Unlocking access to future ATMPs in the UK

Comparing international approaches

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abpi

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Executive summary

The UK demonstrated early leadership and proactive support for the evolution of an ATMP ecosystem

The UK government has provided investment and support for the development of the advanced therapy medicinal products (ATMPs) sector. The establishment of the Cell and Gene Catapult in 2012 marked the start of a range of initiatives designed to create the right conditions for the development and manufacture of ATMPs in the UK, as well as enabling patient access.

This investment has paid dividends in ATMP clinical trials, where 14 per cent per cent of all global phases I-III commercial ATMP clinical trials are conducted in the UK.[1] The number of UK ATMP trial numbers has remained steady between 2022 and 2023, despite a 10 per cent decrease in the overall numbers of global ATMP clinical trials.[2] The UK's sizable share of global ATMP clinical trials is particularly positive in the context of the broader clinical trials environment, where the number of clinical trials taking place in the UK has been in steep decline since 2017, well before the pandemic.

UK-based ATMP manufacturing has continued to develop, with an increase in the overall number of dedicated ATMP manufacturing organisations operating in the UK (26 dedicated cell and gene therapy manufacturers in 2023 compared to 22 in 2022)[3] and a 20 per cent increase in the number of full time employees in the ATMP manufacturing workforce in 2023.[4]

The transformative potential and unique challenges of ATMP access

These efforts recognise that ATMPs have the potential to deliver transformative benefits to patients, caregivers, the wider UK health system and society, by addressing the root causes of otherwise untreatable diseases.[5] At the same time, however, the transformative nature of ATMPs presents novel access challenges for all healthcare systems. From an access perspective, these challenges can be split into three key themes:

- **Affordability:** benefits to patients from ATMPs are frequently delivered in a one-off rather than ongoing intervention, and payments have traditionally been aligned to delivery of the treatment. Payers often need to pay a relatively high upfront cost for long-term benefits.
- **Uncertainty:** although ATMPs may have potentially long-lasting – even lifetime – benefits, the durability of effect may be uncertain in the early years, as clinical trials tend to be conducted over a relatively short time.
- **Infrastructural requirements:** as ATMPs are specialised medicines utilising advanced technologies, they can require specialised infrastructure to identify patients eligible for the treatment, deliver the therapy and monitor the outcome.

Due to the excitement about the potential benefits for patients, but also the novelty of the challenges, there has already been substantial interest in the UK and further afield in understanding how patient access to ATMPs can be enabled.

In England, 14 ATMPs have been reimbursed since the first ATMP received European Medicines Agency (EMA) approval in 2009. There have been several instances in the UK where more flexible and innovative approaches to the assessment and commissioning of ATMPs have ensured that they can deliver life-changing benefits to patients when they otherwise might not have achieved market access. These approaches have included using existing mechanisms such as the Cancer Drugs Fund (CDF) and Highly Specialised Technologies (HST) programme.[6] Patient access has also been enabled by provisions in the wider access environment, such as cross-stakeholder collaborations to support treatment infrastructure readiness.

Additional momentum has been generated by NHS England's (NHSE's) commitment to deliver two innovative payment model pilots for ATMPs in the 2024 voluntary scheme for branded medicines pricing, access and growth (VPAG).[7]

The past is not a predictor of the future – challenges posed by the ATMP pipeline

Ongoing efforts are required to build on the early leadership that the UK has demonstrated in ATMP research, manufacture and patient access. This is because the ATMP pipeline is evolving, presenting new opportunities to treat unmet health needs, but also new challenges requiring sustainable solutions. ATMP clinical trials, whilst in a relatively strong position now, are not immune to the wider challenges facing clinical trials more broadly. In addition, ATMP manufacturing requires ongoing investment and policy support to enable it to scale and mature.

Over the next five years there will be substantial growth in the number of ATMPs launching in the UK – we find a potential increase from around two approvals per year to 10 to 15 per year by 2030 – and in the diversity of ATMPs: although many future ATMPs will continue to share the key characteristics of those that are available today, there will also be new types of ATMPs that will have their own set of challenges for ensuring patient access. For example, the affordability challenge will be exacerbated for ATMPs targeting more common diseases.

The increased number and diversity of ATMPs becoming available may also lead to some existing assessment and commissioning pathways (such as the CDF and HST programme) becoming less relevant for a larger proportion of ATMPs. For example, the entry criteria for the HST programme are already narrow (i.e. not more than 300 people in England can be eligible for the licensed indication),[8] which means that a smaller proportion of ATMPs will benefit, as many of these have much larger patient populations. Likewise, the CDF, which has been routinely utilised to temporarily reimburse CAR-Ts, has the obvious limitation that it is restricted to oncologic therapies. The Innovative Medicines Fund (IMF) was introduced to provide a similar managed-access process for non-cancer medicines.

Learnings from other countries – international case studies on readiness for the ATMP pipeline

This report seeks to bring the end-to-end ATMP pathway to life, by recognising the breadth of the ecosystem that needs to function for the UK to fulfil its potential as a global leader in ATMPs, and the interconnectivity between its different elements. From manufacturing, research and regulation through to access and uptake, each component of the ATMP ecosystem is connected and UK performance across all elements determines the overall competitiveness of the UK.

However, the report is principally focused on access issues because these are frequently cited as a key consideration for companies contemplating investment in ATMP development and launch in the UK.

Challenges for enabling access to ATMPs – both existing challenges and new ones posed by the ATMP pipeline – are not of course unique to the UK, so it is useful to understand if other countries are using different approaches to those in place in the UK, which could inform the ongoing evolution of the UK's ATMP ecosystem to enable patient access and support health system readiness for these innovative therapies as the current pipeline matures. Therefore, the purpose of this report, which was informed by research conducted by Charles River Associates on behalf of the ABPI, is to draw on the range of international experiences for improving access to ATMPs and to identify learnings for the UK. Although many of the examples in the report focus on England, the intention is for the learnings and recommendations to be useful across the devolved nations also.

In this report we describe a range of international case studies that illustrate how access to ATMPs in the UK could keep pace with the evolving ATMP pipeline by addressing current challenges in the UK ATMP ecosystem. Our analysis focused on five countries – Belgium, France, Germany, Italy and Spain – with certain strengths in the ATMP environment, such as tailored policies, the data collection environment, provisions for treatment infrastructure, and value assessment and reimbursement pathways. The primary solution identified in several of these countries is the use of innovative payment models: we have considered any approach affecting the reimbursement or funding of an ATMP beyond the routine market-access pathways in a given country. In interviews, payers from most of these countries considered innovative payment models as necessary for supporting patient access to ATMPs, and there have been successful examples of these being used where innovative payment models are not commonly used for other therapy types. Other key findings from the interviews were that payers expect the need for such innovative arrangements to evolve as the ATMP pipeline changes (including new types of contract), and it was emphasised that innovative payment models must be complementary to, rather than a substitute for, routine access approaches that are appropriate for the value assessment and commissioning of ATMPs.

Despite the UK's current strengths in ATMPs, there is much more to do to ensure that patients here will be able to access the number and variety of ATMPs expected to become available in the coming years.

Based on the learnings from other countries, several important actions are needed for the UK to build on its current momentum to improve the future readiness of the ecosystem.

Access and uptake recommendations for the UK

1. **The National Institute for Health and Care Excellence (NICE) should utilise the existing flexibility to apply the 1.5 per cent discount rate for ATMPs where relevant to ensure its appraisal process does not disadvantage future innovative treatments with long-term benefits, including many ATMPs.** This would reflect evolving Health Technology Assessment (HTA) academic best-practice developments and the experience of several counties of periodic revisions to discount rates, and ensure that access to pipeline ATMPs is made possible through appropriate recognition of their value.
2. **NHSE and NICE should work with industry to accelerate the implementation of a rapid entry to managed access (REMA) process by using ATMPs to pilot new approaches.** Currently, the CDF and IMF require a full appraisal both on entry into and exit from managed access, which increases the burden on NICE and other stakeholders involved in technology appraisals, risking delays as the number of future ATMPs increases. A REMA process would help provide a sustainable solution to these challenges. Learnings from the pilots could also help identify options to streamline the appraisal process for transitioning from managed access to routine commissioning.
3. **NHSE should ensure timely preparation for the launch of new ATMPs by being open to discussions with companies on the potential role for innovative payment models prior to marketing authorisation.** Although NHSE already offers engagement with health technology developers, the specific issue of innovative payment models is not meant to be discussed until after the NICE process. In many cases, this is far too late to avoid delays in patient access if a more innovative contract is negotiated. Therefore, NHSE should align with the company earlier on the challenge facing a particular ATMP and the range of alternative options that might be investigated, rather than assuming a simple commercial discount is the solution, which will not be appropriate for many ATMPs.
4. **NHSE should implement its commitment in the 2024 VPAG to undertake two innovative payment model pilots in a timely manner. At least one of the pilots should be for an outcomes-based agreement with payments spread over a longer contract duration than those used to date.** The decision in the 2024 VPAG to pilot innovative payment models is welcomed, considering the urgency of acting to support patient access to the ATMP pipeline, and it will be important to realise the opportunities of these pilots to identify more sustainable solutions to patient access. This should include the possibility for contracts of longer durations than those used to date, as uncertainty over treatment outcomes may extend for several years longer than NHSE is currently accustomed to.
5. **Accounting regulations have long been identified as an issue for ATMPs, but action has not been taken to address the problem. NHSE, the Department of Health and Social Care (DHSC) and HM Treasury should explore how accounting rules can be adjusted to enable payments over multiple years.** The UK is lagging behind other countries in addressing the uncertain impact of these rules and should instead implement any changes needed to enable the use of spread payments. NHSE's commitment in the VPAG to undertake two innovative payment model pilots provides an opportunity to explore amendments to accounting regulations that are necessary to implement the pilots.
6. **NICE should increase flexibilities in evidence requirements and adopt a more risk-neutral approach to managing uncertainty for all ATMP appraisals.** A clear strategy for health data in the context of ATMPs will become increasingly important as the role of real-world evidence is expected to increase for both managed-access approaches for supporting technology appraisals and for innovative payment models that use patient outcomes. To enable this and address the uncertainty, NICE and NHSE should support greater consistency in data collection to facilitate NICE's continued use and acceptance of real-world data in appraisals.

7. **NHSE, NICE, the Medicines and Healthcare products Regulatory Agency (MHRA) and industry should work together to establish a single national platform for collecting data on ATMP treatment outcomes that could support innovative access models.** This would draw on other countries' learnings on overcoming data-collection challenges, and should also enable secure and appropriate utilisation of patient data.
8. **ATMPs recommended for use by NICE should be included in the NHSE Innovation Scorecard and Estimates Report to understand whether uptake is in line with NICE eligible populations. This data should be scrutinised by an action-orientated cross-sector working group with policy makers, with plans put in place to understand and address instances of lower-than-expected uptake.** This will help to deliver on the promise of a streamlined end-to-end pathway for ATMPs, which is vital for underpinning the attractiveness of the UK to this sector.
9. **The UK government and devolved governments should establish a coordination group for ATMPs to share learnings across the UK nations and support capacity planning and decision-making across the respective health services.** As shown by the example of the Genome UK Implementation Coordination Group, collaboration at UK level is consistent with the devolved nature of healthcare policy and could support maintaining equitable access across the UK.

