AAC (05)

ACCELERATED ACCESS COLLABORATIVE

ADVANCED THERAPY MEDICINAL PRODUCTS (ATMPs)

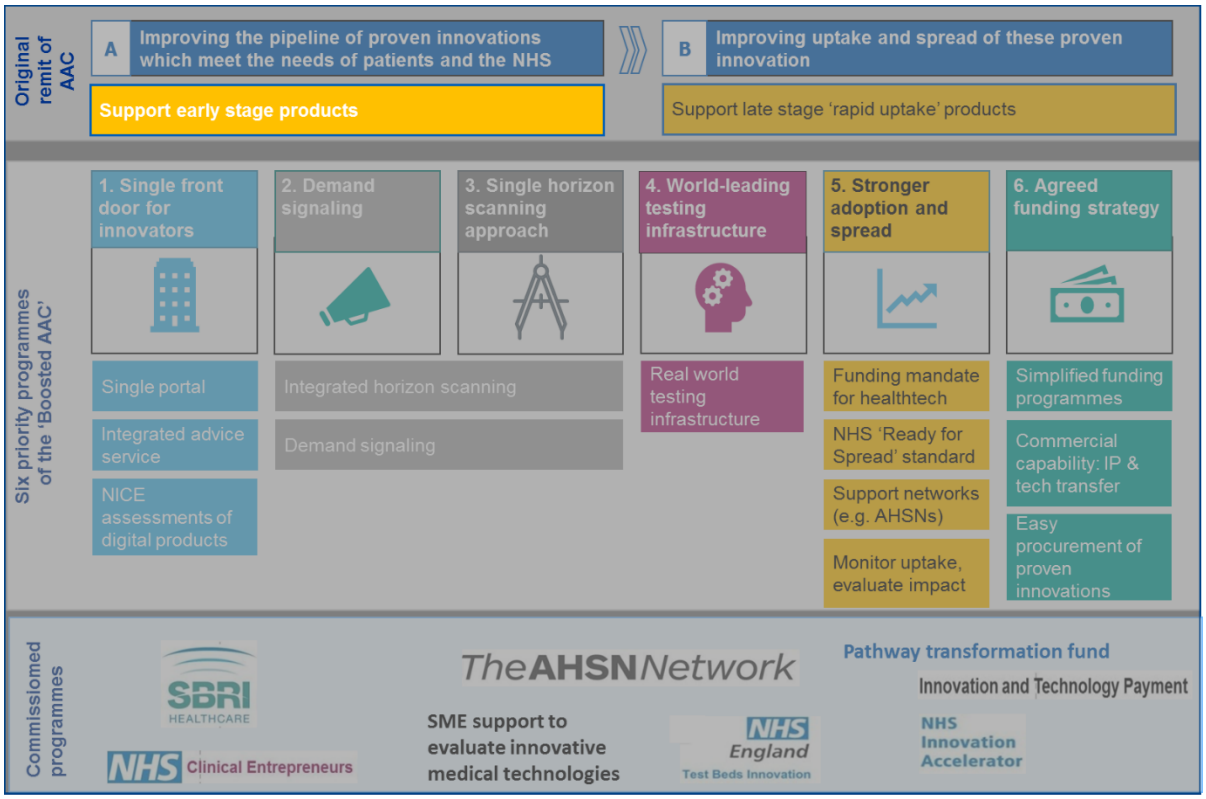
Executive summary

- At the meeting in June, the AAC Board agreed to prioritise advanced therapy medicinal products (ATMPs) for early stage support.
- These early-stage products face a number of barriers to adoption which can be supported by the AAC and its partners, with an opportunity to learn from our experience delivering CAR T, which has been considered exemplary.
- Eight workstreams have been identified for collaborative action:
    - Workstream 1 proposes to **engage with patients and the public**, so they can contribute to discussions on a product-specific basis;
    - To speed up regulatory approvals and manage the NHS' capacity for licensing, the next three workstreams propose to: (2) streamline horizon scanning so that **the same data** can be used across planning, appraisal, commercial discussions and service planning; (3) develop a map of system roles and responsibilities which **outlines the existing support available** to ATMPs; (4) test options for regulation including **possible standardisation** of product specifications, clinical trial design and manufacturing.
    - To address barriers associated with **uncertain evidence** which may lead to ATMPs not being able to prove clinical/cost-effectiveness or getting conditional approval, partners see an opportunity in collection of 'real world data'. Workstream 5 focuses on identification of common requirements to **secure clinical registry capacity and access**.
    - To address challenges for NICE's health technology assessment associated with **high upfront costs and potential extended accrual of benefits** over many years, Workstream 6 proposes that AAC partners **support NICE's review of its methods** with potential use of ATMPs as an exemplar.
    - To support management of potential risks to the NHS related to affordability, compounded by clinical benefit uncertainty, Workstream 7 focuses on **exploration of reimbursement approaches**, linked to real-world data.
    - To address service and infrastructure barriers to sustained uptake, Workstream 8 focuses on **pathway preparedness** from diagnosis through delivery
- **The AAC Board is asked to:**

- **Consider whether the key issues for ATMPs have been identified; and**
- **Approve the establishment of the ATMP Accelerated Access workstreams as outlined above.**

- The next step is to develop a more detailed operational plan to update the Board on progress in March 2020.

