely patient access while the evidence is immature."

Access Options Currently Available in the UK

- Since their introduction, PASs have evolved. Currently, simple discount (confidential upon request) and complex schemes are available. However, the introduction of NHS England also led to Commercial Access Agreements (CAAs) and Market Access Arrangements (MAAs) (Table 1), and the range of options in the future may need to be even more innovative.

Table 1. Currently Available Access Options

Simple PAS	Complex PAS	CAA	MAA
Standard approach used to achieve reimbursement when drugs are routinely commissioned. Must follow PPRS criteria.	Standard approach used to achieve reimbursement when drugs are routinely commissioned. Must follow PPRS criteria.	A financial agreement among NHS England, NICE, and the manufacturer	Applies to drugs when additional data are required, most commonly those approved through the CDF
A single discount proposed by the manufacturer applied to list price	Many possible approaches, including dose caps, free stock, response-based schemes, and those that combine financial and clinical elements	NHS England works with NICE and the manufacturer to identify an arrangement appropriate for the NHS, patients, and the manufacturer	MAA includes a Data Collection Arrangement (DCA) and CAA
NHS England-preferred PAS	Considered complex to manage Cumulative burden in some disease areas	May be part of a CAA for drugs with an MAA	DCA is to allow collection of additional data to add certainty to cost-effectiveness estimates
Once agreed, should be used across all indications for that therapy	Once agreed, should be used across all indications for that therapy	May differ from a previously agreed PAS for the therapy in a different indication	MAA provides interim funding during the data collection period, after which the product is reappraised
Discount remains confidential	Scheme is made public	Remains confidential	DCA is publicly available; CAA remains confidential
All schemes are managed by NHS England			

- From October 2009 to October 2018, simple discount schemes were the most common, and the majority of PASs and CAAs were for oncology products (Figures 1 and 2).[2] As of October 2018, there were 178 operational schemes across 40 companies; Novartis has more operational schemes than any other company (Figure 3).[2]
- As shown in Figure 2, the majority of operational schemes are within the oncology and arthritis disease areas. The administrative burden of operating these schemes is usually concentrated within an NHS Trust's Pharmacy Department.

Operational Schemes, October 2009 to October 2018

Figure 1. By Type

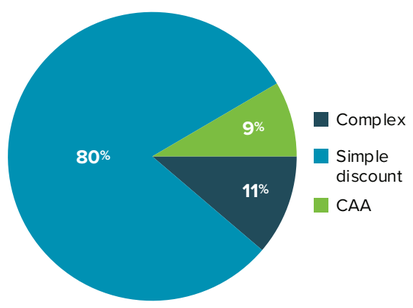


Figure 2. By Disease Area

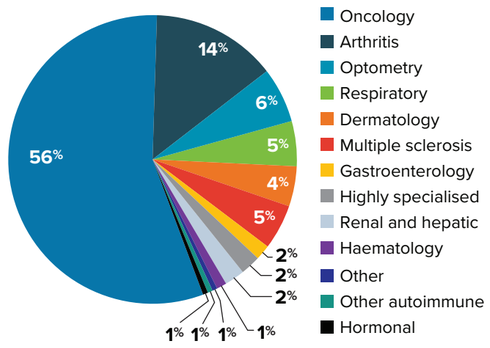
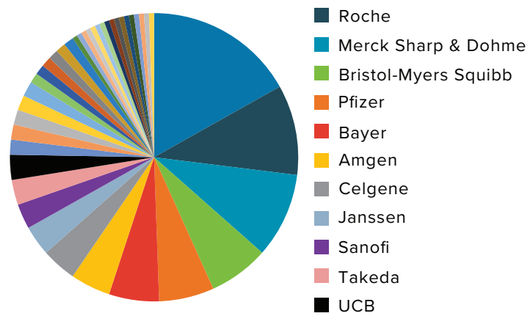


Figure 3. By Company



Adapted from: NICE (2018).[2]