Wider pathway recommendations for the UK

10. **The UK must continue to develop ATMP manufacturing activities, including both early-stage and late-stage production and the effective targeting of research and innovation funding, as well as capitalising on the opportunity afforded by the new £520 million multi-year Life Sciences Capital Grants Facility.** This will help to secure future, larger manufacturing operations and maintain 'sticky', high-value ATMP manufacturing jobs that have been created.
11. **The government should prioritise improving the UK ecosystem for delivering commercial clinical research, which will increase the attractiveness of the UK as a preferred destination for ATMP clinical trials. This should include implementation in full and at pace of the recommendations of the O'Shaughnessy Review, and passing outstanding UK clinical trials legislation to enhance the UK's attractiveness for inward investment.** New clinical trials legislation is essential following the UK's exit from the European Union. However, this faced delays in the previous Parliament, causing uncertainty and enabling the UK's competitors to gain an edge in attracting R&D investment.
12. **A strengthened and refreshed Innovative Licensing and Access Pathway (ILAP) should offer a streamlined end-to-end pathway for ATMPs that helps align all system partners from development to patient access. The MHRA should ensure it has the right levels of expertise and capacity to support the delivery of timely scientific advice, and clinical trial and drug licensing approvals as the evolving ATMP pipeline matures.** The regulatory environment is key to unlocking growth and attracting and retaining inward investment to the UK.

1. Introduction

The Association of the British Pharmaceutical Industry (ABPI) asked Charles River Associates (CRA) to compare the readiness of the UK to other countries in terms of challenges associated with the ATMP pipeline. Therefore, the overarching objective of this report is to understand how the challenges of providing patients with access to ATMPs will evolve over the next five years, and to learn from international experiences of improving access to ATMPs to develop lessons that the UK can draw upon. In doing so, the report identifies several important actions that are needed for the UK to build on its current momentum in a way that will improve the future readiness of its access environment and stresses the importance of ensuring a well-functioning end-to-end ATMP pathway.

ATMPs have the potential to deliver transformative benefits to patients, caregivers, and the wider UK health system and society, by addressing the root causes of diseases.[9] Based on genes, tissues or cells (box 1), these innovative medicines have the potential to offer ground-breaking new opportunities for the treatment of diseases, and in some cases have already provided patients with life-changing solutions where there were previously few or no effective treatments.

Box 1: Definition and types of ATMP

Advanced therapy medicinal products (ATMPs) are treatments that include either a gene therapy medicinal product, a somatic-cell medicinal product or a tissue-engineered product:[10]

- **Gene therapy** contains genes that lead to a therapeutic effect by inserting 'recombinant' genes created in the laboratory into the body.
- **Somatic-cell therapy medicines** contain cells or tissues that have been manipulated to change their biological characteristics or not intended to be used for the same essential functions.
- **Tissue-engineered medicines** contain cells or tissues that have been modified so they can be used to repair, regenerate or replace human tissue.

The UK was one of the first countries to recognise the potential of ATMPs, with the government providing investment and policy support to demonstrate commitment to the field, and progress driven by effective collaboration across key stakeholder groups, including industry. The establishment of the Cell and Gene Therapy Catapult in 2012 sent a signal of commitment to the research-based pharmaceutical industry and has facilitated a helpful focus on many aspects of the UK ATMP ecosystem, from manufacturing and research to training and market access. This collaborative approach has paid dividends in manufacturing and clinical trials, in particular.

In manufacturing, the joint UK government and Medicines Manufacturing Industry Partnership (MMIP) 2016 Advanced Therapies Manufacturing Action Plan set out six key asks to anchor commercial scale manufacturing of ATMPs in the UK. Following this, the Industrial Strategy Challenge Fund invested in a holistic UK ATMP ecosystem by: delivering increased viral vector manufacturing capability and capacity with the expansion of Oxford Biomedica, Cobra Biologics and the Cell and Gene Therapy Catapult; initiating an end-to-end UK-wide talent plan of relevant skills via the Advanced Therapy Apprenticeship Programme (ATAC) and Skills and Training Network (ATSTN); establishing a world-first network enabling best practice and NHS readiness for ATMPs via the Advanced Therapy Treatment Centres (ATTCs); and providing joined-up, innovative and responsive regulation via theMHRA. UK-based ATMP manufacturing has continued to develop, with an increase in the overall number of dedicated ATMP manufacturing organisations operating in the UK (26 dedicated cell and gene therapy manufacturers in 2023) and a 20 per cent increase in the number of full-time employees in the ATMP manufacturing workforce in 2023, compared to 2022.[11]

The UK has also demonstrated strengths in supporting ATMP clinical trials. Fourteen per cent of all global phases I-III commercial ATMP clinical trials are conducted in the UK.[12] The number of ongoing UK ATMP trials increased annually from 2012 to 2021[13] and has remained steady between 2022 and 2023, despite a 10 per cent decrease in the overall number of global ATMP clinical trials.[14] The UK's attractiveness for ATMP trials is particularly positive in the context of the broader research environment, where the number of clinical trials taking place in the UK has been in decline since 2017, leaving the UK in 10th position globally, having fallen from its fourth-place global ranking five years ago. Recommendations in the government's independent review of commercial clinical trials conducted by Lord O'Shaughnessy in 2023 in response to this decline have been accompanied by a government implementation plan to accelerate recovery.

One of the review recommendations that will directly benefit ATMP trials is the adoption of the National Contract Value Review, which is now mandated for all late-phase studies, and will speed up and streamline setup times.

However, the UK must remain vigilant to maintain its strong global position in ATMP clinical trials and should respond nimbly to respond to advances in the field. This is particularly important in the context of the wider UK ATMP ecosystem, as trials provide an opportunity for the NHS to build experience with these products, increasing the chances of rapid adoption following NICE recommendation.

The transformative nature of ATMPs presents novel access challenges for all healthcare systems. These challenges have traditionally been split into three key themes: affordability, uncertainty and infrastructural requirements.[15]

- First, ATMPs can generate an affordability challenge: because their benefits to patients are often delivered in a one-off (rather than an ongoing) intervention and payments have traditionally been aligned to delivery of the treatment, this means the payment is upfront. As such, relatively high upfront cost must be paid for benefits that are delivered to patients in the future.
- Second, ATMPs are associated with additional uncertainty regarding their long-term effectiveness. This is because they have potentially long-lasting – and in some cases perhaps lifetime – benefits, but clinical trials are inevitably over a relatively short time.
- Third, healthcare systems need to address the infrastructure challenges of delivering access to ATMPs to patients: as ATMPs are specialised medicines utilising advanced technologies, they can require specialised infrastructure to identify patients eligible for the treatment, deliver the therapy and monitor the outcome.

Together these challenges help explain why the number of reimbursed ATMPs is currently relatively low across countries.[16] In the UK, 14 ATMPs have been reimbursed (through routine or managed-access processes) since the first ATMP received EMA approval in 2009. Although these challenges are not unique to ATMPs, they are exacerbated considerably for these therapy types due to their transformative nature and often one-time administration.

Due to the excitement about the potential benefits for patients, but also the novelty of the challenges, there has already been substantial interest in enabling patient access to ATMPs. This is particularly because there can be a narrow treatment window opportunity in which delivering the therapy to patients is most effective, demonstrating the importance of minimising access delays. Interest in addressing this challenge has generated extensive academic literature, as well as initiatives from health authorities, developers, patients and physicians.[17, 18, 19] A specific focus has been on addressing the uncertainty and affordability challenges that ATMPs create for payers.[20] However, much of this is conceptual and does not relate to individual countries, and many of these existing approaches do not consider the number and variety of treatments that will be available in five years' time. As a result, it is sometimes assumed that past experience of successful delivery of ATMPs to patients will be replicated in future.

This consideration is particularly relevant for the UK as it is sometimes used as a case study for how access to ATMPs can be achieved.[21] Indeed, it is certainly the case that the UK government and NHS have implemented several initiatives to facilitate patient access to these therapies, in recognition of their potential benefits. Most recently, the DHSC, NHSE and the ABPI reached agreement on the 2024 VPAG, which included a commitment from NHSE to deliver two innovative payment model pilots for ATMPs.[22] The importance of ATMP access is also recognised in the DHSC's 'England rare diseases action plan 2023', which commits NHSE to developing a strategic approach to ATMPs. Similar initiatives can also be found in the devolved nations. For example, in 2019 the Welsh Government published an 'Advanced therapies statement of intent', outlining its intention to create a sustainable platform to enable NHS Wales to provide patients with access to these therapies.[23]

However, progress to date does not guarantee readiness for the future. In this report, we consider how UK health authorities can continue to build on their current momentum to ensure that the evolving challenges for ATMP access are addressed. Furthermore, we assess whether there is more that the UK can learn from international experiences of improving access to ATMPs to ensure its approach is robust enough to manage the number and variety of ATMPs in the pipeline. Although many of the examples in the report focus on England, the intention is for the lessons and recommendations to be useful across all four UK nations. An outline of the methodology used to develop the report – which was primarily comprised of a literature review and interview programme with international payer experts – is provided in the appendix.

2. How access challenges will evolve given the number and diversity of pipeline ATMPs

Access to ATMPs in the UK today

Over many years, health authorities and policymakers in the UK have committed to ensuring patients have access to innovative medicines, including ATMPs.[24] The 2021 NHSE commercial framework for new medicines emphasises the role that NHSE commercial activity plays in enabling patient access to new therapies,[25] while in 2022 NICE introduced additional flexibilities in the new combined methods and processes manual, including those that are likely to benefit ATMPs.[26] In recognising that routine access pathways may not always be appropriate for assessing and commissioning ATMPs, there have already been several cases of patients accessing these treatments through flexibilities in the NICE and NHSE processes for appraisal and commissioning. An overview of the approaches that have been used for the evaluation and reimbursement of ATMPs in England is shown in figure 1. It should be noted that while the single technology appraisal (STA) and HST programmes are alternatives, the CDF and IMF provide funding during a managed

-access period in which additional data is collected to enable a decision through either the STA or HST process.

