Achieving Accelerated Patient Access to Cancer Care in Europe (APACE)

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Executive Summary

In recent years, the European Medicines Agency (EMA) has introduced several accelerated pathways (APs) to enable earlier access to promising therapies where there is high unmet medical need, particularly in oncology. However, while regulatory acceleration has been achieved, value assessment processes as part of Health Technology Assessment (HTA) and pricing & reimbursement (P&R) across EU member states have not changed consistently in response. National HTA and P&R processes have differing evidentiary requirements and timelines compared to regulatory approval, leading to fragmented access pathways in individual member states. As a result, patients in Europe often do not receive fast access to these treatments, and significant inconsistencies persist across countries. HTA agencies typically request more robust data than what is available at the point of accelerated regulatory approval, and flexible reimbursement and HTA models, such as risk-sharing agreements and reassessment, are underutilised. The upcoming Joint Clinical Assessment (JCA) process may support alignment, but its uptake and impact remain uncertain.

To address these challenges, the Office of Health Economics (OHE) has developed an Accelerated Patient Access to Cancer Care in Europe (APACE) framework for promising oncology treatments targeting conditions with high unmet need, that are perceived to lack mature enough evidence for traditional HTA and P&R pathways. The framework lays out the key principles and processes for the HTA and P&R components of an accelerated pathway. This framework should initially be implemented at the national level, with countries agreeing and consistently adhering to the key principles. As the EU moves toward greater harmonisation of HTA processes, the APACE framework should evolve in parallel, supporting access and evidence generation at a multi-national level. While pricing and reimbursement (P&R) decisions will remain under the authority of national payers, the intrinsic link between value assessment and P&R highlights the importance of developing core principles that can be adapted at the national level.

The APACE framework was developed through a four-phase structured engagement process conducted between November 2024 and February 2025, involving European stakeholders—including regulators, HTA bodies, payers, patient representatives, economists, and industry representatives—from six countries.

The APACE framework outlines a structured pathway for managing the uncertainty of promising treatments for oncology. Key components include:

- **Eligibility Phase:**
    - Treatments must address a condition with a significant and urgent unmet need and show promise of demonstrating effectiveness for HTA appraisal
- **Initial Assessment:**
    - HTA bodies assess expected value and scientific uncertainty. Treatments qualify for managed access if uncertainties are resolvable to an acceptable level and if expected value justifies provisional reimbursement.
    - A Data Collection Agreement (DCA) defines the studies needed to resolve specific uncertainties to an agreed upon level, with reassessment timelines.

- **Reassessment:**
    - Takes place at the agreed-upon reassessment point. If available, new evidence informs updated expected value and assessment of whether uncertainties have been resolved to an acceptable level.
    - Depending on evidence, or lack thereof, treatments may enter traditional reimbursement pathways, with either the same or an adjusted price, or are delisted.
    - Resolution mechanisms for remaining uncertainties are set out.
- **Exit Phase:**
    - Outlines conditions for entering the traditional reimbursement pathway or removal from reimbursement status, including obligations to patients and penalties for non-compliance.

There was broad support for the APACE framework among stakeholders. However, certain issues remained unresolved, including how to quantify eligibility criteria, define relevant outcomes and finalise a suitable P&R model under uncertainty. The resulting recommendations for further work and actions to progress the implementation of the framework are:

1. **Generate and agree clear eligibility criteria** – Develop measurable and balanced criteria for eligibility based on unmet needs and urgency of condition, supported by stakeholder consensus and EU-level validation.
2. **Align regulatory and HTA requirements** – Strengthen collaboration between regulators and HTA bodies to streamline eligibility and evidential standards and improve access timelines.
3. **Define relevant and feasible outcomes** – Create EU-endorsed criteria for relevant outcomes and involve patients early to capture relevant, meaningful endpoints to be used in HTA assessments.
4. **Agree on principles and methods for replicable assessments of uncertainty** – Adopt consistent methods to measure and manage evidential uncertainty in early and ongoing assessments.
5. **Strengthen national and pan-European real-world evidence infrastructure** – Enhance national data collection systems, cross-country data integration and quality to support broad, effective real-world evidence use in evaluation.
6. **Progressing implementation of alternative P&R models** – Encourage outcome-based agreements aligned with treatment value and evidence generation incentives.
7. **Creating legal enforcement mechanisms for exit process** – Introduce enforceable legal frameworks to ensure timely delisting of treatments that no longer meet APACE criteria.
8. **Define funding arrangements** – Establish dedicated short-term funds at the national level and long-term plans to sustainably finance accelerated access to ATs.
9. **Determine how APACE will integrate into EU HTA regulation (EU HTAR) processes** – Improve EU-wide alignment in terms of timelines of assessments, evidence requirements and payment models used in accelerated pathways, to ensure APACE can fit well into JCA and other EU HTAR-related processes.

The APACE framework provides a structured, stakeholder-endorsed approach to accelerating access to oncology medicines targeting unmet needs across Europe. It seeks to bridge the gaps between regulatory approval and reimbursement by enabling conditional access paired with evidence development. To realise its potential, further policy work is needed to resolve outstanding issues and ensure consistent implementation across countries.

1 Background

There are a number of programs to accelerate access to medicines in regulatory contexts in the European Union, overseen by the European Medicines Agency (EMA). These accelerated pathways (APs) include conditional marketing authorisation, accelerated assessment, exceptional circumstances, and the PRIME initiative (EMA, 2016). Most of these AP schemes are designed to provide support and/or accelerated approval to medicines targeting a condition with a "medical need for severe, life-threatening or rare diseases" when comprehensive clinical data are not available. They may also be used when early-stage trials show the potential of a substantial effect size to address "medical need". APs counted for 36% of all EMA approvals between 2018-2022, but this share has decreased since 2020 (CIRS, 2024). A much larger proportion of APs is observed in the US, where 75% of new molecules between 2018-2022 had at least one AP.

Health Technology Assessment (HTA) bodies require different types of evidence compared to the EMA's regulatory procedures, reflecting the different objectives of each process. The requirement for HTA agencies to assess comparative efficacy or cost-effectiveness can necessitate evidence that is often not feasible for medicines typically eligible for APs (now referred to as Accelerated Treatments — ATs). These challenges are especially frequent in oncology, a field where high unmet need and rapid innovation often lead to the use of APs. However, these therapies frequently face challenges in meeting traditional evidence standards at the time of approval. For example, overall survival (OS) data may be immature, and generating comparative data is difficult due to evolving standards of care and parallel development of treatments. Patient reluctance to participate in randomised trials—especially when placebo arms are involved—further limits the availability of robust evidence (Kim, Goodall & Liew, 2019).

Despite these constraints, HTA bodies may still expect conventional comparative data to justify reimbursement, without fully accounting for the unique context of oncology and ATs (Rejon-Parrilla et al., 2023). Moreover, while centralised regulatory pathways aim to speed up access, national HTA and reimbursement processes often remain misaligned, leading to inconsistencies in patient access across Europe.

This mismatch between regulatory and HTA pathways is supported by evidence on timelines. A Centre for Innovation and Regulatory Science (CIRS) report analysed rollout times of new active substances in a selection of European countries, Canada and Australia. They found that combined regulatory and HTA approval times were the same as or longer in conditional regulatory approval processes compared to non-conditional approval processes in the majority of countries analysed, with a similar effect seen when focusing on HTA timelines specifically (CIRS, 2024). This demonstrates that current APs in regulatory settings are not having the desired effect of accelerated access for patients.

These discrepancies lead to an inconsistent pathway to access for ATs across countries. Dedicated pathways exist in some countries, such as the Cancer Drugs Fund (CDF) and Innovative Medicines Fund (IMF) in England, the innovation funding or early access authorisation programme (autorisation d'accès précoce or AAP) in France, and the Innovative Medicines Fund in Italy for oncological and non-oncological medicines (NHS England, 2016, 2022; HAS, 2021; AIFA, 2024). However, these pathways are limited to a narrow set of countries, and their processes are unlikely to apply on a pan-European level. These pathways have also faced challenges in generating additional evidence and addressing uncertainties, suggesting that some of their components may need to be changed to achieve accelerated access for oncology medicines across Europe (Wiedmann, Cairns and Nolte, 2024; Trigg et al., 2023).

In addition, dynamic reimbursement models with risk-sharing arrangements that could address these challenges are not utilised in most European countries. Without such

models, payers are unlikely to enter into accelerated access agreements due to the uncertainty around the effectiveness of ATs, which increases uncertainty around their reimbursement decisions.

Finally, the developing European HTA regulation (EU HTAR) offers potential opportunities, but also complicates matters. Whilst currently, individual member states drive value assessments and reimbursement decisions, the new Joint Clinical Assessment (JCA) has the prospect of facilitating a convergence of method guidelines and evidence requirements across Europe (European Commission, 2024). However, in its initial phases of implementation, there is uncertainty around the approach each member state will adopt to incorporating JCA reports in decision-making. Therefore, any new framework for the value assessment of ATs must account for changes associated with adoption of the new EU HTAR and also build on the opportunities it offers.

The challenges associated with collecting evidence that meets current HTA standards, persistent differences in member state requirements, and lack of dynamic reimbursement models, increase the inequity of patient access to oncology medicines across the EU and provide inconsistent signals to innovators about the sort of technologies to research and develop. There is a need to develop a clear and shared policy framework for generating and assessing evidence on ATs for oncology, as well as defining the most appropriate reimbursement models to complement assessment processes. This builds on work from the Bellberry Limited international workshop, which recommended specific changes to HTA appraisal pathways and reimbursement processes for ATs (Phillips et al., 2024; Ollendorf et al., 2024).

The project Accelerated Patient Access to Cancer Care (APACE), led by the Office of Health Economics (OHE), aims to develop such a framework for accelerated access to promising treatments based on an engagement process with stakeholders. The framework and its principles should be considered by individual member state HTA agencies and payers for their national processes, and also for pan-European collaborative initiatives. Whilst the framework focuses on oncology medicines, we recognise that it has potential applications to a range of therapeutic areas that face similar challenges in terms of unmet need and evidence generation, such as rare diseases.

2 Methods

We recruited a panel of 11 European stakeholders covering the following countries: UK, Italy, Spain, Sweden, Norway and Belgium. They represented multiple stakeholder groups including HTA bodies, regulatory bodies, payers, patient organisations and health economists. Some HTA stakeholders also brought the perspective of EU HTA and other regional HTA collaborations amongst European countries. Global industry representatives were also part of the panel.