THE CHALLENGE OF TRANSFORMATIVE THERAPY

- A key driver for more innovative approaches comes from groundbreaking new regenerative therapies, such as CAR T-cell therapy in oncology. CAR T-cell therapy is administered once, and patients whose disease remains in remission for over 5 years are considered cured.
- Tisagenlecleucel has recently been approved for use in the NHS for patients aged 3 to 25 years with relapsed or refractory B-cell acute lymphoblastic leukemia (ALL) via the CDF,[3,4] and innovative approaches to reimbursement were not required. The product is still under review in adult patients with relapsed or refractory diffuse large B-cell lymphoma after 2 or more lines of therapy, and the current appraisal consultation document[5] does not recommend its use.
  - Nonetheless, NICE "would welcome further discussions on its cost-effectiveness,"[6] and it is possible that further discussions between Novartis and NICE/NHS England will occur before the next Appraisal Committee Meeting.

"CAR-T therapies at present only target haematological cancers; in this space, with 3-year long-term data, you can establish curative status. This makes CAR-T reimbursement less dependent on the more innovative pricing schemes (Kymriah for ALL [in patients aged 3-25 years] was admitted to the CDF so no sophisticated pricing scheme here).

However, when it comes to gene therapies for haemophilia, thalassaemia, etc., it becomes much more important to leverage long-term outcomes-based pricing schemes because having the clinical data that establishes curative status for the remainder of the patient's life is challenging at launch."

The Cell & Gene Therapy Catapult; 20 September 2018

INNOVATIVE APPROACHES

- Challenges for transformative therapies include those also seen for other therapies, including small non-randomised studies, high levels of variation in response, use of surrogate outcomes, and immature data at the time of appraisal. However, they are likely to be more common for transformative therapies. The University of York and NICE assessed various pricing models, including discounts, performance-related schemes, and technology leasing (Table 2).[7]
- Hettle et al.[7] considered a leasing payment model for CAR T-cell therapy to be worthy of further exploration. This model would spread out the cost of providing patient treatment; however, potential barriers exist, including the standing operating protocol and standing financial flows within the NHS.

Table 2. Summary of Alternative Pricing Schemes

Traditional PAS	Leasing Scheme	Pay for Performance
• Standard simple discount • May be combined with leasing or pay-for-performance schemes to form a complex scheme	• Product is "leased" from the company • Monthly "lease" payments are made, based on dividing the total cost over the expected survival duration • Payment continues as long as the patient's disease remains in remission	• Payment is made retrospectively, only for patients who achieve a specific outcome (e.g., clinical remission) by a certain time point • An alternative is one up-front payment, followed by a separate "clawback" agreement for patients who do not achieve the specified outcome
• The NHS bears the risk associated with the uncertainty around efficacy	• Decision uncertainty remains but the consequences to the NHS are reduced	• Reduces both the level of decision uncertainty and the consequences to the NHS
• In line with current approaches, no change in process required	• Limits the risk to the NHS of paying up-front for a product that does not achieve the anticipated clinical outcomes • Provides an "exit strategy" for the NHS • Changes to financial flows would be required	• More complex to manage, in line with other outcomes-based complex options • This would require additional patient monitoring and outcomes to be measured; currently not operating as a PAS

Adapted from: Hettle et al. (2017).[7]

CONCLUSIONS

- It is clear from the current and potential options available that further consideration is needed to ensure that market access funding arrangements for new products are fit-for-purpose going forward.
  - Output of the PPRS (2014) review to include more innovative options?
  - Increased NHS financial flow flexibility—to accommodate the flow of money when there is no tangible product?
  - A shift from paying for products to paying for benefits—when they are high-cost, one-off regenerative technologies?
- The incremental burden of innovative approaches must be minimised, particularly when they apply to oncology and arthritis disease areas. Therefore, within the context of the issues to be addressed above, any innovative or 'alternative' arrangement to fund new curative treatments must be as simplistic as possible in these disease areas.

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Presented at: ISPOR Europe 2018; 10-14 November 2018; Barcelona, Spain