Figure 1: Evaluation and reimbursement processes used for ATMPs in England[27,28]

	Approach	Description	Number of ATMPs
NICE assessment processes	Single technology appraisal	• Routine NICE process for evaluating the clinical and cost-effectiveness of a single technology for a single indication • Recommends new medicines based on the incremental cost-effectiveness ratio	6 Recommended for routine commissioning
NICE assessment processes	Highly Specialised Technologies programme	• Designed to be used in exceptional circumstances for treatments for ultra-rare diseases • Provides a more flexible approach and a higher cost-effectiveness threshold than the STA process	5 Recommended for routine commissioning
Managed access fund	Cancer Drugs Fund	• Provides access to promising new cancer treatments via managed-access arrangements while further evidence is collected to address clinical uncertainty	3 Recommended for use within the CDF
Managed access fund	Innovative Medicines Fund	• As per the CDF but for promising non-cancer medicines	1 Recommended for use within the IMF

Note: one treatment, axicabtagene ciloleucel, has been included in the number of ATMPs for both the CDF and STA process, as-has-an indication both in routine commissioning and in the CDF. The routine-commissioned indication was previously recommended for use in the CDF.

Although these different processes create some flexibility in the UK system to account for the unique challenges for ATMPs, they were not designed specifically for ATMPs. Therefore, it is not surprising that there are several challenges with applying these approaches. If we start with the STA process, as noted in box 2 there is a challenge around the discount rate used, which values longer-term costs and health benefits less than short-term outcomes. This is a particular challenge for ATMPs, which may offer lifetime benefits but whose costs are one-off. Furthermore, ATMP innovations that address patients with high unmet needs and no effective treatment can paradoxically face greater hurdles in the NICE process, because there is no current treatment to offset costs. Additionally, if the lack of historical treatment results in an initial surge of patients at launch, this can exacerbate the challenge of the discount rate, as these costs will not be discounted while the resulting long-term benefits will be.

Box 2: Challenges in the STA process for ATMPs

The standard NICE threshold for cost-effectiveness is £20,000 to £30,000 per quality-adjusted life year (QALY).[29] Recommendations based on a cost/QALY threshold are likely to be particularly challenging for ATMPs for several reasons: they do not capture the wider benefit for patients beyond the QALY, nor the indirect benefits to patients and the broader benefits to caregivers, families and society. The STA process is also ill-equipped to deal with the uncertainty associated with ATMP evidence bases at the time of launch.

There is a particular challenge around the discount rate used in the assessment process. NICE has traditionally used a standard 3.5 per cent discount rate for costs and effects, although it can apply reduced discount rates in specific circumstances where long-term benefits (over 30 years) are anticipated.[30] Although NICE has stated that there is an "evidence-based case" for changing the reference base discount rate – which would be in alignment with HM Treasury's Green Book guidance – there have not yet been any changes to this.[31] While in theory NICE can reduce the discount rate to 1.5 per cent in specific circumstances, this has rarely been applied in practice.[32]

The second pathway is the HST process, introduced in recognition of some of the challenges for appraising rare-disease medicines (which most available ATMPs to date have targeted). This pathway offers more flexibility in the evidence requirements and approach to managing uncertainty, including a higher cost-effectiveness threshold of £100,000 per QALY (rising to £300,000 in some circumstances), compared to £20,000 to £30,000 under the STA.[33] However, HST is limited to ultra-rare diseases, and is not expected to be applicable if more than 300 people in England are eligible for the licensed indication.[34] As a result, it is anticipated that only a small number of HST approvals will occur per year, and few ATMPs to date have been appraised through the HST programme. In fact, many ATMPs already available or in the pipeline are for rare diseases with high unmet needs, which are not eligible for the HST process but still face challenges in meeting the STA cost-effectiveness

threshold. The limitations of the HST process as a sustainable solution will be further exacerbated by the increasing number of ATMPs launched for larger populations.

The final mechanism often referred to is the CDF, which has the obvious caveat that it is limited to oncologic therapies. The IMF was introduced to provide a similar managed access process for non-cancer medicines. One ATMP has been entered the IMF since it was launched in June 2022. However, it was not used at all until November 2023.[35] Potential reasons for this include the criteria for entry, the difficulties with replicating data infrastructure (which has often been better established in oncology than in some other therapy areas), and the level of risk that can be reasonably taken by pharmaceutical companies, which may have to fund the full cost of treatment in perpetuity for any treatments that are not subsequently recommended by NICE.[36,37]

Although flexibilities have been found in the current processes and there are ATMP success stories in the UK, these results should not be a cause for complacency. In terms of flexibilities in the evaluation and reimbursement process, current approaches primarily manage shorter-term uncertainties, rather than longer-term uncertainty and affordability challenges, and the barriers for gaining access to these are very high. All existing mechanisms have notable shortcomings regarding provisions for supporting patient access to these innovative therapies. Ultimately, the extent of the current flexibilities is insufficient, particularly in terms of how ATMPs are commissioned: although in theory the NHSE commercial framework sets out opportunities for different commercial arrangements, it states that a simple discount is always the preferred option, and most types of novel payment models, such as an outcomes-based agreement, have never been used for ATMPs.[38]

It is worth noting that different approaches to market access for ATMPs can also be found in the UK's devolved nations. In Scotland, the Scottish Medicines Consortium (SMC) provides advice about the value of new medicines. Medicines recommended by the SMC may receive funding from the New Medicines Fund, which contributes to the cost of orphan, ultra-orphan and end-of-life medicines for patients.[39] In Wales, the All Wales Medicines Strategy Group (AWMSG) does not usually appraise new therapies if NICE guidance is expected, and expects most ATMPs to be appraised by NICE.[40] Newly recommended medicines may receive extra funding from the Welsh Government's New Treatment Fund.[41]

The past is not a predictor of the future – challenges posed by the ATMP pipeline

The challenges that the UK will face in the future become more complex when considering the expected evolution of the ATMP pipeline.

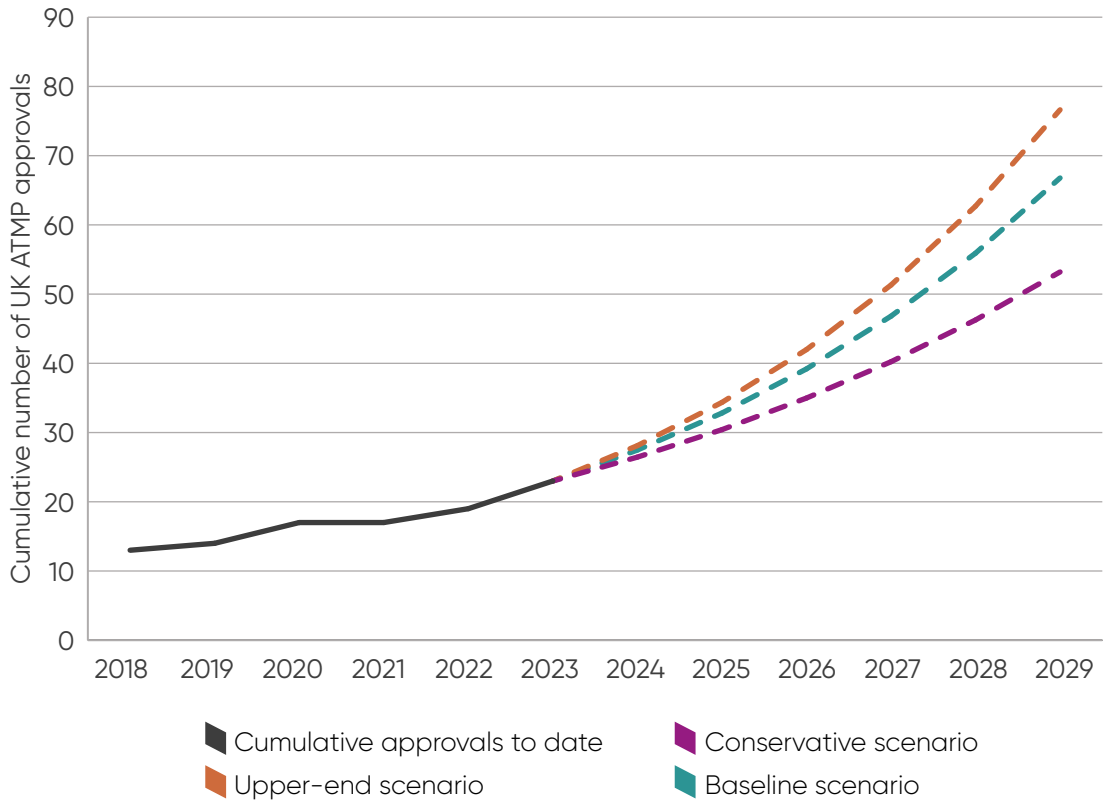
First, there will be a significant acceleration in the number of ATMPs launched. Although it is challenging to predict the exact number of approvals, the literature on modelling the future ATMP landscape all predicts the number of available therapies to rapidly increase in the next five years (figure 2), with the cumulative number of marketing authorisation approvals in the UK potentially increasing from 23 at the end of 2023 to nearly 80 by 2030. Please note that the 23 UK approvals (marketing authorisations) referenced in this report include six ATMPs that subsequently had their marketing authorisation withdrawn or not renewed, and so are no longer licensed in the UK.

To put this in context, over the previous five years an average of two ATMPs per year have been approved by the MHRA (range of zero to four). This could increase to 10 to 15 per year by 2030. Using the baseline of the number of ATMPs already approved in the UK, we considered three scenarios for how approvals will evolve:

- A conservative scenario in which the number of approvals increases by 15 per cent each year: this is based on the Economic Impact (2022) study, which assumed per cent growth each year for most countries (including the UK) from 2022 to 2030.[42]
- A baseline scenario of 19 per cent growth each year: this is based on Young et al. (2022), which estimated the number of cumulative approved therapies in the US as 64 by 2030 (19 per cent annual growth).[43]
- An upper-end scenario of 22 per cent growth each year: this is based on a previous version of the above modelling on the expected number of US approvals and estimated that 45 cell and gene therapies would be launched by 2029 (equivalent to 22 per cent growth each year).[44]

Although only one of these studies addresses the UK specifically, we assume that there are potential similarities in the trajectory of ATMP approvals across different countries, and so consider it possible to use the international literature to model the potential cumulative number of ATMP approvals in the UK in the future (figure 2).