To iteratively gather the views of the panel and develop agreement around key aspects of the APACE process, we engaged the stakeholder panel in a four-phase process, undertaken between November 2024 and February 2025:

- Pre-meeting survey — to identify areas of agreement and disagreement and frame the discussion at the first virtual roundtable. It focused on the need for APACE, eligibility of treatments, evidential requirements and reimbursement processes. The survey included questions that asked participants to rate their level of agreement with statements, as well as comment boxes in which they could raise additional points.

- First virtual roundtable — to discuss the challenges of developing a framework for APACE. This involved relaying the results of the pre-meeting survey to highlight key areas of convergence and divergence of positions. The panel discussed what components should be included in a framework for APACE in light of these challenges.

- Second pre-meeting survey — to feedback on the initial framework for APACE that was developed utilising the results from the first two phases. This framework was presented to participants prior to the second virtual roundtable alongside a survey that gathered agreement on the phases of the framework and remaining areas of contention. The survey included questions that asked participants to rate their level of agreement with statements, as well as comment boxes in which they could expand further or raise additional points.

- Second virtual roundtable — to present the second survey results and discuss remaining areas of disagreement. The aim was to facilitate convergence and identify areas that would require further investigation and engagement, beyond the scope of this project.

The surveys and roundtable discussions identified areas of consensus and divergence on the key components of an accelerated access pathway for oncology medicines. Based on these insights, we developed a general APACE framework outlining the core principles and processes that should underpin APACE. Materials in the survey and roundtable were informed by desk research. Evidence from the literature also supplemented the insights from the surveys and roundtable where possible.

2.1 This report

This report presents a framework for APACE based on our findings in the literature and the stakeholder engagement process. It details the justification for each phase of the framework, as well as remaining areas of disagreement and solutions required to address these areas. Finally, it lays out the steps needed to implement such a framework.

While we recognise that other alternative access pathways exist, such as Switzerland's Article 71, which allows reimbursement of treatments that are not currently insured or even regulatorily approved (Swissmedic, 2024), we focus instead on pathways for treatments with immature clinical data that can be addressed with further evidence collection as part of an interim funding period.

3 A framework for APACE

The APACE framework is a value assessment and reimbursement process designed for ATs that show promise of demonstrating effectiveness for HTA appraisal but face substantial evidential uncertainty, making them unsuitable for traditional reimbursement pathways. To deal with this uncertainty, managed access agreements (MAAs) for treatments that meet certain criteria can be implemented, whereby manufacturers and HTA bodies/payers enter an arrangement for an AT to be reimbursed for a preset period whilst additional evidence is gathered. Movement into the traditional reimbursement pathway depends on whether initial uncertainty has been resolved through further data collection, allowing the HTA body to be sufficiently confident they are reimbursing an effective and, when applicable, a cost-effective treatment.

The framework is designed to be high-level and applicable across EU countries, despite particularities in each jurisdiction. To facilitate broad application, alignment across countries on certain processes may be required (see recommendations in section 5). Below, we outline the phases of the APACE framework and map the process in Figure 1.

The first stage is to assess whether an AT meets the **eligibility criteria** for consideration to enter the process, with criteria based on the characteristics of the condition they are treating. The three eligibility criteria are:

1. **major therapeutic gaps**, which refer to the lack of effective treatments for the disease in question.

2. **urgency of condition**, which refers to the critical and often life-threatening nature of diseases like cancer, where delays in access to treatment can significantly impact patient survival and quality of life.

3. **promise of demonstrating effectiveness for HTA appraisal**, which refers to the likelihood the treatment will generate meaningful improvements in patient outcomes sufficient for a positive HTA recommendation.

These criteria ensure that APACE is used only for treatments targeting the conditions with the greatest medical need. Where possible, the criteria should be judged by quantitative metrics, such as lack of approved treatments for major therapeutic gaps or rapid disease progression for urgency of condition. These criteria differ from the conditions for entry into managed access, which require a more comprehensive assessment of the treatment's value for money.

For eligible treatments, the next stage is an **initial assessment** to evaluate whether a treatment should enter a MAA, and the conditions under which it should do so. The initial assessment involves a full assessment of the expected value of the treatment by the HTA body, as well as an assessment of the scientific uncertainties that remain. The AT enters the MAA if it satisfies the following conditions:

- It has scientific uncertainties that are too significant for traditional reimbursement processes to address.

- It has scientific uncertainties that are, however, resolvable to a satisfactory level during a reasonable period of managed access.

- It has a high likelihood of being value for money to the payer based on an initial payer assessment of expected value and a confidential price, which is acceptable to both the payer and manufacturer.

During initial assessment, a data collection agreement (DCA) should be created, setting out what type of evidence should be collected and paid for by the manufacturer to address key uncertainties, and when the reassessment period should take place. The DCA should be designed and agreed upon by both the payer and manufacturer.

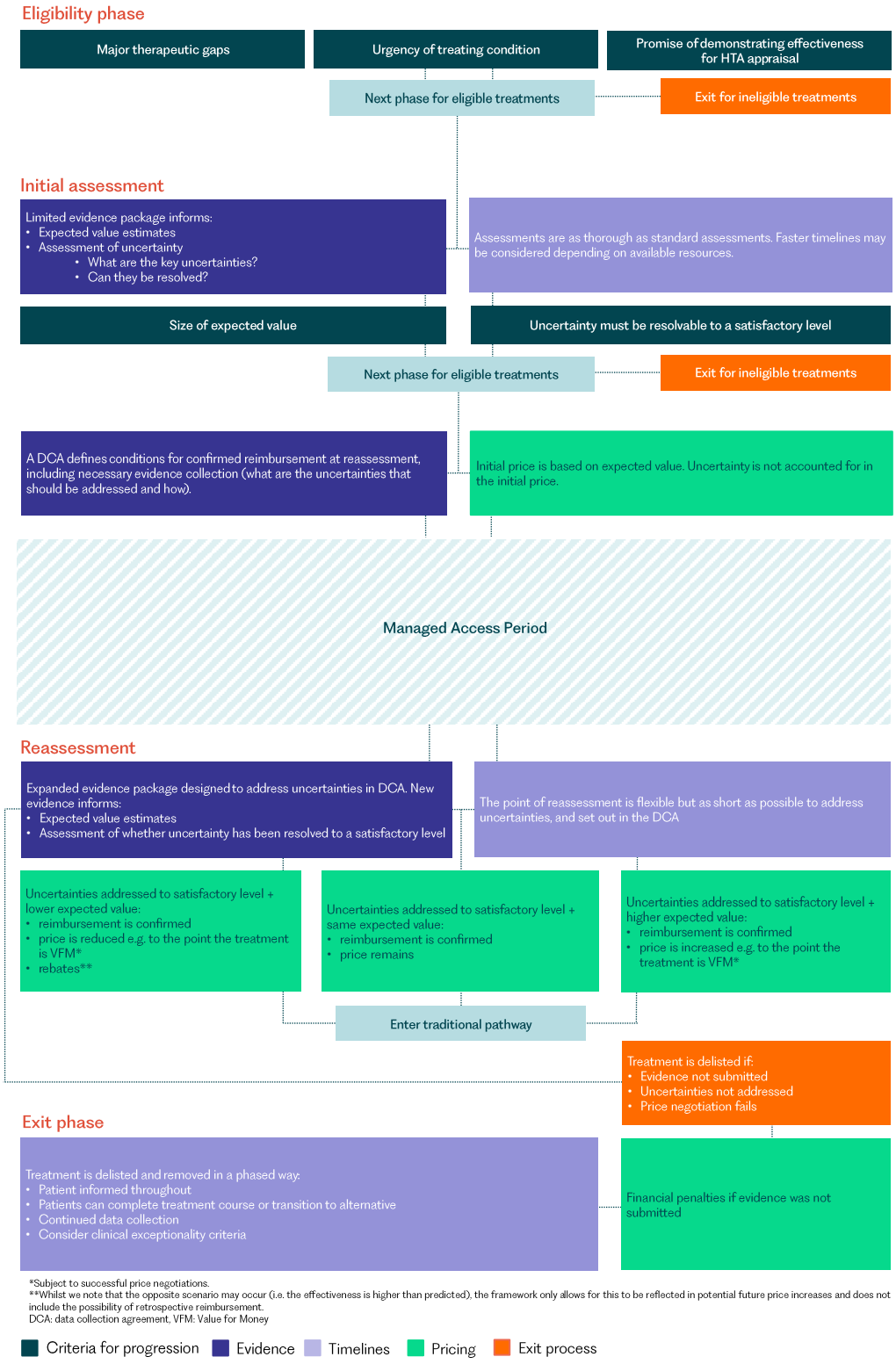
The **reassessment** takes place at a point in time stated in the DCA. It evaluates whether the uncertainties set out in the DCA have been addressed to a satisfactory level and whether new evidence changes the assessment of expected value. If uncertainties have been sufficiently addressed, the confidential price may be adjusted up or down depending on the change in expected value. Such price adjustments are conditional on successful negotiations between payer and manufacturer.

Payment models can vary depending on the AT and condition under question and can include rebates or outcome-based agreements.

The **exit phase** details the process of leaving the accelerated access pathway. If reimbursement is confirmed and the price is successfully negotiated, the AT exits the process and enters the traditional reimbursement pathway. However, the AT may also be delisted in the cases where evidence is not submitted, fails to address uncertainties, or price negotiation fails. When an AT is delisted:

- clinicians are recommended not to prescribe new courses of the AT.
- patients on the AT are informed about reasons for delisting.
- patients can be allowed to complete their course of the AT, paid for by the manufacturer, or are transitioned to a safe alternative.
- patients remaining on the AT are monitored to gather data on the safety and efficacy until the course of therapy is complete.
- payers will consider if individual patients should remain eligible under clinical exceptionality criteria at the payer's expense and without any data collection requirements for the manufacturer.
- financial penalties will be levied on manufacturers who fail to submit evidence within the agreed upon timelines, in line with the value of the uncertainty the evidence was intended to address. This will involve a discount on the prices paid by payers during the managed access period.