Position of this work within the remit of the AAC



Background

1. Advanced Therapy Medicinal Products (ATMPs) change the relationship between drug treatments and clinical services. This change increases the importance of partnership working with patients, clinicians, providers, commissioners, the pharmaceutical industry and others coming together to support discovery, development and adoption.

2. In the NHS in England, there is strong support for the introduction of ATMPs where they offer significant potential health benefit. Partnership working has been working well, with the Accelerated Access Collaborative providing further opportunity to bring together key partners. However, if health systems and industry are to achieve faster adoption of the most promising ATMPs, it will require a scale up of collaborative efforts to overcome the implementation challenges.

3. The experience of introducing CAR T has demonstrated that issues related to planning, preparing and providing for adoption of clinically and cost-effective ATMPs are not

unique to individual products. However, it cannot be assumed that the approach developed for CAR-T will apply to all other ATMPs. Some products may be more straightforward to implement in the NHS, and others may need significant changes to patient pathways, with implications for staffing, training and infrastructure.

4. Key issues that partners and stakeholders have raised in relation to ATMP adoption fall into five themes, which are set out in this paper:

    - Patient involvement and communication
    - Regulatory procedures, approval times and the pace of innovation
    - Data and dealing with uncertainty
    - Cost effectiveness assessment, affordability and reimbursement options
    - Service and infrastructure requirements

What the NHS has done and learnt so far

5. The NHS led the world in providing patient access to CAR T cell therapy just weeks after the products received marketing authorisation, following appraisal by NICE and agreement of a commercial deal. The Association of the British Pharmaceutical Industry (ABPI) and the Cell and Gene Therapy Catapult (CGT Catapult) have publicly stated that the NHS's introduction of CAR T cell therapy has been an exemplar in the way health systems can help accelerate the rate of adoption of cost effective ATMPs and that the NHS is world leading in this regard.

6. NHS England and Improvement (NHSE/NHSI) took a proactive partnership approach to the introduction of ATMPs. During the first year of implementation, lessons learnt sessions were held which reiterated the need for proactive engagement, timely communication, clear NHS input into the NICE value assessment and joined up working within the NHS. These lessons have been informing preparatory work for subsequent ATMPs.

7. The AAC has a mandate for accelerating the adoption of promising products which are early stage (pre-NICE approval) and late-stage (post-NICE approval). There are ATMP innovations in the pipeline that represent opportunities for patients and the NHS. The system may not yet be ready for these innovations for a range of reasons, including complex regulation, disruptive care pathways or limited capacity for real world testing.

Issues and Proposed Collaborative AAC Action on ATMPs

Patient involvement and communication

8. Partners have raised the importance of ensuring that patient groups can contribute to discussions on the practical and emotional considerations of introducing ATMPs into the NHS, and that the wider public voice is accounted for when considering the implications for care of the population as a whole.

- **Workstream 1: Engagement with patients and communications**: We propose to establish mechanisms to ensure collaboration and engagement with relevant patient groups and other stakeholders on a product-specific basis.

Regulatory approval, the pace of innovation and NHS readiness

9. Many ATMPs are achieving early regulatory approval and licensing, indicating that regulators are content that they meet clinical and safety requirements at a relatively early stage in their life cycle. There is a general desire to speed up overall regulatory approval times and the MHRA's corporate plan[i] 2018-2023 summarised in Appendix 1 outlines their approach to support innovation and wider Government work on Life Sciences and Growth.

10. Industry feedback has highlighted a tension between the need for individual companies to ensure compliance with the requirements of multiple regulators whilst developing specific standardisation procedures required to increase the efficiency of NHS adoption.

11. Horizon scanning indicates that NICE is due to assess around 30 ATMPs by 2023. The current pipeline is detailed in Appendix 2. The analysis suggests fast follow-on of product 'upgrades' from the same supplier; multiple suppliers in the same disease areas; and the same technology applicable in a wide range of disease areas. The Food and Drug Administration (FDA) in the United States predicts that by 2025, they will be approving 10-20 cell and gene therapies a year.

12. The number of products in the pipeline raises questions about the capacity for timely licensing, value assessment, service delivery changes and post authorisation data collection to match the speed of innovation, and to avoid delays whilst making good investment decisions and enabling the NHS to secure the best deals.