Figure 2: Using international literature to model the potential cumulative number of future ATMP approvals in the UK

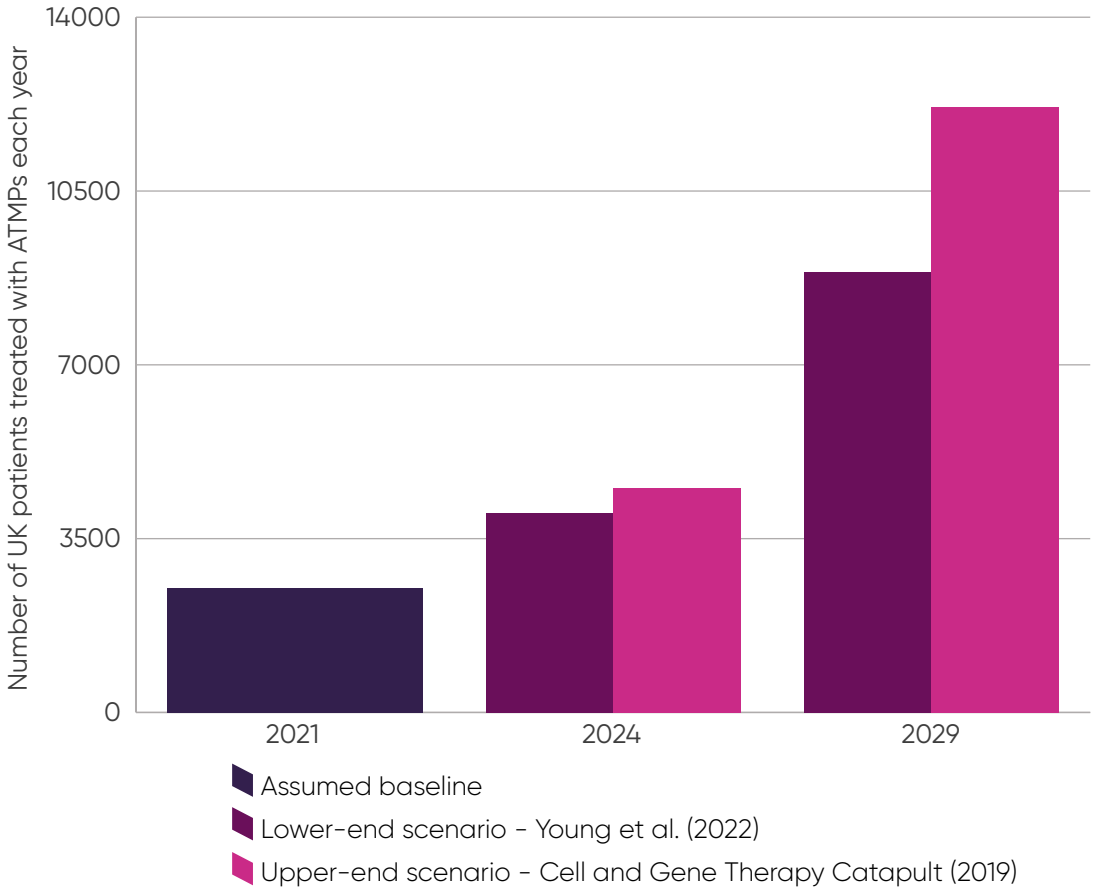


The growing number of available ATMPs is expected to result in more patients benefiting from these therapies: although reliable data on the number of UK patients treated to date with ATMPs is limited, one estimate found that 2,500 patients were treated with ATMPs in 2021.[45] Taking this as the baseline, the literature provides two scenarios for future potential patient numbers:

- An upper-end scenario of 22 per cent annual growth: this is based on the Cell and Gene Therapy Catapult (2019), which forecast that the number of patients could reach 10,000 by 2028 (22 per cent annual growth).[46]
- A lower-end scenario of 17 per cent annual growth: this is based on Young et al. (2022), which estimated an increase in patients treated in the US from 22,500 in 2021 to 99,400 in 2030 (so it is assumed that this 17 per cent annual growth is one possible scenario for the UK).[47]

The impact that these growth rates would have on the number of patients treated is shown in figure 3.

Figure 3: Using international literature to model the potential number of UK patients treated with ATMPs each year



However, these may be relatively conservative scenarios considering alternative forecasting approaches: according to a model developed for France, as many as 117,000 patients there could be treated annually by gene therapies by 2030 (which would result in a similar estimate in the UK, considering similar total population sizes).[48] Regardless of the precise numbers, under any of these scenarios the potential number of patients treated with ATMPs will rapidly increase. These findings reiterate the importance of ensuring that ATMPs can be appropriately assessed and commissioned so that more patients can access their benefits, as well as building sufficient ecosystem capabilities to cope with this volume in both assessment and delivery.

In addition to the growing number of ATMPs, new challenges will be created by the diversity of ATMP types in the pipeline. Today, the majority of ATMPs share several characteristics: they are limited to rare and ultra-rare diseases and so often target small patient populations; they are often one-off interventions with potentially curative intent; and they are generally offered to patients who have no existing or limited effective available treatment options. However, based on the types of ATMPs currently being studied in clinical trials, the UK health system will have to adapt to several new types of ATMPs, which will create additional access challenges.

Although there are many factors that will differentiate future ATMPs – including increased diversity of treatment indications, mechanisms of actions and manufacturing techniques – here we focus on: (1) the population size, which will include more non-rare diseases; (2) the treatment approach, which will comprise more chronic or preventative treatments; and (3) the availability of alternatives, which will involve more ATMPs being launched in indications where there are already therapeutic alternatives and with earlier positioning in the standard of care. These new characteristics may pose new access challenges, which will require cross-sector collaboration to overcome if UK patients are to continue to benefit from the next wave of these treatments (table 1).

Table 1: Additional challenges of future ATMP characteristics

Although many of the future ATMPs will continue to share the key characteristics of those available today, there will also be new types of ATMPs that will have their own set of challenges for ensuring patient access			
	Population size	**Treatment approach**	**Availability of alternatives**
Challenges of current ATMP characteristics	**Rare/ultra-rare diseases:** • Evidence developed in small clinical trial sizes, compounding uncertain durability of clinical effect	**One-off and potentially curative treatments:** • High upfront cost under traditional payment approaches, with uncertainty over long-term durability of effect	**No existing or limited effective available treatments:** • Value assessment more challenging with lack of appropriate benchmarks
Additional challenges of future ATMP characteristics	**Larger patient populations:** • Greater affordability challenge due to higher patient numbers • Continued uncertainty regarding long-term effectiveness despite potential for larger trial populations • Patient volume places greater demand on specialist infrastructure	**Chronic or preventative treatments:** •Greater lag between delivery of the treatment and seeing improvements in outcomes, especially if administered in pre-symptomatic stage • Novelty of endpoints used to demonstrate efficacy or to utilise in managed-access approaches	**Therapeutic alternatives and earlier positioning in treatment paradigm:** •Earlier positioning will increase patient numbers and therefore budget impact/demands on specialist infrastructure • Need to establish clinical benefit and cost-effectiveness compared to alternatives (which may not have been previously reviewed by NICE)

ATMPs for larger patient populations

In the future, ATMPs will target both rare and non-rare diseases, and could be launched for indications with significantly larger populations than has been the case to date.[49] It has been reported that the majority of the ATMP pipeline targets non-rare diseases, with one study finding that in ATMP clinical trials the study target was a rare disease in only 46 per cent of trials, with the remaining 54 per cent targeting non-rare diseases.[50] For example, gene therapies are being investigated in some of the UK's most common neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease (with the caveat that ATMPs would likely target a certain segment of these patients rather than the full population). This trend is in stark contrast to ATMPs currently available: nearly 80 per cent of the ATMPs approved by the end of 2023 (18 out of 23) target rare indications and consequently received orphan drug designation. The development of ATMPs for non-rare diseases will exacerbate the affordability challenge, place greater demands on specialist infrastructure, and also lead to some non-routine access pathways – such as England's HST programme – becoming applicable to an even smaller proportion of ATMPs than at present. Yet the considerable value these potential treatments offer to patients and society means that it is increasingly important to provide timely solutions to these challenges.

Chronic or preventative ATMPs

The majority of existing ATMPs are seen as having potentially curative outcomes from one-off or short-term treatments: at least 13 of the 23 approved ATMPs (as of the end of 2023) can be considered to be potentially curative for patients. Overall, many ATMPs will continue to offer patients potentially curative outcomes. However, an increasing number of ATMPs in the pipeline will have the potential to deliver significant broader benefits to patients. For example, some cell and gene therapies are already showing benefits for patients with chronic disorders without curative intent, such as AAV-based gene therapies for neurodegenerative diseases like Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis. These are expected to target prevention or slow progression rather than curing disease. There is also growing interest in 'preventative' ATMPs, which treat asymptomatic or pre-symptomatic patients who have a known genetic mutation.[51] Preventative ATMPs can increase the long-term benefits from advanced therapies but lead to a greater time lag between treating patients in the pre-symptomatic stage and seeing improved outcomes. There will also be more variability in the size and duration of the effects on patients.

ATMPs in earlier treatment lines or in indications where there are already therapeutic alternatives

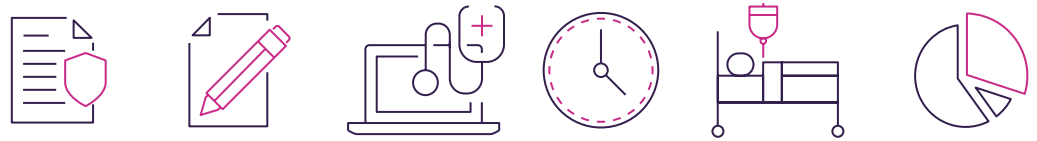
Available ATMPs already differ in relation to existing pharmacological comparator interventions: some of the rare indications for which ATMPs are launching have no available alternatives, while others launch to address unmet needs despite available treatments. Generally, however, patients receiving an ATMP have few therapeutic alternatives. Considering the range of indications for which ATMPs are being developed, in the future there will be a broad variation in the way new therapies can be characterised in relation to the existing standards of care, including more indications for earlier lines of therapy. This may be in the form of available disease-modifying therapies, or even direct ATMP competitors. For example, there are more than 10 gene therapies in development for both haemophilia A and B.[52] As ATMPs move into earlier treatment lines, they may benefit larger population sizes, exacerbating the challenges associated with non-rare diseases. There will also be a need to account for the availability of alternatives within the value assessment and reimbursement process, such as evaluating clinical benefit and cost-effectiveness relative to available alternatives.

3. Lessons from other countries

In this chapter we seek to understand if other countries are already using approaches that can address the anticipated challenges for the ATMP pipeline. Health authorities and policymakers in other countries have already taken a wide range of approaches to facilitate patient access to ATMPs, including but not limited to novel approaches from payers for the assessment and commissioning of new treatments.

Below we describe a range of international case studies that may be relevant for the UK. We looked across the broader environment for enabling patient access to ATMPs (figure 4) and found that much of the focus in other countries has been on how innovative payment models can be used to address access challenges. We therefore provide here a deep-dive analysis of lessons from their use.

Figure 4: Health system characteristics impacting patient access to ATMPs



Broader ATMP policy environment	Regulatory environment	Diagnosis and data	Early access to treatment	Infrastructure for provision of treatment	HTA, pricing and reimbursement and funding
• Focus on ATMPs in rare disease plans or other national policies • Broader policy frameworks	• Dedicated methodology to assess ATMPs • Availability of, and eligibility for, fast-track procedures	• Access to diagnostic testing • Patient registries	• Early-access schemes • Alternative approaches to accelerate access	• Specialised ATMP treatment capabilities and availability	• Flexible value assessment approaches • Support for and use of innovative payment models • Funding opportunities

Ensuring a robust environment that can enable patient access

Broader policies that recognise the need for policy change for ATMP access

Policy recognition of the need for national strategies to support ATMP access has been limited in many countries, particularly with regards to readiness for the ATMP pipeline. The situation in the UK mirrors that in several EU countries, where policy recognition of ATMPs occurs primarily within the context of national plans for rare diseases: while not explicitly mentioned in the UK Rare Diseases Framework, England's Rare Diseases Action Plan includes the action of developing a strategic approach for ATMPs.[53] While further development of such a strategy would be welcome – as would clarity on what has already been developed to support a shared understanding of what else needs to be done – it is important that the challenges of ATMPs are not seen solely in the context of rare diseases, considering the ongoing development of ATMPs in non-rare diseases.