Figure 11 A framework for APACE

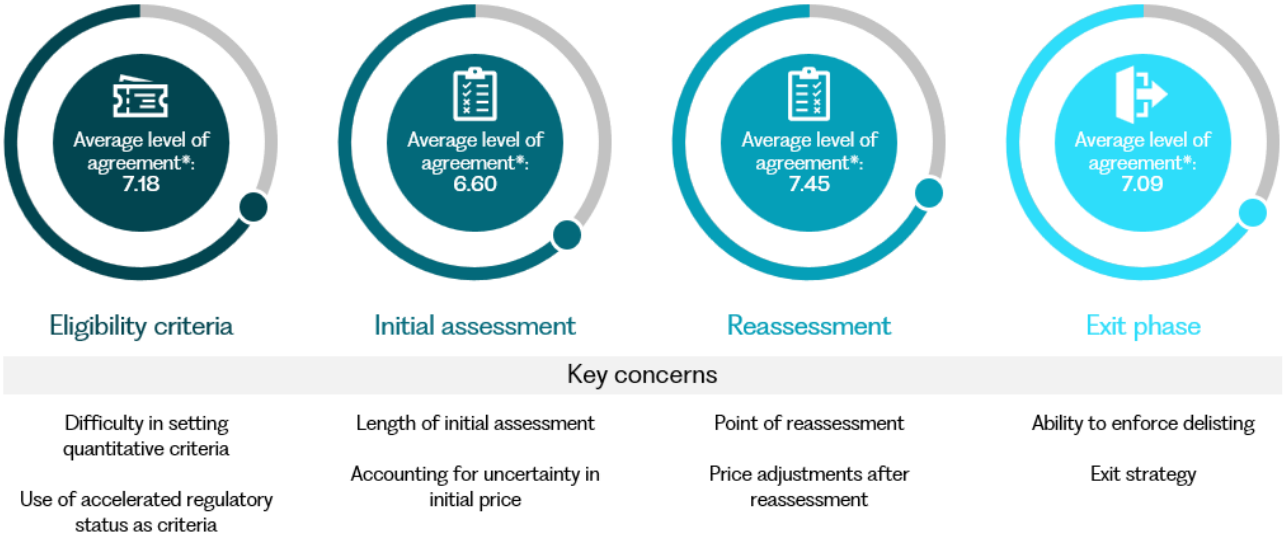


Some countries have already implemented similar frameworks to the APACE proposal, with notable examples in England, France and Italy (NHS England, 2016, 2022; HAS, 2021; AIFA, 2024). Moreover, the World Health Organisation's (WHO) Novel Medicines Platform has been developed to improve affordable and equitable patient access to novel high-cost medicines in the European region, which includes developing principles for their payment, pricing, HTA and reimbursement (WHO, 2023). The APACE framework aims to reflect this growing focus on accelerated access to these medicines. It brings a consistent approach for an accelerated pathway across Europe to minimise market fragmentation and can inform improvements in countries where similar pathways have been introduced.

4 Stakeholder perspectives

This section includes an overview of the level of agreement and key discussions on individual APACE phases from the stakeholder engagement process. Supporting literature is provided for some of the viewpoints where applicable.

Figure 22 Summary of stakeholder engagements for each phase of the framework



**Participants were asked 'To what extent do you agree with the principles outlined for this phase of the framework?' where 1 = strongly disagree, 5 = neither agree nor disagree and 9 = strongly agree*

4.1 Eligibility phase

Eligibility criteria refer to the conditions for a treatment to proceed to the initial assessment and become an AT. Additional entry criteria for entering the managed access period and temporary reimbursement are discussed in the assessment phase.

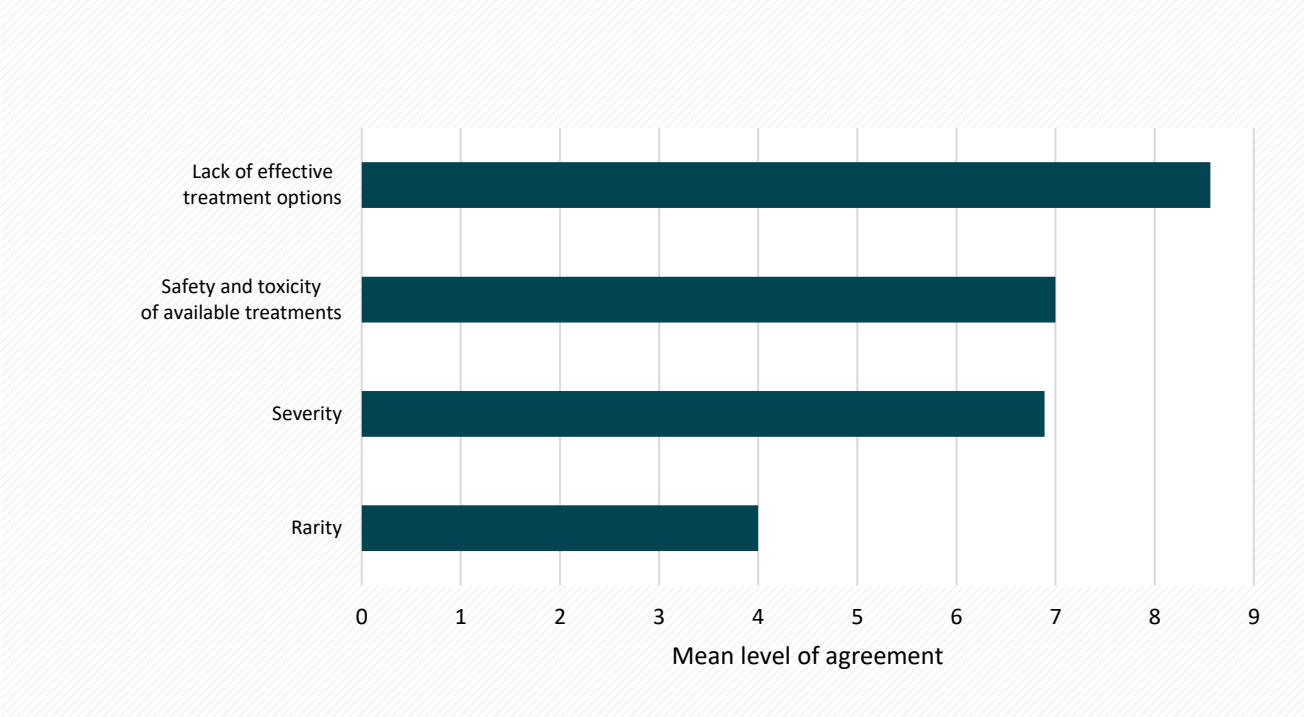
There was strong agreement with the suggested eligibility criteria (see Figure 22). The term "entry" has been updated to "eligibility" to clarify that meeting these criteria allows a treatment to be considered for managed access—not to automatically enter a period of managed access.

What should the eligibility criteria be?

Defining clear eligibility criteria is a crucial component of the APACE framework, ensuring only a limited number of treatments with specific characteristics enter. Unmet clinical need was widely considered to be the most important eligibility criterion by participants. However, it was noted the lack of a common definition of unmet need and different interpretations across stakeholders can lead to inconsistency in decision-making across countries and between HTA bodies and regulators.

Some stakeholders suggested broad definitions of unmet need should be used, encapsulating patient-centric factors such as treatment convenience. However, others warned overly broad definitions could dilute resources and create inefficiencies, as treatments that were not a priority for accelerated access use the limited resources available for such schemes. We explored more targeted definitions of unmet need during the roundtable discussions and surveys.

Figure 3 Level of agreement for unmet need dimensions



**Participants were asked to rate level of agreement for each dimension, where 1 = strongly disagree, 5 = neither agree nor disagree and 9 = strongly agree. The mean level of agreement for each dimension was then calculated.*

Lack of effective treatment options was considered the most important dimension of unmet need by participants, followed by safety and toxicity of available treatments (see Figure 3). To encapsulate both dimensions of current treatment shortfall, the first of our eligibility criteria was named 'major therapeutic gaps'. This definition aligns with previous attempts to define unmet need in the literature, as well as the French eligibility criteria for early access programmes (Farmer et al., 2023; BlueReg Group, 2025). Participants also noted the importance of clearly identifying what constitutes an alternative treatment when assessing such criteria.

Another eligibility criterion suggested was urgency of the condition, to ensure that early access is granted to treatments for severe conditions with irreversible effects, particularly when there are no viable treatment alternatives (as captured in the unmet need criterion). In these cases, the costs of no treatment are substantial and speed of access to potentially effective treatments is particularly important.

The final criterion proposed by participants was promise of effectiveness, ensuring the treatment has the potential to address this unmet need or urgent condition. This criterion aligns with the 'improvement in clinical outcomes' criterion in EMA's PRIME scheme, in which medicines should impact the prevention, onset or duration of a given condition or

improve the morbidity or mortality of the disease (EMA, 2015). PRIME helps manufacturers targeting accelerated regulatory assessment. Alignment between regulatory criteria for accelerated approvals and those set in the APACE framework should be pursued to ensure there is a consistent and efficient access pathway for ATs, within the limits of the different aims of the two processes. In practice, treatments must show promising effectiveness through early clinical evidence that suggests a meaningful impact on desired outcomes, providing a signal strong enough to justify APACE consideration. Whether this criterion is met will depend on the specific context and how it aligns with the other two criteria, with expert judgment guiding the final decision. The number of treatments advancing to initial assessment will also depend on the funding available for implementing APACE and, accordingly, the strictness of this criterion may vary.

Participants did not support the inclusion of an accelerated regulatory approval alone as a criterion for consideration for APACE, given the remaining discrepancies between regulatory and HTA perspectives. As a result, this was removed when finalising the framework. Whilst some of the criteria align with the EMA's regulatory priority medicines (PRIME) scheme, such as unmet need and major therapeutic advantage, there is no explicit mention of *urgency of the condition* in PRIME. Furthermore, regulatory criteria were deemed too vague in their definitions, something addressed in the next subsection. Convergence between regulatory and HTA eligibility criteria is desirable in the long run in order to streamline processes.