13. The proposals for collaborative action in these areas include:

    - **Workstream 2: Horizon scanning:** Development of effective horizon scanning capability, functionality, content and analysis. This work is already in progress, involving NHSE&I, NICE, ABPI, CGT Catapult. The aim is to achieve a cross system integration that enables a single data feed to be used to enable planning, NICE appraisal, commercial discussions and service planning.

    - **Workstream 3: Future state ATMP collaboration:** Develop and test a map of system roles and responsibilities that clarifies support for ATMPs available to product developers, particularly in the development phase i.e. scientific support and advice from the Medicines and Healthcare Products Regulatory Agency (MHRA) and NICE.

    - **Workstream 4: Collaborative solutions for standardisation of system requirements for ATMPs:** Develop and test options of templates for specification of manufacturing requirements, labelling etc.

Data and dealing with uncertainty

14. Many ATMPs receive regulatory approval at a time when the evidence about their long-term impact is unknown or uncertain, making the assessment of the product's value more challenging.

15. This uncertainty may lead to ATMPs not being able to provide definitive evidence of long term clinical and cost-effectiveness. The most well-established conditional approvals exist for cancer indication treatments through the CDF, with over 30 indications gaining reimbursement through managed access. Managed Access Agreements have also been agreed for Highly Specialised Technologies (HSTs). As part of its current Technology Appraisal methods review, NICE is also considering how to support its committees to make decisions when faced with highly uncertain evidence.

16. Industry and other stakeholders have proposed that the ability to collect 'real world data' would help to address the evidence uncertainty and provide the NHS with a mechanism to measure whether ATMPs deliver the desired outcomes in real time. One of the requirements for collecting real world data and data on patient outcomes is the availability of high-quality clinical registries or similar types of data collection mechanisms, as well as accurate and complete data capture by clinicians to the company and payor on agreed metrics. The quality of registries in oncology is relatively good, but ATMPs will go beyond cancer, so there would be benefit in supporting the development of registries in more disease areas.

17. The proposals for collaborative action include:

    - **Workstream 5: NHS Digital and data infrastructure:** Collaboration to identify the common requirements, themes and mitigations to secure robust clinical registry capability and access and develop a shared plan for action. The systems developed should have equal coverage over cancer and non-cancer indications. The contributions of NICE, MHRA, ABPI, Cell and Gene Therapy Catapult and Advanced Therapy Treatment Centres (ATTC), as well as industry and patient groups will be key to this workstream; NHS ownership of the proposed solutions will be key.

Cost effectiveness assessment, affordability and reimbursement options

18. Some stakeholders, including industry, have noted that the high upfront costs of some ATMPs and the potential accrual of patient benefits over many years may create challenges for NICE's health technology assessment. This challenge may be particularly true for products with a one-off treatment and potentially long duration of disease modification.

19. However, while there may be enhancements needed to NICE methods, the assessment of CAR T showed that NICE's current methods could be applied. NICE's review of its methods and processes will be covering many of the issues relevant to the assessment of ATMPs, including types of evidence that are considered in assessment. AAC partners are encouraged to continue engaging in NICE's methods review, to ensure concerns about ATMPs can be considered.

20. Some stakeholders have indicated that ATMPs may present affordability challenges for the NHS, even if they are found to be cost-effective. While commercial arrangements may be considered for addressing individual products, when considered across multiple products there may be a wider affordability challenge.

21. The risk to the NHS is that multiple in-year affordability challenges may prove hard to manage at scale, compounded by the uncertainty of the clinical benefit. This risk is managed to a certain degree by the 2019 Voluntary Scheme for Branded Medicines Pricing and Access and the Statutory Scheme, which aims to control overall spend on branded medicines. However, spending at levels higher than anticipated through the life of the voluntary scheme might mean a higher than anticipated rebate from industry, and it could compromise the ability to negotiate future schemes.

22. Pharmaceutical companies may be able to share the risk of uncertain benefit, such as spreading reimbursement over several years to reflect the uncertainty. This approach could take the form of arrangements with rebates when a patient outcome is not achieved or could mean that payments only occur once patient outcomes have been achieved. The NHS may be able to consider these types of commercial arrangements where ATMPs offer best value to the NHS. Other commercial approaches might include stimulating effective competition between similar products and developing purchasing approaches focused on products offering the greatest health gains and value.

23. The proposals for collaborative action include:

    - **Workstream 6: NICE Methods Review:** AAC partners to support NICE's review of its methods and to consider implications for ATMPs. NICE to consider ATMPs as an exemplar category to stress test whether changes to NICE methods would accommodate the requirements for value assessment of highly innovative products

    - **Workstream 7: Exploration of reimbursement approaches:** NHSE&I to consider, with input from NICE Commercial Liaison and industry, potential reimbursement approaches for ATMPs in line with the commercial framework. This consideration should include ways to incorporate collection of real-world data and longer-term tracking of patient outcomes in non-cancer indications.