The UK could learn from Spain, where there is a dedicated strategy for advanced therapies (box 3). Implemented in 2018, the strategy has been seen as evidence of Spain actively addressing its approach to ATMPs.[54] The strategy has several notable strengths: it recognises the wave of new ATMPs and the increase in patient volume that is expected in the coming years and does not situate ATMP access only in the context of rare diseases. At the same time, its focus so far has been CAR-T therapies, suggesting limited overall scope in terms of ATMP types. Still, it has been reported that the strategy has already resulted in two ATMPs – tisagenlecleucel and axicabtagene ciloleucel being reimbursed much earlier than is typically the case for orphan medicines in Spain.[55]

Box 3: The Spanish National Strategy for Advanced Therapies (2018)

The National Strategy for Advanced Therapies was approved by the Interterritorial Council of the National Health System in 2018 to improve access to ATMPs, specifically CAR-T therapies.[56] The main objective of the strategy was the organisation of equitable, safe and efficient use of CAR-T medications, with a focus on the designation of new hospital centres to the ATMP network to increase capacity for treating patients. The strategy led to a significant expansion in the number of centres authorised to use CAR-T therapies. Although the strategy has been directly linked to access to some CAR-T therapies, some experts and patient societies have advocated for an updated advanced therapies plan to simplify processes and improve equity of access.[57]

Regulatory frameworks that can streamline authorisation and access for ATMPs

It is important that the regulatory processes for ATMPs are as efficient and attractive as possible. For example, until recently, the marketing authorisation approvals of ATMPs in the UK have been primarily driven by the EMA, based on the MHRA's European Commission (EC) Decision Reliance Procedure (ECDRP), a temporary measure from January 2021 to January 2024 that permitted the MHRA to rely on EC decisions.

With the cessation of the ECDRP, there was a risk that the benefits of the EMA's advanced therapies expertise may lessen. In January 2024, the ECDRP was replaced by the International Recognition Procedure (IRP), which enables applications for marketing authorisation based on the same medicine having already been approved by one of the MHRA's seven reference regulators, including the US Food and Drug Administration (FDA) and EU EMA. This has the advantage of offering a potential additional flexibility for medicine developers and may accelerate patient access to new ATMPs if a faster reference regulator – most often expected to be the FDA – grants an earlier marketing

authorisation. However, it is important that the MHRA remains adequately resourced with experienced staff to manage the number of ATMP products likely to come through the pipeline in the coming years.

In 2021, the MHRA launched the ILAP to, "support the safe, timely and efficient development of medicines to improve patient access".[58] The ILAP is open to ATMPs and includes a number of 'permanent' and 'supporting' system partners with the intention of facilitating a more coordinated approach to medicines development and launch in the UK.

The ILAP is currently under review and the strengthened and refreshed ILAP should offer a streamlined end-to-end pathway for ATMPs that helps align all system partners from development to patient access.

Diagnostic and patient data infrastructure for identifying and monitoring patients

Data collection is crucial for supporting payers and physicians in demonstrating the long-term effectiveness of ATMP treatment. Indeed, data collection systems are essential for enabling patient access if they are a component of a payment model used to enable reimbursement of a new ATMP. For example, Italy is often seen to have enabled its pioneering use of managed entry agreements (MEAs) through an extensive national system of online registries (box 4).[59] All MEAs in Italy are based on the Italian Medicines' Agency (AIFA) web registries. For each monitored product, patients are registered in the specific therapeutic indication dynamic monitoring database to collect epidemiological and clinical data. Key successes of the AIFA registries have been their wide applications to different treatment types (both orphan drugs and non-orphan drugs, and for different therapy areas) and the enablement of different types of managed entry agreement (both financial-based and outcomes-based agreements).[60]

Another country with lessons for the UK is Spain, where the Valtermed platform has been an important enabler for implementing payment models that make patient access possible. The Valtermed registry is a national information system that collects real-world evidence on new medicines with a high clinical and economic impact. All five ATMPs available in Spain are reimbursed through an innovative payment model linked to the Valtermed registry.[61,62,63]

These examples demonstrate the impact that well-developed data-collection systems can have on enabling patient access to ATMPs. Approaches to optimising data collection for the purposes of implementing innovative payment models are further assessed in the next section.

Box 4: AIFA registry system

The web-based AIFA registry system has been a key enabler of outcomes-based agreements for ATMPs. The registries monitor innovative medicinal products and are governed by AIFA with funding from pharmaceutical companies. The data collected through registries is owned by AIFA. Initiation of a registry starts with the AIFA Technical-Scientific Commission by issuing a mandate to the AIFA registries office. The registries have been designed to collect patient longitudinal data at public or private (national health service affiliates) hospitals.[64]

The main actors with clinical and administrative responsibilities are pharmacies, regions, district health services and the marketing authorisation holder, and there is no patient involvement at any stage. If an AIFA registry is running, healthcare providers must enter data into the system before they can prescribe the medicine or obtain national health service reimbursement.

Early-access programmes to ensure faster access to medicines for those in need

Speed of access is crucial for patients who may benefit from treatment with an ATMP. These are patients – sometimes newborn babies – who may have life-threatening or severely debilitating diseases with no therapeutic alternatives. Any delay in time to access can have detrimental effects on patients. For this reason, many countries have provided ATMPs to patients through an early-access scheme. For example, most countries have compassionate use or named-patient programmes, which can be used to provide patients with access to a medicine prior to receiving marketing authorisation, partially analogous to the early access to medicines scheme (EAMS) in the UK. However, there have been challenges with providing patients with access to ATMPs through these pathways in several countries. For example, while in theory Italy's law number 648/96 provides an established pathway for access to not-yet-authorised medicinal products, in practice its application to ATMPs has been limited: from 2017 to 2021, only three requests for ATMPs under law 648 were evaluated, and only one of these received a positive opinion.[65]

International experience with early-access schemes for ATMPs provides lessons for a key challenge seen in the UK and elsewhere: the feasibility of providing medicines like ATMPs free of charge during the early-access period. It has been previously documented that it can be commercially unviable to apply unfunded early-access schemes to single-administration high-cost therapies, especially for treatments with small patient populations, as there is no prospect for the manufacturer to recoup any costs for that particular patient in the future if a positive reimbursement decision is subsequently made.[66] While full funding during access prior to full HTA is rarely considered, other countries do have lessons as to how the use of early access can be made more feasible. For example, France's early-access authorisation programme (AAP) and compassionate use programme provide access prior to marketing authorisation (box 5). The AAP includes the previous authorisation for temporary use (ATU) mechanism and allows early access and free pricing by the company, alongside a payback clause. Of the first 13 ATMPs with favourable reimbursement assessments from France's Haute Autorité de Santé (HAS), nine were granted early access under the AAP scheme or its predecessor the ATU, while to date, no ATMPs on the AAP/ATU were subsequently denied reimbursement by HAS.[67,i] France's success in delivering fast access to ATMPs for patients demonstrates the benefits of a highly structured early-access programme with public funding, and one that can cover the pre-marketing, post-marketing and pre-reimbursement phases.[68]

Systems like the ATU are also linked to the overall attractiveness of countries to be the location of the development and launch of innovative medicines. In fact, in addition to accelerating patient access, early-access mechanisms support innovative activities, such as by supporting the generation of real-world evidence.[69]

Box 5: Early access in France

France's authorisation for temporary use (ATU) programme was a funded pathway for supporting early access prior to marketing authorisation, divided into six sub-systems. In 2021, ATU was reformed into two new mechanisms: the early access authorisation programme (AAP), which incorporates the previous cohort ATU, and a compassionate access programme, which incorporates the former nominal ATU.[70]

The AAP is granted and administered by the main HTA authority, Haute Autorité de Santé, at the request of the health technology developer. During the AAP period, the manufacturer freely sets the price of the medicine but is subsequently subject to mandatory rebates according to the final price negotiated with the French medicine pricing committee (CEPS). Specifically, a yearly rebate is applied dependent on the sales amount, with an additional rebate applied retroactively equal to the differences between the sales amount billed during the AAP (less the above rebate) and the sales amount that would have been billed had the final negotiated price applied.[71] CEPS may increase the rebate amount in the absence of an agreement with the manufacturer on setting the price within a fixed deadline following the request for registration for reimbursement.[72]

i ATMPs that have been included in the ATU/AAP in France include the following: Idecabtagene vicleucel, Ciltacabtagene autoleucel, Tabelecleucel, Tisagenlecleucel, Atidarsagene autotemcel, Voretigene neparvovec, Brexucabtagene autoleucel, Eladocagene exuparvovec, Axicabtagene ciloleucel and Onasemnogene abeparvovec

Infrastructure to ensure patients can benefit from new ATMPs

For ATMPs to be delivered to patients, there needs to be sufficient capacity in the health system infrastructure. As the number and type of ATMPs increases, ensuring sufficient specialised ATMP treatment capabilities and availability will become increasingly important for converting the transformative potential of ATMPs into benefits for patients. In the UK, there are already some notable initiatives underway to accelerate the NHS's ability to routinely deliver ATMPs to patients. Of particular note is the Advanced Therapy Treatment Centres (ATTC) project, which aims to develop robust systems for the routine delivery of ATMPs as a standard of care throughout the NHS.[73] Operating within NHS frameworks, the ATTC is coordinated by the Cell and Gene Therapy Catapult and has established a network of three regional UK centres: Innovate Manchester Advanced Therapy Centre Hub, Midlands and Wales Advanced Therapy Treatment Centre (hosted by University Hospitals Birmingham NHS Foundation Trust) and Northern Alliance Advanced Therapies Treatment Centre.

There are similar initiatives underway in several countries. These include:

- **INTEGRATE-ATMP in Germany:** a collaboration between specialised German treatment centres to develop harmonised treatment plans and quality assurances for delivery of ATMP treatments[74]
- **ATMP Sweden:** a national network of researchers, healthcare professionals and industry partners supporting the development of novel solutions to support patient access to ATMPs[75]

The UK appears to be a frontrunner in developing systems for rapid and more extensive ATMP uptake that other countries may be able to learn from, which is to be welcomed. However, this is also a reflection of a widespread issue that health authorities in many countries do not appear to be fully engaging with the anticipated challenges in capacity posed by the ATMP pipeline.