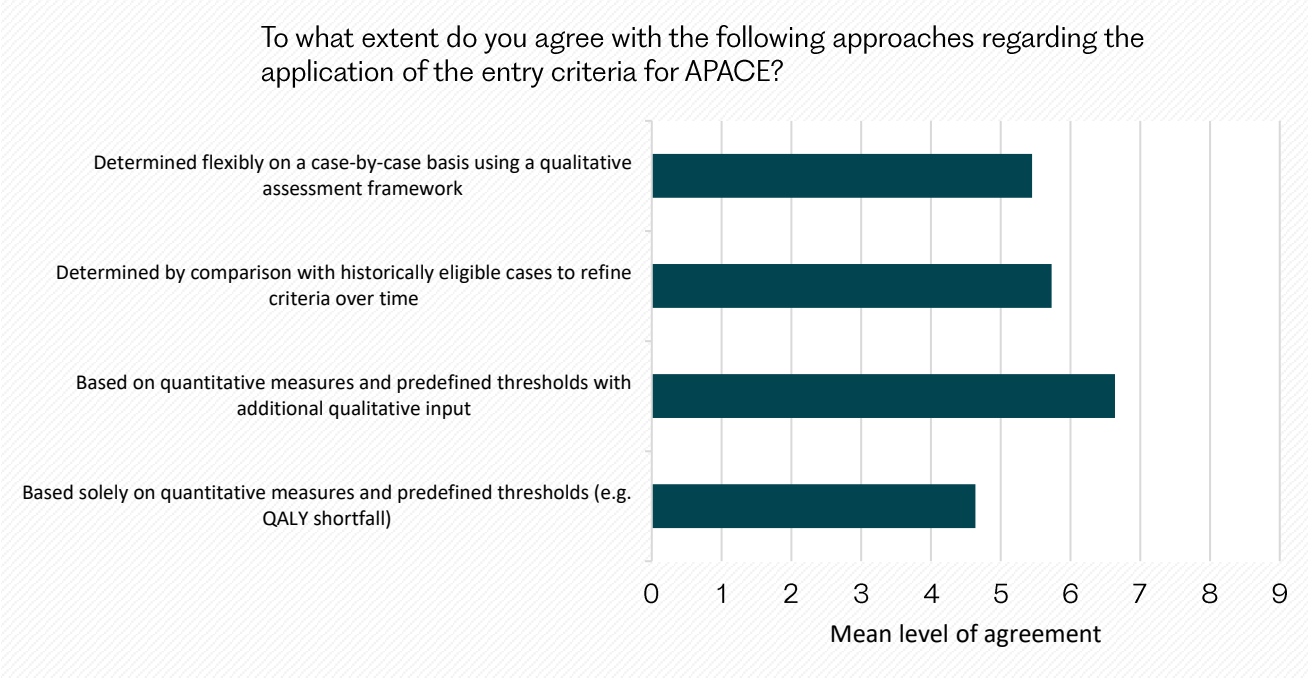
How should the criteria be judged?

Participants acknowledged the benefits of using quantitative measures of the agreed criteria, judged against predefined thresholds, to prevent overly broad definitions permitting too many treatments, and to improve transparency of the selection process. This viewpoint supports a European Federation of Pharmaceutical Industries and Associations (EFPIA) report suggesting it is difficult to determine whether a treatment fulfils the European Commission's current unmet need criteria due to their ambiguous nature. For example, assessing when a disease is associated with 'high' morbidity or mortality is open to interpretation (EFPIA, 2023).

One participant noted that a robust methodology linked to QALYs to measure the severity of a condition (i.e. proportional shortfall) has been used by some HTA systems (i.e. England and the Netherlands) and can be implemented in this context too. However, participants also recognised that setting quantitative criteria can be difficult in some situations due to the lack of clinical data inherent to ATs, and qualitative deliberations are also required (see Figure 4). They stressed the need for qualitative criteria to be transparent and accepted by stakeholders prior to implementation.

Stakeholders proposed one possible way of setting criteria is using case histories, whereby the current case is compared to previously eligible cases. These could be used to set predefined quantitative thresholds or provide definitions where quantitative setting is not possible. However, they noted that a challenge with this approach is that many past eligibility decisions are considered inappropriate by payers, creating a risk of reinforcing poor treatment selection. Nonetheless, case histories could form a starting point for stakeholder consultation over defining major therapeutic gaps, for example, with criteria continuously refined with experience.

Figure 4 Level of agreement for criteria application



**Participants were asked to rate level of agreement for each approach, where 1 = strongly disagree, 5 = neither agree nor disagree and 9 = strongly agree. The mean level of agreement for each approach was then calculated.*

4.2 Assessment phase (initial assessment and reassessment)

The initial assessment phase received the lowest overall agreement of all phases, which appeared predominantly driven by concerns over the length and thoroughness of initial assessment, whether risk was appropriately shared, and whether uncertainty should be accounted for in the initial price. The reassessment phase achieved good average agreement, with some concerns raised over how the price would change upon reassessment (see Figure 22).

We combine the roundtable discussions on the initial and reassessment phases, structuring through themes of evidence, timelines and pricing, which spanned both phases. For example, risk sharing-mechanisms are developed during the initial assessment and continued until a decision is made at reassessment.

Evidence
What type of studies should be accepted at the initial assessment phase?

Roundtable participants broadly agreed that a limited evidence package may be accepted as part of the initial assessment, in recognition of challenges associated with generating randomised controlled trial (RCT) data for many ATs, which can include treatments for rare diseases.

Whilst there was a preference for RCTs, there was also an acceptance that evidence may need to be in the form of single-arm studies in some situations. Single-arm trials can be particularly important for ATs for severe or rare cancers as the ethical basis of conducting RCTs in these circumstances is questionable (Wang et al., 2025). Moreover, for rare cancers, recruiting a sufficient sample size for RCTs may not be feasible. For tumour-agnostic therapies targeting rare biomarkers across multiple tumour types, single-arm basket trials are commonly used, as RCTs are often unfeasible due to low prevalence and tumour heterogeneity. The limitations of single-arm trials were noted, such as the lack of comparators and compounded uncertainty when combined with non-OS outcomes. Single-arm trials are often considered to demonstrate clinical efficacy and safety in the regulatory process, and methods such as external control arms and platform trials were suggested as potential avenues towards consideration in HTA processes as well.

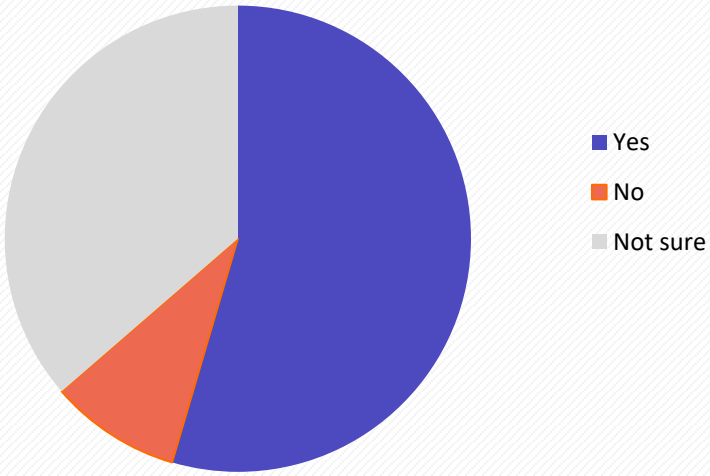
In such situations, accepting single-arm trials as the basis for initial appraisal in the absence of comparative trials aligns with the principles of APACE — it accelerates access to ATs to patients with urgent unmet needs, before more robust evidence or other sources of evidence are available. Single-arm trials are sometimes the basis for the original appraisal for the Cancer Drugs Fund (CDF) in England (Kang and Cairns, 2023; Wu, Zou and Zhang, 2024).

What role does overall survival (OS) have to play in the assessment phases?

The surveys and roundtables included discussions over the role of non-OS outcomes in value assessments as part of the APACE framework, though an in-depth analysis and discussion of the topic was not in the scope of this study. Some participants suggested the acceptance of non-OS outcomes at initial assessment depends on the possibility of OS data being available at reassessment, as OS remains the gold standard outcome that the evidential process should be geared towards. Others felt validation of the surrogate is sufficient, though this would have to be limited to validation within similar indications. No consensus was reached regarding their use at the reassessment stage (see Figure 5).

Figure 5 Question on non-OS outcomes at ressassement

Should non-OS outcomes inform estimates of effectiveness at the reassessment stage?



However, some felt the focus on OS was inappropriate since many cancers have evolved into long-term conditions, and OS data may not be available over a reasonable period of managed access. In particular, whilst OS may be appropriate for late-stage cancers where treatments can feasibly impact survival and OS may become available, for early-stage cancers, collection of OS data is more challenging. Within the CDF, OS is the most common source of uncertainty at initial assessment but often that uncertainty has not been resolved by resubmission (Simmons, Lilley and Lee, 2022; Trigg et al., 2023). Positive recommendations are still made despite remaining uncertainty. For example, NICE noted that there were insufficient data at reassessment to determine how much nivolumab increases OS for the treatment of melanoma in adults with lymph node involvement or metastatic disease but still recommended its use upon exit of the CDF. Similarly, in Germany, maturity of survival data and clinical benefit ratings did not change in the majority of reappraisals compared to the initial appraisal, highlighting that current evidential frameworks within these agreements may fail to raise additional insights beyond the initial assessment (Wiedmann, Cairns and Nolte, 2024).

Participants noted that even when OS data becomes available, its reliability can be undermined by patients using other treatments and the influence of unrelated health events, both of which can obscure the true impact of the AT being studied. For example, crossover of control group patients to taking the treatment under study may underestimate the OS impact of said treatment. Darolutamide for men with non-metastatic prostate cancer reduced risk of death by 31% when using intention-to-treat analysis, compared to 41% when adjusting for crossover (Shore et al., 2023). Participants also raised the point that OS may not capture all that is important to patients, with quality of life commonly mentioned as an important alternative outcome.

As such, some participants recommended that the acceptance of non-OS outcomes or alternative outcomes at both initial assessment and reassessment should be considered in some cases. For ATs targeting short-term survival, OS being available at reassessment can be a condition of managed access. For ATs resulting in longer-term OS, other outcomes may be acceptable, and these should be specified in the DCA. We include flexibility within our framework to reflect these differences.

Which ATs should enter the MAA?

A limited evidence package is likely to be associated with significant clinical uncertainties. Roundtable participants agreed that acceptance of such evidence rests on the knowledge that uncertainties will be addressed by more mature evidence, or more robust or expanded studies (e.g. longer follow-up for the RCT), at a later stage. They stressed the need for an assessment of what the uncertainties are and whether they can be resolved to a reasonable extent during an appropriate data collection period (maximum of 5 years). This perspective aligns with principles set out in the IMF, which states "Any data collection for managed access must be feasible to undertake, have a credible chance of addressing the uncertainties and avoid adding undue burden for patients and/or clinicians" (NHS England, 2022). As a result of these discussions, resolvableness of uncertainty was included as an entry criterion for managed access in the framework.

A further condition for entering the MAA is the potential size of relative benefit. In practice, this means the treatment should show a high likelihood of cost-effectiveness according to country assessment guidelines, or the 'expected value' of the treatment should demonstrate cost-effectiveness. The expected value will be updated as longer-term or more robust evidence is generated, such as at the point of reassessment, but an assessment based on the more limited evidence package at initial assessment must be made to judge eligibility for managed access.

What should a data collection agreement look like?

When developing a DCA, roundtable participants noted the need for absolute clarity in what the uncertainties are and how they are to be resolved, so when a reassessment occurs, it is obvious what the studies provided by the manufacturer should show to confirm reimbursement. This involves distinguishing between resolvable and irreducible gaps in evidence, and the extent to which the irreducible gaps are acceptable and how they may be mitigated. Participants also stressed the need to identify the most important uncertainties that may have an impact on the assessment of cost-effectiveness.