Service and infrastructure requirements

24. There are three main issues in preparing for and securing sustained uptake of approved ATMPs: (a) lack of clinical data about patient outcomes; (b) limited experience in implementing ATMPs in joint pathways between the NHS and industry; and (c) variation in the clinical areas and use of ATMPs.

25. The first and second relate to clarity and agreement on patient numbers, placement on the patient pathway, diagnostic requirements, and co-location. There are also longer-term implications regarding the transition away from chronic disease management models of care. The third relates to variation of manufacturing and implementation including workforce training requirements and onboarding for providers. Without collaboration ahead of value assessment, there are risks of delay to adoption

downstream. Greater consideration of implementation at development and licensing stages is required.

26. The proposals for collaborative action include:

- **Workstream 8: Pathway preparedness:** NHSE&I to lead a workstream to ensure from diagnosis to delivery, the service implementation issues are understood at category and individual product-level and from different perspectives to inform strategic thinking and planning. This will include developing a road map for early industry engagement and key information required by NHSE&I for adoption.

RECOMMENDATIONS

27. The AAC Board is asked to:

- **Consider whether the key issues for ATMPs have been identified; and**
- **Approve the establishment of the ATMP Accelerated Access workstreams as outlined above.**

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Appendix 1: MHRA Corporate Plan Summary:

Corporate Plan summary

Public health and partnerships	1	We will protect public health and promote patient safety by ensuring the safety, efficacy and quality of medicines and health care products in the UK and internationally, including:	1a:	with Government and strategic partners, we will prioritise action to deliver our statutory functions in response to the challenges of exiting the EU
			1b:	with Government and strategic partners, we will deliver our statutory functions to protect public health and ensure the safety and quality of medicines and health care products in the UK
			1c:	we will enhance our public health impact through building stronger partnerships, collaboration and engagement across the UK healthcare sector to improve clinical practice and protect public health
			1d:	we will enhance our public health impact through building stronger partnerships, collaboration and engagement including through further development of our international strategy
Enhancing innovation	2	We will support and enhance innovation and accelerate routes to market to benefit public health and be a magnet for life sciences including:	2a:	we will support innovation and growth in Life Sciences
			2b:	we will develop and deliver innovative regulatory and legislative measures including through our offer to research and clinical trials
			2c:	we will be responsive to priority areas of scientific development including new products, product types and production methods and methodologies
Proactive, robust surveillance	3	We will deliver robust proactive surveillance for medicines and medical devices to achieve measurable public health benefit including through:	•	improved use of real world data
			•	enhanced information sharing
Secure global supply chains	4	We will ensure the safe production and supply of medicines and medical devices through:	•	enhanced systems
			•	strong international partnerships
			•	educating consumers
Organisational excellence / efficiency	5	We will be an exemplar organisational excellence and efficiency:	5a:	through our operational transformation programme, we will deliver a flexible and efficient organisation able to respond effectively to market and customer requirements
			5b:	we will build staff resilience and deliver a people strategy to ensure the Agency has the skill mix to adapt to changing regulatory models across the next five years and beyond

[i] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/702075/Corporate_Plan.pdf

Appendix 2: ATMPs that may undergo NICE assessment in the next 3 years*

	Product	Company	Indication
1	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]
3	[redacted]	[redacted]	[redacted]
4	[redacted]	[redacted]	[redacted]
5	[redacted]	[redacted]	[redacted]
6	[redacted]	[redacted]	[redacted]
7	[redacted]	[redacted]	[redacted]
8	[redacted]	[redacted]	[redacted]
9	[redacted]	[redacted]	[redacted]
10	[redacted]	[redacted]	[redacted]
11	[redacted]	[redacted]	[redacted]
12	[redacted]	[redacted]	[redacted]
13	[redacted]	[redacted]	[redacted]
14	[redacted]	[redacted]	[redacted]
15	[redacted]	[redacted]	[redacted]
16	[redacted]	[redacted]	[redacted]
17	[redacted]	[redacted]	[redacted]
18	[redacted]	[redacted]	[redacted]
19	[redacted]	[redacted]	[redacted]
20	[redacted]	[redacted]	[redacted]
21	[redacted]	[redacted]	[redacted]
22	[redacted]	[redacted]	[redacted]
23	[redacted]	[redacted]	[redacted]
24	[redacted]	[redacted]	[redacted]
25	[redacted]	[redacted]	[redacted]
26	[redacted]	[redacted]	[redacted]
27	[redacted]	[redacted]	[redacted]
28	[redacted]	[redacted]	[redacted]
29	[redacted]	[redacted]	[redacted]
30	[redacted]	[redacted]	[redacted]

Note: product reviews subject to change due to volume of assessments, emerging evidence and regulatory decisions in multiple jurisdictions