Despite these, the UK appears to be the frontrunner in having systems in place for rapid and more extensive uptake of the current generation of ATMPs and is demonstrating clear progress in developing ATMP treatment capabilities that other countries may be able to learn from. However, no health authorities in the countries we studied appear to be fully engaging with and preparing for the anticipated challenges in capacity posed by the ATMP pipeline.

As the pipeline for ATMPs matures, the ABPI would welcome a transparent approach to reviewing UK adoption and uptake. The NHSE Strategic Metrics Board Medicines Subgroup's remit has been refreshed to align with key commitments in the 2024 VPAG and the Life Sciences Vision. It will continue development of uptake measurement tools, including the Innovation Scorecard and Estimates Report, to track variation in uptake of NICE-recommended medicines between Integrated Care Boards. Including ATMPs in the Estimates Report would allow policymakers to scrutinise ATMP adoption and uptake and proactively address unwarranted variation. This will help to deliver on the promise of a streamlined end-to-end pathway for ATMPs, which is vital for underpinning the attractiveness of the UK to this sector.

Unlocking patient access to ATMPs with innovative payment models

A key theme of the international case studies is the role played by innovative payment models in improving or accelerating patient access to ATMPs. An innovative payment model can be any approach affecting the reimbursement or funding of an ATMP beyond the routine market-access pathways in place in a given country. A selection of the innovative payment models that have been used to date is shown in table 2. Notably, innovative contracts do not have to be limited to one of these types but can combine components of each.

In this section, we outline key findings from the literature review and series of 10 interviews with international payer experts regarding the role of innovative payment models in improving access to ATMPs. The findings can be summarised as follows:

- innovative payment models are widely considered to be an important option that is often necessary for supporting patient access to ATMPs
- manufacturers and payers value flexibility in the establishment of innovative payment models for ATMPs
- successful implementation of innovative payment models requires appropriate infrastructure
- payers expect the need for innovative payment models to evolve as the ATMP pipeline changes
- innovative payment models must be complementary to, rather than a substitute for, routine access approaches

Table 2: International examples of innovative payment models that have been used for ATMPs[76]

Category	Description
Coverage with evidence development	Temporary reimbursement with a specific requirement for the collection and presentation of further evidence at the population level
Outcomes-based agreements	Payment is linked to outcomes achieved at the individual patient level by either requiring rebates if the therapy is unsuccessful or only paying once continued success has been demonstrated
Spread payments	Treatment cost is split into several smaller payments over a fixed period
Subscription models	Payer provides manufacturer with a fixed revenue regardless of actual volume used
Expenditure cap	Fixed amount that total spending on the medicine cannot exceed, such as by requiring the company to pay back excess sales revenue

Innovative payment models are widely considered to be an important option that is necessary for supporting patient access to ATMPs

Payers, health-technology developers and patients organisations from around the world are increasingly recognising the benefits of innovative payment models for improving access to ATMPs.[77] In fact, innovative payment models have now been used to support access to ATMPs in many countries (a selection of which are shown in figure 5), and it has been reported that, in Europe at least, innovative contracts are now discussed in nearly all negotiations undertaken in European countries for ATMPs.[78]

One notable European healthcare system where there has been significant use of innovative payment models is Italy. Specifically, Italy has had extensive experience with outcomes-based reimbursement implemented through AIFA's registry platform, which has been the main enabler of managed-entry agreements for a multitude of both ATMP and non-ATMP treatments.[79] In total, five of the first six reimbursed ATMPs in Italy used outcomes-based agreements.[-] For example, in the case of the CAR-T cell therapy tisagenlecleucel, payments are split over three separate instalments: one after 45 days if the patient is still alive, the second after six months if the patient remains alive and progression free, and a final payment after 12 months assuming no progression or death.[80] These agreements are generally proposed during the negotiation with AIFA – for example, AIFA might require an outcomes-based agreement on condition of a higher price – but in several cases the company entered the negotiations with a proposal for a managed-entry agreement.[81]

Significantly, the perception of payers in Italy is that the motivation behind the AIFA registry platform was not to generate financial savings for the health system, but to make reimbursement of certain therapies possible.[82] Indeed, considering the challenges with assessing ATMPs under routine approaches in many countries, this case study points to a wider finding that there are cases where patient access has only been possible through the implementation of an innovative contract. For example, in Spain there is only one standardised HTA pathway, and so innovative reimbursement approaches have been the only mechanism for bringing some of these medicines to market.

Given these potential benefits, there is increasing agreement in several countries between different stakeholders – including payers, patients and the industry – on the importance of being open to innovative payment models. Notably, this view was formally codified in France in 2021: the Accord-cadre (2021) agreement between the pharmaceutical industry association (Les Enterprises Du Médicament) and the pricing committee (CEPS) stipulates the use of payment models if certain conditions apply.[83] These can be proposed by the Transparency Committee or the manufacturer if there is uncertainty in the clinical evidence that can be addressed through such a contract.

In addition to enabling patient access to ATMPs, payers also recognise that innovative payment models can alleviate some of the administrative burden on healthcare authorities. This is especially the case if a full HTA is required both on entry into and on exit from managed access, as is the case in England. For example, in South Korea, the government has implemented cost-effectiveness analysis exemptions on entry into a risk-sharing agreement for certain treatments in the context of high unmet need. This approach was applied to the gene therapy tisagenlecleucel, which will have its cost-effectiveness evaluated after four years of collecting additional data, and in an agreement that was considered essential for providing access to patients in South Korea.[84]

Figure 5: Example countries where innovative payment models have been used for ATMPs[85,86,87]

US
Outcomes-based agreements and subscription models

Netherlands
Pay-for-performance for a gene therapy

Germany
Outcomes-based rebates linked to individual patient data

Spain
Payment by results with data collected through Valtermed registry

Denmark
Outcomes-based agreement for a gene therapy

Italy
Payment at results and payment by results enabled by AIFA registries

France
Coverage with evidence development with annual health technology reassessments

Belgium
Pay-for-performance with spread payments for CAR-T therapy

South Korea
Cost-effectiveness exemptions alongside outcomes-based risk-sharing agreement

Originator companies and payers value flexibility in the establishment of innovative payment models for ATMPs

International experiences with innovative payment models suggest that they are most beneficial for patient access when there is flexibility in how they are established, how it happens and on what terms, from both payers and the ATMP developers. In Italy, for example, an innovative payment model can be proposed by either the originator company or AIFA, generally at some point during the negotiation. However, there have also been some cases where an innovative payment model was suggested at the outset by the manufacturer.[88] Furthermore, in 2020 AIFA updated its pricing and reimbursement dossier guidelines to explicitly invite manufacturers to outline proposals for MEAs, including a list of several financial-based and outcomes-based MEAs to choose.[89] While there have been discussions about reducing the use of outcome-based MEAs, given their administrative complexity, it has also been recognised that they are one of the best payment options for ATMPs, and the use of these outcome-based payments models is continuing for these products.

The Italian case study illustrates a broader point: formally codifying opportunities to propose an innovative payment model is not incompatible with flexibility in the form that such a contract can take. For example, in Belgium the relevant legislation (Article 81) explicitly describes the potential role for managed-entry agreements, but there is sufficient flexibility in the legislation for any kind of innovative contract to be implemented in practice.[90] As noted below, flexibility in the process for negotiating an innovative payment model and in the form that such models will take will likely become increasingly important as new types of innovative payment model are needed to account for the changing characteristics of ATMPs being developed. This perspective on the potential benefits of innovative payment models also stands in stark contrast to the UK: while in the UK a simple discount is taken as an assumed starting point, in countries such as Italy contracts like outcomes-based agreements have been actively encouraged by payers.

Successful implementation of innovative payment models requires appropriate infrastructure

The experience of other countries demonstrates that willingness from payers and manufacturers to implement innovative payment models is only impactful if there are the necessary wider frameworks and infrastructure in place to implement them. The two main perceived challenges in the UK reflect those that almost all other countries have had to address in some way to support patient access: ensuring that accounting and budgetary regulations permit appropriate innovative payment models and having infrastructure in place to collect the data needed to implement certain types of contract (such as outcomes-based agreements).

The first of these issues is frequently attributed to national and EU-level accounting regulations acting as a barrier to innovative payment models. Specifically, it is often said that compliance with the European System of Accounts is an issue for spread payment or annuity-based funding opportunities, which separate the treatment cost into multiple payments.[91] Additional hurdles can also arise from national-level laws. National trade associations – both the ABPI in the UK and several of its European counterparts – have repeatedly sought clarity from national authorities on what is possible under existing regulations. While in most countries it is understood that accounting rules have not been the main obstacle to the agreement of an innovative contract,[92] in England it is perceived that the Treasury rules prevent the cost of a medicine being spread over multiple years if it is delivered in a single upfront dose. Our case studies provided several different approaches to how this issue may be resolved. Some of these were in the direct context of ATMP innovative payment models, while others were tied to broader financial reforms:

- **Adaptation of budget cycles to enable spread payments:** the NHS Finances (Wales) Act 2014 introduced the possibility of health boards using three-year rather than annual budget periods, with the objective of supporting longer-term decisions.[93]
- **Clarification on the types of spread payments that are and are not possible:** in Belgium, the trade association pharma.be clarified with the Ministry of Finance that spread payments were entirely possible as long as there was an aspect of uncertainty associated with the agreement.[94,95]
- **Commitment to implementing necessary legal changes:** in France, the Accord-cadre (2021) specifically mentions payment in instalments as an option to address uncertainties associated with ATMPs. This option would be implemented once necessary legislative and regulatory changes had been made.[96]

The other key issue for the successful implementation of some innovative payment models is the infrastructure and systems needed to monitor usage of medicines. This is because many innovative payment models require the monitoring of patients following the delivery of an ATMP. This is most clearly the case for outcomes-based agreements, such as payment by results or payment at results, but could also include less complex models that do not require tracking individual patient data, such as those linked to overall usage of the medicine or healthcare costs. There are some challenges in adopting the necessary infrastructures and collecting these patient data, including ethical concerns about the use of patient-sensitive information. While these payment models may not be justified where other options are available, ATMPs may represent an exception where outcome-based agreements could be valuable. As noted above, Spain and Italy provide two examples of where a single system can enable systematic data collection on ATMPs. Although payers recognised that the registry system can add to the administrative burden for healthcare providers – and therefore emphasised the importance of managing the burden on physicians in terms of data collection – ultimately these payment models have been required for enabling patient access to ATMPs, and so identifying how the administrative requirements could be overcome was highly beneficial.[97]

However, there are several broader implications from the case studies on how to improve data collection for ATMPs. Specifically, healthcare providers must be sufficiently incentivised and resourced to carry out the requisite data collection. In Spain, for example, entering data into Valtermed is a requirement for reimbursement for the medicine, and additionally some hospitals are supported by a dedicated data manager to alleviate the administrative burden on physicians.[98] Likewise, in Italy, if an AIFA registry is running, healthcare providers must enter the data into the registry before they can prescribe the therapy or obtain reimbursement.[99]

In the UK, there has been some recognition from both the industry and in academic literature that improved data capabilities will be essential for the UK to improve patient access, such as through using real-world evidence for outcomes-based agreements.[100,101] In fact, data infrastructure is already in place, to an extent, for routine collection of oncology data, with the National Cancer Registration and Analysis Service, including the Systemic Anti-Cancer Therapy (SACT) database in England (although this is not expected to be an entirely sufficient database to support outcomes-based agreements).[102] Key issues include ensuring that robust data governance can maintain compliance with legal, privacy and security controls on data usage, and improving consistency in the quality and quantity of data collection between different therapy areas. While a full consideration of data governance issues is beyond the scope of this report, it can at least be concluded from the international case studies that the option of innovative payment models that can use real-world evidence can be highly impactful for addressing evidence uncertainties, and that in other countries the barriers to data collection infrastructure have not been insurmountable.