These discussions reflect findings in Trigg et al. (2023), who found that fewer than half of the treatments entering the CDF had a DCA that fully considered uncertainties raised by NICE committees at initial appraisal. To reflect these findings, we highlight the need for the DCA to be specific and comprehensive in its assessment of uncertainties and their potential resolution.

It was noted that, during the data collection period, additional uncertainties may emerge—uncertainties that neither the manufacturer nor the HTA body could have anticipated at the time of the initial assessment and that cannot be addressed through a detailed DCA. In such cases, a resolution mechanism is needed to ensure that these uncertainties can be addressed through further evidence, while still allowing for timely access to treatment.

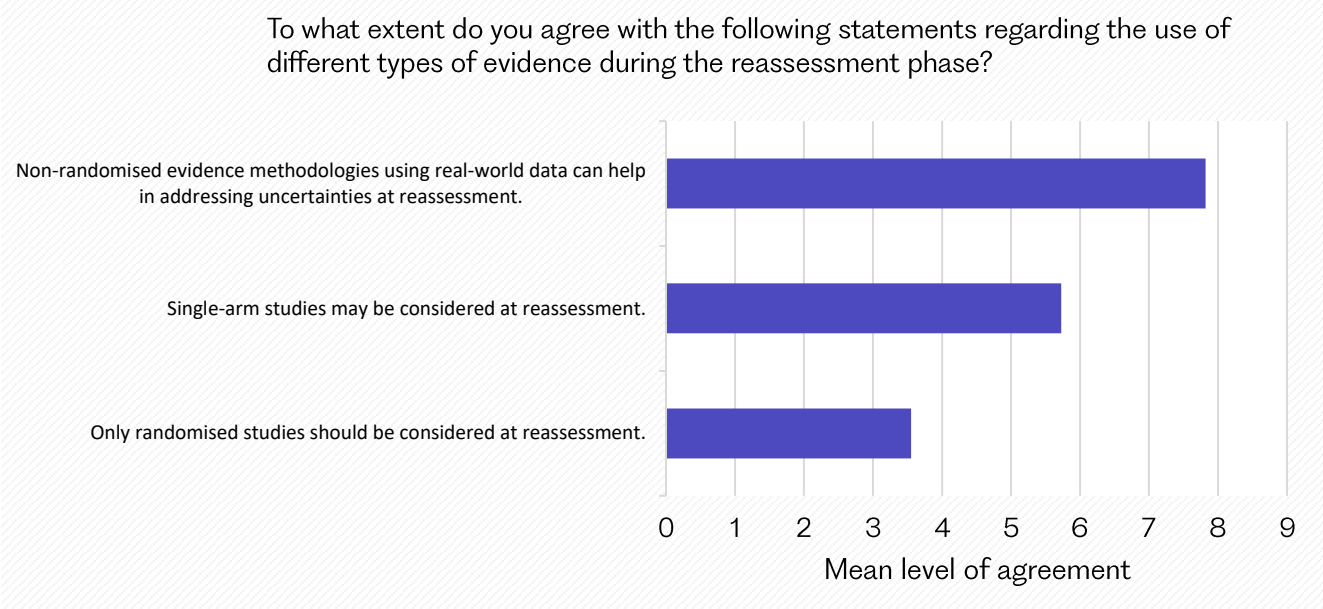
Participants also raised the need to take advantage of opportunities for collaboration, such as when systems with similar evidential requirements have similar clinical uncertainties. Manufacturers can take advantage of more efficient evidence generation processes and avoid conducting separate studies for multiple countries. However, participants also recognised that differing decision-making contexts and decision uncertainties across countries might require country-specific evidence generation.

What type of studies should be accepted at the reassessment phase of the framework?

There was agreement across stakeholders that the evidence package should be expanded for reassessment, compared to the initial assessment phase. As previously discussed, RCTs may not be feasible for some patient populations, including rare cancers, and therefore, single-arm trials and/or real-world evidence (RWE) can play a significant role. Participants agreed the use of RWE can help in addressing uncertainties (see Figure 6). This reflects a growing acceptance of RWE, as demonstrated by a study showing that RWE plays an important role in confirming efficacy and safety data from RCTs and informing oncology reassessment decisions (Bharmal et al., 2024).

Moreover, the roundtable participants emphasised that RWE addresses important real-world aspects that cannot be addressed by RCTs. For example, it can provide data on treatment effectiveness in more diverse populations than seen in RCTs and additional data on how treatments work in practice, outside of the controlled settings. Given 'generalisability of the trial population to the UK' and 'generalisability of treatment pathways' were two of the most prevalent uncertainties identified in a review of CDF data collection agreements, there are clear gaps that RWE is particularly suited to addressing (Trigg et al., 2023). RWE, therefore, forms an important part of the evidential studies that may be submitted at reassessment in APACE.

Figure 6 Level of agreement for acceptable evidence at reassessment



**Participants were asked to rate level of agreement for each statement, where 1 = strongly disagree, 5 = neither agree nor disagree and 9 = strongly agree. The mean level of agreement for each statement was then calculated.*

Timelines
How long should the initial assessment be?

The length of the initial assessment was a key area of debate during the survey and roundtable. Some participants suggested the initial assessment of an APACE framework should be faster than the traditional assessments, as otherwise the accelerated aspect of the process is less pronounced. However, others noted that given the large uncertainties inherent to this stage of the process, the initial assessment would need to be as thorough if not more so than traditional assessment processes, which may preclude the possibility of a faster assessment. A faster yet thorough process is possible but would require significant additional resources that may not be available in many jurisdictions.

Efthymiadou and Kanavos (2022) found that in Australia, England, Scotland, and Sweden the average time from original submission to final funding decision was larger for submissions with an MAA compared to those without (452 days compared to 404 days). Whilst this included the managed access period, they suggested one of the reasons could be the need for stakeholders to align on the required data for a final decision. This suggests shorter initial assessment timelines in a MAA may be unrealistic, and the framework instead prioritises a focus on the thoroughness of the initial assessment. Despite potentially longer initial assessment timelines, patients will still access drugs long before they otherwise would have without a managed access agreement.

JCA aims to centralise the HTA evaluation of clinical evidence in the EU to avoid or minimise duplications of assessments and streamline processes. Some participants suggested JCA offers scope for faster timelines, especially in countries where current evidential requirements are less clear. However, others questioned whether the JCA would meaningfully impact timelines given it only covers the clinical assessment and much of

the broader assessment (including cost-effectiveness in some countries) will still be conducted at the national level in accordance with country-specific evidence standards and processes.

How the JCA will be incorporated in accelerated access pathways remains an area requiring further discussion and analysis, particularly exploration of the impact it may have on the start and speed of the initial assessment. The impact could be neutral if countries can decide to pursue APACE without considering the JCA outputs and timelines. Alternatively, the impact could be positive, if JCA reports identify key uncertainties that can inform the DCA at the initial assessment phase (such as a common protocol to be pursued in APACE processes).

Additionally, the Joint Scientific Consultation (JSC), which provides early advice to manufacturers on regulatory and HTA evidential requirements, could also play a role by ensuring studies are designed efficiently and include the necessary components for every stage of an accelerated pathway, from regulatory to reassessment, potentially impacting initial assessment and MAA period timelines.

When should reassessment take place?

Roundtable participants agreed that a fixed timepoint did not account for the variability in uncertainty and evidence across treatments. Bee et al. (2024) found median data collection in MAAs in England ranged from less than 1 year to more than 5 years. They also found a correlation between MAAs relying on later phase trials and shorter data collection, compared to early phase trials/real-world data (RWD)-based MAAs, which required longer data collection, supporting points raised in the roundtable. Participants raised the need to build in sufficient time for data collection and preparation for submission, as well as review points to ensure monitoring of evidence generation. These review points mirror those seen in the AAP programme in France, where periodic submissions of a summary report of data are required (BlueReg, 2022).

However, there was also an acknowledgement that the managed access period must be as short as possible. If uncertainty takes too long to resolve, a treatment should not be eligible for the APACE pathway. This relates to the assessment of uncertainty described above - it must be resolvable within a reasonable timeframe, so payers do not have to live with uncertainty for too long.

Furthermore, if the managed access period is too long, the possibility of the treatment landscape evolving further as new competitor treatments enter the market complicates the reassessment process and can impact price. To reflect these points, the framework includes scope for flexibility in the reassessment point, but at a maximum of 5 years, to be agreed on a treatment-by-treatment basis as part of the DCA. There was also recognition that after 5 years, new lines of therapy may be available that represent improvements on the studied AT.

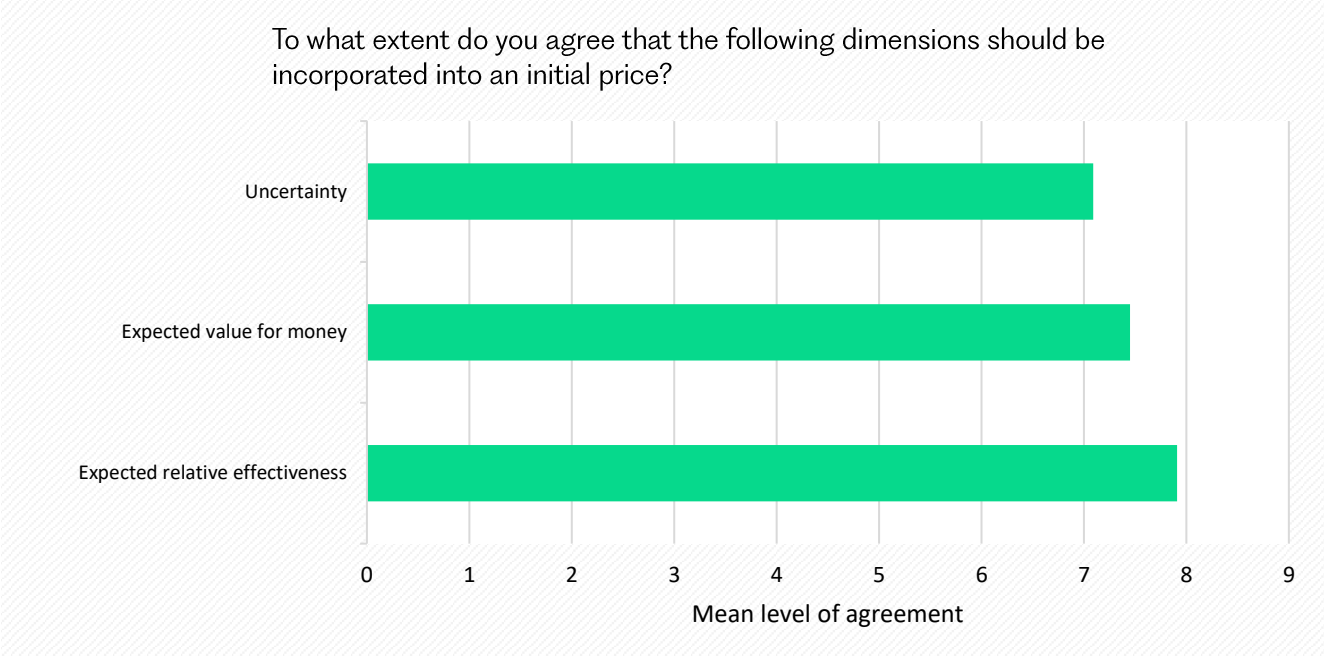
Pricing

What P&R models should be used?

One of the most debated areas among roundtable participants was which payment models should be adopted (as shown, for example, in Figure 7) —specifically, whether uncertainty should be addressed upfront through fixed pricing discounts or via schemes where the price is aligned with expected value at all times with no discount for uncertainty. Such agreements tie the *final* payment for the medicine to the effectiveness or cost-effectiveness of the medicine only. This can include outcome-based payments at the

patient level and also rebates based on the reassessment of effectiveness at the population level.

Figure 7 Level of agreement for dimensions in initial price



**Participants were asked to rate level of agreement for each dimension, where 1 = strongly disagree, 5 = neither agree nor disagree and 9 = strongly agree. The mean level of agreement for each dimension was then calculated.*

McElwee et al. (2025) suggested either conditional coverage with a fixed price or pricing based on effectiveness are suitable payment models when dealing with the contracting problem of uncertainty around effectiveness. It was important to understand whether participants felt one of these payment model categories was preferable to the other.

In the proposed framework, price is aligned with the payer's assessment of the treatment's expected value at all stages, including the initial assessment, without applying a fixed discount for uncertainty on the initial price. To ensure the final price aligns with effectiveness or cost-effectiveness and payers do not end up paying more for the AT than effectiveness suggests, rebates or other payment models can be used. Some participants supported this approach, arguing that pricing should reflect expected value, and that additional uncertainty should be resolved through the data collection agreements and rebates, rather than embedded into the initial price. France's early access scheme shows rebates after a lower price adjustment are possible. Prices are set freely by the manufacturer during the early access period but are subject to a double system of rebates: 1) yearly rebates depending on sales volume, 2) a retroactive rebate equal to the sales amount during the early access period minus the yearly rebate, and the sales amount had the final negotiated price been in place during the early access period (Haute Autorité de Santé, 2025; Abdelghani et al., 2023).

This expected value approach aligns with the approach detailed in Towse and Fenwick (2024), who propose a performance-based risk-sharing agreement (PBRSA) integrated with value of information (VOI) analysis to ensure that providing early access during a managed access period can be acceptable for both payers and manufacturers. They identify the issue that if a manufacturer believes the expected value of its treatment is larger than the expected value proposed by a payer, they may be unwilling to accept a further perceived price reduction to provide market access. A risk-sharing mechanism, whereby the initial price aligns with payer expectations of value and the 'final' price with

evidence at reassessment can enable the new price of the treatment to be higher or lower and encourages both parties to enter into a PBRSA. There is an incentive for the manufacturer to generate more evidence to demonstrate the expected value of their treatment, due to the potential of confirmed reimbursement at an increased price. For the payer, who is assumed to be risk neutral, the risk is shared as price aligns with their expected value, and there is potential to reduce the price and/or receive rebates if effectiveness is proved to be lower at reassessment, if further research is not provided or uncertainties have not been addressed. The option of retrospective rebate to the manufacturer in the case of the price being higher than the payer's initial assessment implies is not included in the framework.

However, some participants preferred fixed discounts, as simplicity is preferred by some payers over complex pricing arrangements that can be challenging to implement. They also suggested that some payers have doubts around receiving the money back in the form of rebates, which highlights issues of trust among the parties involved. This view is supported by a recent paper that assumes payers are risk-averse, and this risk aversion should be reflected in a reduced price based on the level of uncertainty at initial assessment (Jiao et al., 2025). This contrasts with the assumption of risk neutrality made in our framework. Participants noted that the discount implied by risk aversion could lead to less ATs being proposed by manufacturers in the first place. It was stated that the approach should be pragmatic and implementable but that does not necessarily imply the need for simple discounts.

Due to the incentives generated by aligning price with expected value with no discount for uncertainty - ATs are not held back *and* there are incentives for evidence generation - the final framework proposes this scheme, with mechanisms to ensure the payer does not end up paying more than the final assessment of AT effectiveness. Different types of agreements may be implemented, such as patient-level outcome-based schemes or rebates based on the reassessed level of effectiveness, but the P&R model should ultimately be tied to AT effectiveness. However, patient-level outcome-based payments were discussed, and roundtable participants noted their complexity and burdensome data requirements.

The APACE framework supports a consistent approach to P&R by aligning on key principles, such as not applying discounts for uncertainty, linking price to expected value, and enabling price adjustments upon reassessment. It also supports alignment with timelines of established European processes. Importantly, while supporting greater consistency, P&R processes and decisions will continue to fall under the jurisdiction of individual countries with the ability to establish confidential prices.

Should the price be adjusted upon reassessment?

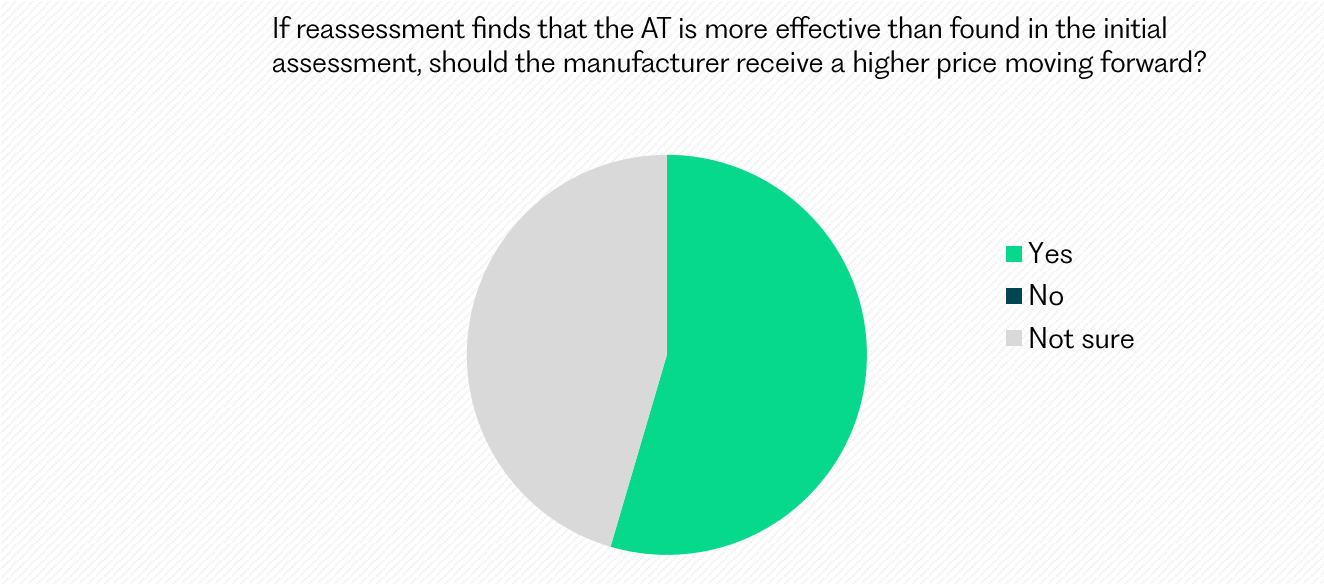
A related area where there was no consensus was whether the price should be adjusted upon reassessment. Figure 8 shows that a substantial number of participants were not sure if the manufacturer should receive a higher price moving forward if the AT was found to be more effective (i.e. it had a higher expected value than at initial assessment). However, there was general agreement that the manufacturer needs to be incentivised to collect evidence. This supports earlier findings that manufacturers should take responsibility for evidence collection, as payers are unlikely to engage in MAAs if they must also allocate resources for evidence generation in addition to monitoring and negotiation efforts (Cole, Cubi-Molla and Steuten, 2021).

Some participants said manufacturer evidence collection could be incentivised by discounts for uncertainty in the initial price being removed upon reassessment if uncertainties are resolved. They noted simple discounts to the initial price are preferred by payers as they are simpler and less resource-intensive to implement.

However, others suggested simple discounts for uncertainty fail to incentivise manufacturer evidence collection and may mean manufacturers do not enter into agreements in the first place as the price for the managed access period is too low. Others supported the alternative, where price aligns with expected value at all stages of the assessment process. Under this model, manufacturers would be incentivised to collect evidence as they expect the value of the AT will be shown to be higher than the initial price as judged by the payer at initial assessment. This view is supported by Towse and Fenwick (2024), who suggest that the prospect of price increases in line with expected value incentivises the manufacturer to bear the costs of evidence generation. Without such price increases and the prospect of decreases in the case evidence at reassessment shows lower effectiveness, there is an active disincentive to collect evidence and generally to engage in any agreements. Such incentive is an important foundation of accelerated access agreements, spurring evidence generation that benefits patients and advances scientific knowledge. Our suggested framework, therefore, includes the possibility of future price adjustments, both up and down. As noted above, these prices will ultimately be based on country-specific confidential negotiation.

A further incentive for evidence generation includes financial penalties when required evidence has not been submitted. Without such penalties, manufacturers who do submit and end up paying rebates would have to pay more than those who do not submit at all, creating disincentives for evidence generation. The penalty should be set to effectively deter non-submission.

Figure 8 Question on price adjustments moving forward



4.3 Exit phase

The exit phase achieved broad agreement across participants in the second survey (see Figure 22). The main concerns surrounded the enforceability of the delisting process, which is discussed further below.

What should the exit process be?

The exit process includes HTA bodies issuing the drug with 'not recommended' status and informing clinicians and patients of their decision and supporting reasons, under certain conditions. Roundtable participants suggested manufacturers must then pay for current patients continued treatment and prospective patients' treatment, where some still want to take the drug in absence of alternative treatments. This would be agreed in the commercial agreement, to ensure payers are not paying for ATs that are not considered to provide value for money.

Roundtable participants agreed with the steps laid out in the exit process but had concerns about implementation. In reality, treatment withdrawal may come up against strong resistance from patient organisations both for existing patients and prospective patients who want to take the drug. This is likely to be a particular issue for orphan conditions, where the absence of viable alternatives means patients may still value the AT as their only option. However, this might be mitigated by the introduction of other promising therapies.