Payers expect the need for innovative payment models to evolve as the ATMP pipeline changes

Due to the future evolution of the ATMP pipeline, payers from other countries expect that the ways in which innovative payment models are used will also need to change. This is likely to include new types of innovative payment models to account for the changing characteristics of ATMPs, as well as new considerations as to the respective role of routine alongside more innovative access approaches.

First, as experience and evidence of ATMPs continues to broaden, payers expect that many ATMPs will not require an innovative approach to enabling patient access, at least in terms of managing evidence uncertainties. This is because payers will likely become more confident in the long-term benefits of ATMP treatment once certain mechanisms of action and treatment types become better established. This trend is already underway to a degree in the US, where payers are reverting from outcomes-based contracts for CAR-T therapies to simpler financial contracts.[103]

However, as previously noted, the ATMP pipeline will also generate a wide range of therapy types – ones that have different mechanisms of action and target different types of diseases – which existing innovative payment models may not suit. One of the key findings of the external interviews was that payers from most countries acknowledge gaps in the types of contract that have been used to date. While the appropriateness of different models will vary depending on the specifics of the product at hand, payers suggested several types of innovative payment models that could be valuable in addressing the challenges associated with the changing characteristics of future ATMPs:

1. **Subscription models for ATMPs in non-rare diseases:** in non-rare diseases, the greatest concern is likely to be the budget impact volatility over time due to patient eligibility, and so payers would welcome a contract that fixes their annual payments to the developer regardless of the number of patients treated.
2. **Cost-based outcomes-based agreements for ATMPs that slow disease progression:** outcomes-based agreements could have wider applications by using a broader range of outcomes to reflect the different types of ATMP in the pipeline. For example, patient healthcare costs could be used to address uncertainties over the long-term cost savings that ATMPs generate for payers.
3. **Treatment switch coverage for ATMPs positioned where there are already therapeutic alternatives available:** as ATMPs move into areas where there are treatment alternatives, payers may be required to fund additional treatments if there is insufficient success with the ATMP. To account for this, the manufacturer could contribute to the treatment costs if patients need to be moved on to a different treatment.

All these payment models have already been used in other countries, though not all for ATMPs. In fact, some of these agreement types have already been used in the UK for other types of therapy. For example, NHSE negotiated a deal with no cap on patient numbers to provide access to a company's cystic fibrosis portfolio.[104] However, it is not surprising that payers suggested non-ATMPs agreements could provide lessons for the ATMP pipeline, considering the new characteristics that it will present. Examples of the use of these payment models are shown in table 3.

Table 3: Case studies of payment model types

	Payment model	Case study	Details
1	Subscription model	 US insurer providing unlimited access to ATMPs	Health plans and employers can pay a per-member monthly fee for unlimited access to certain ATMPs[105]
2	Cost-based outcomes-based agreements	 US insurers using both health and cost outcomes in a diabetes outcomes-based agreement	Increasing rebate payments were required if the total cost of care was greater for the group not receiving the medicine[106]
3	Treatment switch coverage	 Multiple sclerosis therapy developer pays additional costs if patients switch treatment	In the event of insufficient success with their treatment, the developer covers additional costs if patients are switched to another therapy[107]

Innovative payment models must be complementary to rather than a substitute for routine access approaches

Although the key debates in other countries have focused on the potential role for innovative payment models, it is important to note that they should be seen as an enabler of patient access alongside the routine market-access pathways that are also in place. In other words, innovative payment models must be complementary to market-access pathways that can address the distinct characteristics of ATMPs, rather than acting as a substitute for them.

As noted above, one of the key challenges in the UK is that the NICE discount rate means the long-term health benefits of ATMPs are not fully captured. The suitability of the 3.5 per cent discount rate has been discussed extensively, reflecting a key methodological debate that many HTA bodies have been engaging with. In several countries, discount rates have been periodically revised downwards, reflecting evolving HTA academic best-practice developments, changing economic conditions and increased value being placed on investing in long-term health benefits.[108] For example, in Canada the discount rate used for the base case analysis was reduced from 5 per cent to 1.5 per cent in 2017, with a recommendation that additional scenarios can be assessed using discount rates of 0 per cent and 3 per cent.[109]

Although most countries discount costs and health effects at the same rate, there is an increased trend internationally towards differential discounting, which places greater value on future health benefits than the costs of achieving them.[110] For example, in Belgium future costs are discounted at a rate of 3 per cent, and future benefits at a rate of 1.5 per cent. While not justified with reference to ATMPs specifically, the rationale for this is to avoid overly strong penalisation of interventions that generate most of their benefits in the future, such as vaccinations. A similar logic could be applied to ATMPs considering their potentially life-long benefits for patients.

4. Recommendations for the UK

Despite the progress made so far in some areas – such as supporting access to some ultra-rare and oncologic therapies and launching initiatives to support treatment infrastructure – the ATMP ecosystem is still developing, and there is much more to do to ensure that patients in the UK will be able to access the number and variety of ATMPs expected to become available in the coming years. Although there is no single country that is fully prepared to address the anticipated challenges posed by the ATMP pipeline, some of the systems and pathways already in place are more 'futureproof' than others and have addressed challenges that are likely to come to the fore in the coming years, and which remain unresolved in the UK at this time. As such, the international cases studies provide several key lessons to inform how the UK decides to build on progress made to date to improve the future readiness of its access environment.

Access and uptake recommendations

1. **NICE should utilise the existing flexibility to apply the 1.5 per cent discount rate for ATMPs to ensure its appraisal process does not disadvantage future innovative treatments with long-term benefits, including many ATMPs.**

   As the number of ATMPs launching in the UK increases, it will be crucial for routine and more flexible assessment pathways to complement one another. However, there are several challenges with the NICE STA process for ATMPs, and a particular risk that several ATMPs will never be appropriately valued due to a discount rate of 3.5 per cent that does not reflect the long-term benefits of treatment with these therapy types. Therefore, NICE appraisals should reflect evolving HTA academic best-practice developments and ensure that the existing flexibility to apply the 1.5 per cent discount rate is implemented in practice where long-term benefits are expected, bringing it in line with the Treasury Green Book guidance.

   In its 2022 revised methods and processes manual, NICE introduced changes to allow flexibility in cases where it is particularly difficult to generate evidence, including "where the new treatment is innovative or complex", which would likely apply to many ATMPs.[111] However, to date this has not been significantly put into action. For example, at least two companies have made a case for the 1.5 per cent discount rate to be applied, which have not been granted.[112] As the number and diversity of future ATMPs increases, ensuring that this provision is implemented in practice will become increasingly important for adequate recognition of the value of these treatments.

2. NHSE and NICE should work with industry to accelerate the implementation of a Rapid Entry to Managed Access process by using ATMPs to pilot new approaches.

Although NICE has had some important success stories of delivering patient access to ATMPs (such as through the CDF), both the CDF and IMF require a full HTA on entry into and on exit from managed access. As more ATMPs launch in the UK, the burden on NICE and other stakeholders involved in technology appraisals will increase, risking delays in patient access. Approaches for streamlining this duplicated requirement, such as recognising the need for alternative approaches to value assessment on entry into managed access, would both alleviate the resource burden for NICE and accelerate patient access. For example, the case study of South Korea providing cost-effectiveness exemptions on entry into managed access illustrates how flexibility in assessment methods can be used to accelerate access if accompanied by full assessment once additional evidence has been generated during the managed-access period.

NICE and NHSE are already working to understand how REMA approaches could be used to enable earlier patient access. ATMPs would be suitable candidates for a pilot to explore these new approaches, similar to the 2024 VPAG commitment to pilot innovative payment models. This would not only support access to ATMPs, but also have potential implications for how similar approaches could be applied to other innovative health technologies in the longer term.

As NICE continues to investigate other opportunities to address complex HTA challenges, it may also need to consider the exit process for transitioning from managed access to routine commissioning. For example, there may be opportunities to streamline this transition in some circumstances, such as if certain pre-specified outcomes are attained.

3. NHSE should ensure timely preparation for the launch of new ATMPs by being open to discussions with companies on the potential role for innovative payment models prior to marketing authorisation.

In the future, a range of innovative payment-model types will be needed to account for the new characteristics and increased variety of the ATMP pipeline. Although NHSE already offers engagement with health technology developers, the specific issue of innovative payment models is often not discussed until during the NICE process. In many cases this is too late to avoid delays in patient access if a more innovative contract is needed. NHSE should align with the relevant company earlier on the challenge facing a particular ATMP and the range of alternative options that might be investigated, rather than assuming a simple commercial discount is the solution, which will not be appropriate for many ATMPs.

Another key issue that would improve the early advice process is greater discussion on how NHSE would use a pipeline ATMP once launched. This is because the delivery process for ATMPs can be particularly impacted by considerations around their formulation and storage once in clinical practice.

4. **NHSE should implement its commitment in the 2024 VPAG to undertake two innovative payment model pilots in a timely manner. At least one of the pilots should be for an outcomes-based agreement with payments spread over a longer contract duration than those used to date.**

   The number of ATMPs launched is already accelerating, and action to support their delivery to patients is needed urgently. To date, the UK's willingness to engage with innovative contracting has been largely limited, and NHSE has an explicit preference for simple discount agreements.[113] Yet the experience from other countries shows that greater use of innovative payment models can be mutually advantageous to all stakeholders, and ultimately be highly significant for accelerating patient access to ATMPs. For this reason, NHSE, NICE and their counterparts in the devolved nations should prepare for the coming wave of new ATMPs by enabling greater use of innovative payment models. For example, in other countries payers do not take a certain type of managed-entry agreement as the default – unlike the assumed starting point of a simple discount for NHSE. Instead, they invite manufacturers to submit proposals from a range of managed-entry options, as in the AIFA dossier guidelines, or more formally institutionalise the procedures for negotiating different types of agreement, as in Belgium's Article 81. The experience of other countries demonstrates that as these agreements are implemented more readily it becomes increasingly straightforward to negotiate them.