Participants also stressed the need to strictly define clinical exceptionality criteria to avoid gaming the system. Within the literature, Farmer et al. (2023) highlight the psychological burden felt by patients during MAAs due to evidence generation and uncertainty over continued access, and the subsequent need to keep them informed throughout the process.

Finally, participants encouraged continued reassessment of ATs with confirmed reimbursement status using real-world data, given that even confirmed reimbursement may rely on short-term data for some conditions.

5 Limitations

First, our stakeholder panel consisted of 11 participants from six EU countries. While these individuals brought valuable insights, the views expressed may not be fully representative of all EU member states or the broader range of stakeholder perspectives.

Second, due to time and resource constraints, we were unable to conduct multiple rounds of consultation that might have been necessary to reach a broader consensus on the APACE framework. Although this limited the depth of validation, we view the process as a valuable agenda-setting exercise. It helped to surface key issues that warrant further exploration and could inform future, more extensive stakeholder engagement, potentially through methods such as Delphi panels or surveys involving a larger sample of stakeholders and experts.

Finally, while desk research supplementing the roundtable findings included key articles reviewing current schemes, our analysis could have benefited from a more systematic search and review of their advantages and disadvantages.

6 Summary and next steps

A consistent and aligned process for appraising and reimbursing oncology medicines targeting unmet clinical needs through accelerated pathways is currently lacking at the European level. Stakeholders from different countries hold differing views on how such pathways should be implemented, making even existing pathways the subject of ongoing debate. Additionally, current accelerated appraisal and reimbursement decisions are driven by individual member states, resulting in unequal patient access across Europe. To address this, the Accelerated Patient Access to Cancer Care in Europe (APACE) framework was developed, informed by a range of stakeholder perspectives to promote broad acceptance of its underlying principles. APACE aims to enable earlier access to innovative oncology treatments, faster than traditional pathways allow, by streamlining the process from regulatory approval through health technology assessment (HTA) to reimbursement. These accelerated pathways are conditional, with continued evidence collection post-approval to ensure ongoing assessment and are reserved for treatments meeting specific criteria.

To support the development of APACE, we conducted surveys and roundtable discussions to identify areas of consensus and divergence on its key components. Based on these insights, we developed a general APACE framework outlining core principles and processes. While there was broad agreement with the proposed framework, some areas remained unresolved during the roundtable discussions and require further dialogue. These included the quantification of eligibility criteria, the definition of acceptable non-overall survival (non-OS) outcomes, and the final structure of the P&R model.

Although limited in scope, this consultation helped surface key issues around the APACE framework. Rather than offering final recommendations, it serves as a useful agenda-setting step, highlighting areas for deeper exploration through broader stakeholder engagement and dialogue. While we focus on oncology medicines, many of the key principles may be applied in other disease areas with unmet need and challenges in generating evidence. However, there may be particularities in these disease areas that we have not covered here, and these should be considered if applying APACE's principles elsewhere.

The next steps below aim to set out actions that can aid in the implementation of the APACE framework and resolve the remaining areas of disagreement:

1. **Generate and agree clear eligibility criteria**
   a. There is a need to identify indicators used to define each criterion. KCE in Belgium conducted such a process, listing indicators for various dimensions of unmet need and the corresponding data collection methods as part of the NEED framework (KCE, 2024). However, they highlight the resource intensity in generating measurable indicators, with patient heterogeneity within the same disease further complicating the process. A balance between collecting measurable indicators and qualitative judgements will therefore need to be struck to ensure feasibility. The NEED framework provides a possible starting point, and validation at the EU level has begun (Claerman et al., 2024). Its implementation requires adaptations to be used for HTA (as it was created to drive R&D investments), stakeholder endorsement and alignment on definitions and data collection processes.
   b. Threshold-setting for the entry criteria should be agreed among stakeholders, for example, to define situations when there are major therapeutic gaps and the condition is considered *urgent*. Initially, cut-off points might also be informed by the allocated funds and the maximum number of initial assessments that HTA agencies can conduct as part of APACE.

2. **Align regulatory and HTA requirements**
   a. Ensuring alignment between regulatory and HTA processes is essential to prevent scenarios where HTA bodies evaluate ATs that meet regulatory standards but fail to satisfy their own evidential requirements. This can also accelerate the overall access pathway, from regulatory through to reimbursement.
   b. For example, convergence on eligibility criteria and the evidence needed to satisfy such criteria will ensure the mismatch between acceptability of treatments at regulatory and HTA level do not persist.
   c. A recent EMA workshop convened regulators and HTA representatives to identify the key challenges and potential solutions with regards to HTA-regulator collaboration (EMA and HAG, 2025). Recommendations included improving collection and analysis of outcomes beyond primary outcomes in clinical trials and collaboration in clinical trial study design.
   d. Going forward, it is recommended that regulatory and HTA bodies reinforce existing collaborative mechanisms and provide sufficient resources to new formal processes (such as the Joint Scientific Advice) for ongoing collaboration and communication on topics such as evidence standards, also at the product-specific level. This includes joint workshops, shared databases, and coordinated efforts in clinical trial design and outcome analysis. Such initiatives will ensure that both regulatory and HTA standards are met, ultimately facilitating faster and more efficient access to ATs for patients in need.

3. **Define relevant and feasible outcomes**
   a. Given the difficulty in validating non-OS outcomes, such as progression-free survival (PFS) for oncology treatments, and the changing landscape of cancer care, alternative outcomes should be developed and discussed in order to reflect these issues.
   b. Most importantly, there is a need for payers to engage with patients and clinicians over other outcomes that are not necessarily related to OS but remain important. Early engagement is critical to ensure outcomes are collected from the start of clinical trials. There must also be work done to highlight the standalone value of outcomes alternative to OS, either by linking them to traditional quality of life measures or demonstrating long-term clinical and economic benefits associated with such outcomes (Fameli et al., 2023).

4. **Agree on principles and methods for replicable assessments of uncertainty**
   a. To facilitate judgements of whether uncertainty at initial assessment is resolvable to a satisfactory level, it is important that it can be measured in a replicable way. Examples of methods to quantify uncertainty include VOI analysis, whereby the cost is compared to the value of collecting additional evidence (Towse and Fenwick, 2024). Such methods would enable a decision over whether it is worth resolving uncertainty to be made at initial assessment, and at reassessment whether continued evidence still needs to be collected.

5. **Strengthen national and pan-European Real-World Evidence infrastructure**
   a. To maximise the benefits of RWD and RWE, cross-country collaboration is required so ATs can be assessed in larger and more diverse populations. For this to be achieved, data must be accessible across a range of countries and in line with national laws. Currently, data may be of variable quality and stored in databases that are not compatible with each other, meaning they cannot be combined for analysis. The European Health Data Space has the potential to address these issues and enable a standardised collection and processing of RWE on a pan-European basis (EFPIA, 2025).
   b. Other European initiatives exist, such as DARWIN-EU for regulatory decision-making and RWE4decisions for HTA. (RWE4Decisions, 2024; EMA, 2021). The challenge will be ensuring the recommendations generated from these initiatives

are implemented and also coordinated across different RWE decision-making processes.

6. **Progressing implementation of alternative P&R models**
   a. The outcome-based model implemented will ultimately be country-specific, and payers must decide which model works best in their jurisdiction. While the final confidential price will be negotiated on a country-by-country basis, the pricing model should adhere to the principles set out in the framework, such as the final price aligning with expected value and incentivising manufacturers to collect evidence.
   b. This will require resolution of the resistance by payers to potential price increases if reassessment indicates higher effectiveness or cost-effectiveness, which is an important incentive for manufacturers to engage in the outlined agreements.

7. **Creating legal enforcement mechanisms for exit process**
   a. In order for the APACE process to be effective and legitimate, medicines that fit the exit criteria must be delisted, and strict processes, such as the ability of decision-makers to trigger legal action against those who do not comply with the exit process, should be implemented.

8. **Define funding arrangements**
   a. Given the exceptional nature of the APACE process, it is crucial to establish clear and sustainable funding arrangements. National governments should consider creating dedicated funds, which can provide the necessary financial support to kickstart the programme and cover initial costs associated with accelerated access to ATs. While short-term dedicated funds are important for the initial phase, it is equally important to develop long-term sustainability plans. Governments should outline strategies for integrating APACE into the national healthcare budget over time recognising that approved ATs will be delivering health care at prices that meet their value-for-money criteria.
   b. Ring-fenced funds require robust monitoring and accountability mechanisms to ensure that the funds are used efficiently and transparently. Regular audits, performance evaluations, and public reporting can help maintain trust and demonstrate the program's impact on improving access to ATs for unmet medical needs.

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9. **Determine how APACE will integrate into EU HTAR processes**
   a. It is key to clarify how ATs will be assessed as part of JCA and JSC processes. This will require early dialogue among key decision-makers to determine whether a treatment may be eligible for APACE, allowing the JCA timeline to align with the appropriate stage of assessment. It is important to establish whether the JCA reports can inform the initial assessment. If they do, JCA reports could identify key uncertainties and recommendations to address them. Given that these recommendations could apply on a pan-European basis, this opens up the possibility of organising studies that collect data from multiple countries to increase the power and generalisability of conclusions.
   b. Consideration of how the JSC can be utilised is also important. A key part of APACE is ensuring closer alignment among regulatory and HTA processes, and the JSC can facilitate the design of trials and studies that adhere to both sets of requirements, particularly in the context of ATs.
   c. Whilst APACE will, at least initially, be implemented at a country-level, general principles should continue to be refined as part of a continuous pan-European dialogue, with this framework used as a starting point. This will enable countries with limited experience in implementing such pathways to learn from and leverage the expertise of those with more established practices.

The APACE framework provides a structured, stakeholder-endorsed approach to accelerating access to oncology medicines targeting unmet needs across Europe. It seeks to bridge the gap between regulatory approval and reimbursement by enabling conditional access paired with evidence development. To realise its potential, further policy work is needed to resolve outstanding issues and ensure consistent implementation across European countries.

References

Abdelghani, I., Jdidi, H., Chachoua, L., Comiti, A., Hanna, E., Gilles, P., Francois, C. and Rémuzat, C., 2023. HTA353 Analysis of the Impact of Early Access Decisions on Pricing and Reimbursement Decisions in France. *Value in Health*, 26(12), p.S388. 10.1016/j.jval.2023.09.2036.

AIFA, 2024. *Monitoring pharmaceutical expenditure*. [online] Available at: https://www.aifa.gov.it/en/monitoraggio-spesa-farmaceutica [Accessed 7 May 2025].

Bee, C., Austin, C., Wakefield, L. and Williamson, S., 2024. HPR207 How Long Is Long Enough? Data Collection Duration for Medicines in Managed Access in England. *Value in Health*, 27(12), p.S314. 10.1016/j.jval.2024.10.1631.

Bharmal, M., Katsoulis ,Ioannis, Chang ,Jane, Graham ,Alex, Stavropoulou ,Apostolina, Jhingran ,Priti and and Pashos, C.L., 2024. Real-world evidence in the reassessment of oncology therapies: payer perceptions from five countries. *Future Oncology*, 20(21), pp.1467—1478. 10.2217/fon-2023-1004.

BlueReg, 2022. *FR early access programs for your innovative treatments - Blog - BlueReg*. [online] BlueReg Group. Available at: https://blue-reg.com/news/how-to-take-advantage-of-early-access-programs-for-your-innovative-treatments-in-france/ [Accessed 16 Apr. 2025].

BlueReg Group, 2025. *Early Access Programs in France (ex ATU program)*. [online] BlueReg Group. Available at: https://blue-reg.com/service/france-services-early-access-programs/ [Accessed 16 Apr. 2025].

CIRS, 2024. *Centre for Innovation in Regulatory Science. R&D Briefing 93: New drug approvals in six major authorities 2014—2023: Changing regulatory landscape and facilitated regulatory pathways.*

Claerman, R., De Pauw, R., Cleemput, I., Kohn, L., Levy, M., Schönborn, C. and Maertens de Noordhout, C., 2024. Validation of the NEED assessment framework: an EU level Delphi study. *European Journal of Public Health*, 34(Supplement_3), p.ckae144.010. 10.1093/eurpub/ckae144.010.

Cole, A., Cubi-Molla, P. and Steuten, L., 2021. *Making Outcome-Based Payment a Reality in the NHS. Phase Two: Practical Considerations - OHE*. [online] Office of Health Economics. Available at: https://www.ohe.org/publications/making-outcome-based-payment-reality-nhs-phase-two-practical-considerations/ [Accessed 1 Apr. 2025].

EFPIA, 2023. *The Commission's criteria to define unmet medical need and high unmet medical need*.

EFPIA, 2025. *Harnessing RWE to transform healthcare decision-making in Europe*. [online] Available at: https://efpia.eu/news-events/the-efpia-view/efpia-news/harnessing-rwe-to-transform-healthcare-decision-making-in-europe/ [Accessed 13 Apr. 2025].

Efthymiadou, O. and Kanavos, P., 2022. Impact of Managed Entry Agreements on availability of and timely access to medicines: an ex-post evaluation of agreements implemented for oncology therapies in four countries. *BMC Health Services Research*, 22(1), p.1066. 10.1186/s12913-022-08437-w.

EMA, 2015. *PRIME: priority medicines | European Medicines Agency (EMA)*. [online] Available at: https://www.ema.europa.eu/en/human-regulatory-overview/research-development/prime-priority-medicines [Accessed 14 May 2025].

EMA, 2021. *Data Analysis and Real World Interrogation Network (DARWIN EU)*. [online] Available at: https://www.ema.europa.eu/en/about-us/how-we-work/data-regulation-big-data-other-sources/real-world-evidence/data-analysis-real-world-interrogation-network-darwin-eu [Accessed 17 Apr. 2025].

EMA and HAG, 2025. *Joint HTAb-regulatory workshop: understanding key evidence challenges, managing uncertainties and exploring potential solutions*. [online] European Medicines Agency & Head of HTA Agencies Group. Available at: https://www.iqwig.de/printprodukte/joint-htab-regulatory-perspectives-on-understanding-evidence-challenges-final.pdf [Accessed 14 Apr. 2025].

Fameli, A., Paulsson, T., Altimari, S., Gutierrez, B., Cimen, A., Nelsen, L. and Harrison, N., 2023. Looking Beyond Survival Data: How Should We Assess Innovation in Oncology Reimbursement Decision Making. *Value and Outcomes Spotlight*, [online] 9(5). Available at: https://www.ispor.org/publications/journals/value-outcomes-spotlight/vos-archives/issue/view/looking-beyond-survival-data-in-oncology-reimbursement-decisions/looking-beyond-survival-data-how-should-we-assess-innovation-in-oncology-reimbursement-decision-making [Accessed 19 June 2025].

Farmer, C., Barnish, M.S., Trigg, L.A., Hayward, S., Shaw, N., Crathorne, L., Strong, T., Groves, B., Spoors, J. and Melendez Torres, G.J., 2023. An evaluation of managed access agreements in England based on stakeholder experience. *International Journal of Technology Assessment in Health Care*, 39(1), p.e55. 10.1017/S0266462323000478.

HAS, 2021. *Innovation funding: HAS assessment principles*. Available at: https://www.has-sante.fr/upload/docs/application/pdf/2021-10/forfait_innovation_guide_principe_evaluation.pdf .

Haute Autorité de Santé, 2025. *Early access to medicinal products*. [online] Available at: https://www.has-sante.fr/jcms/r_1500918/en/early-access-to-medicinal-products [Accessed 19 June 2025].

Jiao, B., Hsieh, Y.L., Li, M. and Verguet, S., 2025. Value-Based Pricing for Drugs With Uncertain Clinical Benefits. *Health Economics*, 34(4), pp.780—790. 10.1002/hec.4932.

Kang, J. and Cairns, J., 2023. "Don't Think Twice, It's All Right": Using Additional Data to Reduce Uncertainty Regarding Oncologic Drugs Provided Through Managed Access Agreements in England. *PharmacoEconomics - Open*, 7(1), pp.77—91. 10.1007/s41669-022-00369-9.

KCE, 2024. *NEEDS EXAMINATION, EVALUATION AND DISSEMINATION (NEED): ASSESSMENT FRAMEWORK*. [online] Available at: https://kce.fgov.be/en/project-need-unmet-needs [Accessed 14 Apr. 2025].

McElwee, F., Cole, A., Kaliappan, G., Masters, A. and Steuten, L., 2025. Alternative Payment Models for Innovative Medicines: A Framework for Effective Implementation. *Applied Health Economics and Health Policy*. [online] 10.1007/s40258-025-00960-1.

NHS England, 2016. *NHS England » Cancer Drugs Fund*. [online] Available at: https://www.england.nhs.uk/cancer/cdf/ [Accessed 2 Apr. 2025].

NHS England, 2022. *NHS England » Innovative Medicines Fund*. [online] Available at: https://www.england.nhs.uk/medicines-2/innovative-medicines-fund/ [Accessed 28 Mar. 2025].

Ollendorf, D., Henshall, C., Phillips, M., Synnott, P., Sansom, L. and Tunis, S., 2024. Putting meat on the bone: how to fast-track innovative medicines to those who need them and generate data to justify continued use. *Health Affairs Scholar*, 2(8), p.qxae095. 10.1093/haschl/qxae095.

Phillips, M., Synnott, P., Henshall, C., Tunis, S., Sansom, L. and Ollendorf, D., 2024. Towards a coordinated approach for managing accelerated patient access to potentially beneficial medicines: reporting the perspectives of a multi-stakeholder, international workshop. *Health Affairs Scholar*, 2(6), p.qxae069. 10.1093/haschl/qxae069.

Rejon-Parrilla, J.C., Espin, J., Garner, S., Kniazkov, S. and Epstein, D., 2023. Pricing and reimbursement mechanisms for advanced therapy medicinal products in 20 countries. *Frontiers in Pharmacology*, [online] 14. 10.3389/fphar.2023.1199500.

RWE4Decisions, 2024. Stakeholder Actions to Generate Better Real-World Evidence for HTA/Payers. Available at: https://rwe4decisions.com/2024-stakeholder-actions-to-generate-better-real-world-evidence-for-hta-payers/ [Accessed 14 Apr. 2025].

Shore, N.D., Fizazi, K., Tammela, T.L.J., Luz, M., Salas, M.P., Ouellette, P., Lago, S., Bastos, D.A., Jansz, G.K., Cárcano, F.M., Andrade, L., Pliskin, M., Lazaretti, N., Arruda, L., Correa Ochoa, J.J., Kuss, I., Kappeler, C., Sarapohja, T. and Smith, M., 2023. Effect of crossover from placebo to darolutamide on overall survival in men with non-metastatic prostate cancer: sensitivity analyses from the randomised phase 3 ARAMIS study. *European Journal of Cancer*, 195, p.113342. 10.1016/j.ejca.2023.113342.

Simmons, H., Lilley, C. and Lee, D., 2022. *Comparing Outcomes Pre- and Post-Cancer Drugs Fund: What Can We Learn?* [online] Lumanity & The Association of British Pharmaceutical Industry. Available at: https://www.abpi.org.uk/publications/comparing-outcomes-pre-and-post-cancer-drugs-fund-what-can-we-learn/ [Accessed 9 Apr. 2025].

Swissmedic, 2024. *Reimbursement procedures for medicines*.

Towse, A. and Fenwick, E., 2024. It Takes 2 to Tango. Setting Out the Conditions in Which Performance-Based Risk-Sharing Arrangements Work for Both Parties. *Value in Health*, 27(8), pp.1058—1065. 10.1016/j.jval.2024.03.2196.

Trigg, L.A., Barnish, M.S., Hayward, S., Shaw, N., Crathorne, L., Groves, B., Spoors, J., Strong, T., Melendez-Torres, G.J. and Farmer, C., 2023. An Analysis of Uncertainties and Data Collection Agreements in the Cancer Drugs Fund. *PharmacoEconomics Open*, 8(2), pp.303—311. 10.1007/s41669-023-00460-9.

Wang, M., Ma, H., Shi, Y., Ni, H., Qin, C. and Ji, C., 2025. Single-arm clinical trials: design, ethics, principles. *BMJ Supportive & Palliative Care*, 15(1), pp.46—54. 10.1136/spcare-2024-004984.

WHO, 2023. *The Novel Medicines Platform*. [online] Available at: https://www.who.int/europe/groups/the-novel-medicines-platform [Accessed 26 June 2025].

Wiedmann, L.A., Cairns, J.A. and Nolte, E., 2024. Evidence Quality and Health Technology Assessment Outcomes in Reappraisals of Drugs for Rare Diseases in Germany. *Value in Health*, 27(12), pp.1662—1670. 10.1016/j.jval.2024.07.012.

Wu, S., Zou, D. and Zhang, E., 2024. EE338 NICE Reconsideration for Oncology Drugs Based on Single-Arm Trials Referred to Cancer Drug Fund. *Value in Health*, 27(6), p.S119. 10.1016/j.jval.2024.03.636.

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