   For some ATMPs, uncertainty over treatment outcomes may extend for several years longer than NHSE is accustomed to. Previously, NHSE has only agreed to contracts up to seven years in length, so it is essential that accounting and budgetary rules include the possibility for contracts of longer duration than those used to date.

   Considering that NHSE recently committed in the 2024 VPAG to two innovative payment model pilots for ATMPs, it is important that the opportunities to identify more sustainable solutions for patient access are realised. Therefore, an outcomes-based agreement with spread payments over a longer contract duration than those used to date should be included in the pilots.

5. **Accounting regulations have long been identified as an issue for ATMPs, but action has not been taken to address the problem. NHSE, the DHSC and HM Treasury should explore how accounting rules can be adjusted to enable payments over multiple years.**

   While in most countries accounting regulations have been seen as a challenge to the implementation of innovative payment models, they are increasingly considered to no longer be the main barrier, and have not been a major obstacle to the agreement of innovative contracts. The UK is lagging behind in addressing this issue and should implement any necessary changes to accounting rules to enable the use of spread payments. NHSE's commitment in the 2024 VPAG to undertake two innovative payment model pilots provides an opportunity to explore amendments to accounting regulations necessary to implement the pilots.

6. **NICE should increase flexibilities in evidence requirements and adopt a more risk-neutral approach to managing uncertainty for ATMP appraisals.**

   Adoption of a risk-neutral approach with increased flexibilities in evidence requirements in the context of ATMPs will becoming increasingly important as the role of real-world evidence is expected to increase for both managed-access approaches for supporting technology appraisals and for innovative payment models that utilise patient outcomes. To enable this and address the uncertainty, NICE and NHSE should support greater consistency in data collection to facilitate NICE's continued use and acceptance of real-world data in appraisals.

7. **NHSE, NICE, the MHRA and industry should work together to establish a single national platform for collecting data on ATMP treatment outcomes that could support innovative access models.**

   In the long-term, improved capabilities for data collection will be essential if the UK is to maintain its position as a priority launch market, considering the implications for the implementation of innovative payment models. Given the nature of ATMPs, there will inevitably be questions on whether the long-term data supports the continued value of ATMPs. The learnings from other countries demonstrate that the challenges seen to date are not insurmountable, and so all stakeholders should work together to understand how future data-collection practices can be optimised. One solution would be the development of a single national platform, analogous to the AIFA registries of Italy and the Spanish Valtermed system, which enable routine use of outcomes-based agreements. This would ensure mandatory long-term data collection into patient registries and may also require appropriate resourcing of healthcare personnel for data management, such as through dedicated administrative staff (as in some Spanish hospitals).

8. **All ATMPs should be included in the NHSE Innovation Scorecard and Estimates Report to understand whether uptake is in line with NICE eligible populations. This data should be scrutinised by an action-orientated cross-sector working group with policy makers, with plans put in place to understand and address instances of lower-than-expected uptake.**

   This will help to deliver on the promise of a streamlined end-to-end pathway for ATMPs, which is vital for underpinning the attractiveness of the UK to this sector.

9. **The UK government and devolved governments should establish a coordination group for ATMPs to share learnings across the UK nations and support capacity planning and decision-making across the respective health services.**

   In each of the devolved health authorities there has been some notable progress in terms of initiatives to support access to ATMPs. For example, in Wales, the Advanced Therapies Wales programme – which is funded by the Welsh Government – has been established to provide patients with equitable access to ATMPs,[114] and there may also be greater potential for payment models that rely on spread payments due to the possibility of three-year budgets. To ensure equity across the UK, it is important for each of the devolved nations to draw learnings from both other countries and each other concerning how to ensure readiness for the ATMP pipeline. This could be enabled through the establishment of a coordination group for ATMPs. As shown by the example of the Genome UK Implementation Coordination Group,[115] a formal mechanism for collaboration between key stakeholders in each devolved nation is consistent with the devolved nature of healthcare policy and can support collaboration and maintain an equitable and quality service across the UK.

Wider pathway recommendations

10. **The UK should continue to develop ATMP manufacturing activities, including both early-stage and late-stage production and the effective targeting of research and innovation funding, as well as capitalising on the opportunity afforded by the new £520 million multi-year Life Sciences Capital Grants Facility.**

    This will help to secure future larger manufacturing operations and maintain the 'sticky', high-value ATMP manufacturing jobs that have been created.

11. **The government should prioritise improving the UK ecosystem for delivering commercial clinical research, which will increase the attractiveness of the UK as a preferred destination for ATMP clinical trials. This should include implementation in full and at pace of the recommendations of the O'Shaughnessy Review, and passing outstanding UK clinical trials legislation to enhance the UK's attractiveness for inward investment.**

    New clinical trials legislation is essential following the UK's exit from the European Union. However, this faced delays in the previous Parliament, causing uncertainty and enabling the UK's competitors to gain an edge in attracting R&D investment.

12. **A strengthened and refreshed Innovative Licensing and Access Pathway should offer a streamlined end-to-end pathway for ATMPs that helps align all system partners, from development to patient access. The MHRA should ensure it has the right levels of expertise and capacity to support the delivery of timely scientific advice, and clinical trial and drug licensing approvals as the evolving ATMP pipeline matures.**

    The regulatory environment is key to unlocking growth, and attracting and retaining inward investment to the UK.

Glossary

Term	Definition
The All Wales Medicines Strategy Group (AWMSG)	The All Wales Medicines Strategy Group advises the Welsh Government about the use, management and prescribing of medicines in Wales.
Cancer Drugs Fund (CDF)	The Cancer Drugs Fund is a source of interim funding for cancer drugs in England. The CDF provides patients with faster access to the most promising new cancer treatments and helps to ensure more value for money for taxpayers.
Department of Health and Social Care (DHSC)	UK government department responsible for policy on health and adult social care.
Discount rate	The rate at which costs and benefits that occur in the future are adjusted to present values, used in the health-economic assessment of new medicines.
Early access to medicines scheme (EAMS)	A scheme for providing people with access to medicines in the UK that have not yet received a marketing authorisation.
European Medicines Agency (EMA)	The European Medicines Agency is a decentralised agency of the EU, responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU.
Highly Specialised Technologies (HST) programme	NICE evaluations for very rare, and often very severe, diseases that need the specific considerations and flexibilities permitted by the programme. A higher QALY threshold is used for HST appraisals.
Health Technology Assessment (HTA)	An evaluation of the effectiveness and benefits of a health technology, such as a medicine. In the UK, an HTA evaluates the clinical and cost-effectiveness of a new technology in comparison with existing alternatives.
Innovative Medicines Fund (IMF)	A managed-access process used to provide patients in England with access to non-cancer medicines while further data can be collected.
Managed entry agreement (MEA)	An agreement between a payer/provider and health technology developer that enables access subject to certain conditions. These may be financial or outcomes-based conditions.
Medicines and Healthcare products Regulatory Agency (MHRA)	The MHRA regulates medicines and medical devices in the UK. The MHRA decides whether medicines should be granted licenses (also known as marketing authorisations) based on safety, quality and effectiveness data.

Term	Definition
National Cancer Registration and Analysis Service (NCRAS)	A disease registration service within the National Disease Registration Service responsible for cancer registration in England to support cancer epidemiology, public health, service monitoring and research.
NHS England (NHSE)	NHSE commissions specialised services and oversees the budget, planning, delivery and day-to-day operation of the commissioning side of the NHS in England.
National Institute for Health and Care Excellence (NICE)	NICE is an executive non-departmental public body of the Department of Health and Social Care in England, which produces evidence-based guidance on the clinical and cost-effectiveness of health technologies in England and Wales.
Rapid Entry to Managed Access (REMA)	A streamlined approach for accelerating entry of new medicines into managed access agreements such as the Innovative Medicines Fund.
Single Technology Appraisal (STA)	The assessment undertaken by NICE where a new technology (such as a medicine) is compared with standard of care for the indication of interest.
Scottish Medicines Consortium (SMC)	The SMC provides advice to NHS Scotland about the value for patients of newly licensed medicines. Before a medicine can be prescribed routinely in Scotland, it must be accepted for use by the SMC.
Systemic Anti-Cancer Therapy data set (SACT)	Dataset curated by NCRAS (see above) that collects information on the use of systemic anti-cancer therapies across all NHS England trusts.
Voluntary scheme for branded medicines pricing, access and growth (VPAG)	A voluntary agreement between the Department of Health and Social Care, NHS England and the Association of the British Pharmaceutical Industry, which is in force for five years from January 2024. The voluntary scheme aims to promote better patient outcomes and a healthier population, support UK economic growth, and contribute to a financially sustainable NHS.

Appendix: Methodology

The research was informed by a literature review and interview programme with 10 international payer experts and covered a wide range of countries that have taken different approaches to improving access to ATMPs. Specifically, the following steps were taken for each stage of the analysis:

Pipeline analysis:

- We conducted a review of academic articles and grey literature on how the ATMP pipeline is expected to evolve in terms of the number and characteristics of therapies, both in the UK and internationally.
- Based on this review, we identified three scenarios for future growth in terms of percentage changes. These were then applied to baseline current levels of product approvals and patient numbers in the UK.
- All approvals by the EMA up to the end of 2020 – during which period the MHRA and EMA were aligned – and approvals by the MHRA between 2021 and 2023 inclusive, were used for the baseline.
- In terms of number of patients, we used an assumed baseline from the Cell and Gene Therapy Catapult.

Learnings from other countries:

Literature review

- Our primary method was in-depth secondary research of academic publications and grey literature on policies relating to ATMPs, including innovative payment models. We reviewed both cross-country literature on ATMP access and local language literature for key markets, including details of innovative payment models where available.
- A variety of search terms were used in combination, including: 'cell therapy', 'gene therapy', 'reimbursement', 'innovative payments', 'managed entry' and 'outcomes-based agreement'.
- The literature review was conducted between July and October 2023; more than 40 academic articles and more than 150 grey literature sources (including from local health authorities) were reviewed in total.
- An in-depth literature review was conducted for the following countries: Belgium, France, Germany, Italy and Spain. This was supplemented by ad-hoc research for other countries with relevant provisions in place for ATMPs, including the US and South Korea.

Interviews

- We also conducted an interview programme with 10 payer experts. The interviews focused on seven countries where there have been notable developments in supporting access to ATMPs: Belgium, France, Germany, Italy, South Korea, Spain, and the US.
- Two payer interviews were conducted for each of Germany, Italy and Spain due to the greater levels of experience in the use of innovative payment models and the anticipated learnings for the UK.
- The screening criteria for payer experts were as follows: current or former member of a payer organisation (for example, HAS in France, AIFA in Italy and the Federal Joint Committee in Germany) with direct experience with pricing and/or value assessment of at least two advanced therapeutic medical products, and prior involvement with discussions on the use of an innovative payment model for an ATMP.

Recommendations for the UK:

- Recommendations for the UK were based on an assessment of the key learnings from other countries as well as the wider literature on access to ATMPs in the UK.

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