

Solving the challenge of combination treatments: Patient organisation roundtable on access to combination treatments in the UK

Chaired by Professor Sir Mike Richards
Wednesday 9 June 2021, 09:00 – 11:30, held virtually (MS Teams)

Roundtable Report

Introduction

This report provides a summary of a patient organisation roundtable on solving the challenge of access to combination treatments in the UK. The event was co-hosted by Takeda UK Ltd. and the Blood Cancer Alliance and took place on Wednesday 9 June 2021.

All the perspectives captured within this report have been anonymised and attendance at the Roundtable does not indicate endorsement of Takeda's proposed solution.

Those in attendance at the Roundtable have been given the opportunity to comment on this report.

Attendee list

The following individuals and organisations were present during the meeting:

- Professor Sir Mike Richards [Chair]
- Eric Low [Guest speaker], Independent Consultant and Chair of Takeda UK's Combination Treatments Advisory Group
- Shelagh McKinlay [Guest speaker on behalf of Blood Cancer Alliance], Head of Patient Advocacy (Myeloma UK)
- Bradley Price, Director of Research, Policy and Support (Sarcoma UK)
- Dany Bell, Strategic Advisor for Treatment, New Personalised Medicine and Genomics (Macmillan Cancer Support)
- Fiona Hazell, Chief Executive Officer (Leukaemia UK)
- Holly Heath, Policy Manager (Breast Cancer Now)
- Jane Lyons, Chief Executive (Cancer52) – partial attendance
- Laura Szutowicz, Chief Executive (Hereditary Angioedema UK)
- Lorraine Dallas, Director of Prevention, Information and Support (Roy Castle Lung Cancer Foundation)
- Sarah Berry, Policy Lead for England (Crohn's and Colitis UK)
- Steve Cotterell, Head of Advocacy (MPS Society)
- Zack Pemberton-Whiteley, Chief Executive Officer (Leukaemia Care)
- Emma Roffe, Oncology Country Head – UK & Ireland (Takeda UK)
- Jerome Penn, Senior Public Affairs Manager (Takeda UK)
- Helen Taylor, Programme Realisation Manager (Takeda UK)
- Danielle Smith, Head of Professional Relations and Patient Advocacy (Takeda UK)
- Tanja Podkonjak, Director of Access and Reimbursement Policy, EUCAN (Oncology) (Takeda Pharmaceuticals Company Ltd)

The Roundtable report has also been shared with the following representatives who were unable to attend the meeting:

- David Thomas, Head of Policy, Access and Innovation (Alzheimer’s Research UK)

Purpose

The purpose of the Roundtable was to consider combination treatment access challenges and to solicit feedback on a proposed solution developed by Takeda UK, with input from multi-disciplinary experts, to ensure it suitably represents/reflects the perspectives of patients and carers. It also aimed to identify the role patient organisations could play in the potential operation of a solution and how Takeda can partner with patient organisations to ensure implementable solutions are adopted.

The Roundtable covered the following:

- The challenges of access posed by combination treatments
- Takeda’s approach to developing a solution
- Takeda’s proposed solution
- Refining the proposed solution and gathering feedback
- Feedback on Takeda’s engagement strategy
- Involvement of the patient community in the operation of the proposed solution
- Summary of actions and next steps

Takeda’s approach to developing the solution and the components making up the solution are contained within the two Whitepapers: *An Attribution of Value Framework for Combination Therapies* Whitepaper and the *Voluntary Arbitration Framework for Combination Treatments* Whitepaper.

Summary of the key discussion points

The following are the key highlights from the Roundtable and further details around the discussions can be found later in the Report.

- Until the challenges associated with access to combination treatments are addressed, patients may be unable to benefit from the potential of combination treatments due to delays in access or no access at all (*see chapter 1*)
- It is therefore important that all relevant stakeholders come together to find a transactable and implementable solution that aligns with current National Institute for Health and Care Excellence (NICE) and NHS England (NHSE) methodologies and processes (*see chapter 1*)
- Takeda’s proposed solution is just one of a tapestry of proposed solutions being developed by industry and other stakeholders (*see chapter 2*)
- Takeda’s proposed solution is made up of two component “Frameworks” that are intended to be used together; the Attribution of Value Framework (to attribute value to each treatment) and the Voluntary Arbitration Framework (to ensure compliance with competition law) (*see chapter 3*)
- Whilst participants were not asked to endorse a single proposed solution, they welcome all proposed solutions and the opportunity to engage with industry (including Takeda) to identify an implementable and transactional solution (*see chapter 2*)

- It is important for patient organisations, as well as Takeda, to consider the role and opportunities for greater involvement of patients and patient organisations in the implementation of the Voluntary Arbitration Framework and the potential influence that patient organisations can have in ensuring that solutions are adopted (*see chapter 4*)
- Concern was raised about the voluntary nature of participating in the Arbitration Framework and the acceptance of the outcome. Further discussion is required around the merits of a mandatory versus voluntary Arbitration Framework (*see chapter 4*)
- Transparency and appropriate communication associated with the implementation of the Arbitration Framework is of high importance to patient organisations, to ensure there is awareness of industry involvement and the combination treatments being considered for the process (*see chapter 4*)
- Steps must be taken to ensure that the Voluntary Arbitration Framework does not overly increase the time that combination treatments take to complete the NICE process (*see chapter 4*)
- Governance and review of the success of any solution implemented was of high importance to patient organisations (*see chapter 4*)
- Consideration must be given to ensure that smaller companies can afford the cost of engaging 'clean teams' and that the qualifications/criteria of 'clean teams' is clearly outlined in the Voluntary Arbitration Framework (*see chapter 4*)

Detailed report of the Roundtable

1. The challenges posed by combination treatments: a presentation by Shelagh McKinlay

To introduce the Roundtable, Shelagh McKinlay (Head of Patient Advocacy, Myeloma UK and Blood Cancer Alliance representative) was invited to present her perspectives, as an advocate for blood cancer patients, on the difficulties that exist for patients in accessing combination treatments. The views expressed below are those of Ms McKinlay, and not necessarily representative of all participants.

During her presentation, Ms McKinlay outlined that:

- There was recognition in the patient organisation community, nationally and internationally, about the combination treatment issue and the impact it was having on access to new treatments in myeloma, blood cancers generally and beyond
- The patient organisation community understood this to be for a number of reasons and therefore agreed that this was a complex policy area requiring carefully thought through solutions that all stakeholders would find acceptable
- The issue of access to combination treatments had been highlighted in the recent Blood Cancer Alliance 'Rapid Access to New Drugs and Treatments for People with Blood Cancer on the NHS' report, under recommendation 15 and Blood Cancer Alliance is currently discussing the report's findings with decision-makers at NICE and NHS England
- Ms McKinlay pressed upon the group a sense of urgency to resolve the issue as many patients were being denied access to effective and tolerable treatments, with the potential to improve both quality and length of life
- Ms McKinlay referred to the fact that in myeloma, several companies had made the decision to not launch their combination treatments in the UK in recent years due to likely cost effectiveness issues. Further highlighting Blood Cancer Alliance findings which suggest non-submissions are increasing. However, Ms McKinlay did accept that there were perhaps other factors that could influence why a company may choose not to launch in the UK
- Ms McKinlay, while accepting this was a global issue, said she was especially concerned about its impact in the UK given the already very difficult market access and treatment use environment
- To support this view, Ms McKinlay cited that a survey by the Blood Cancer Alliance found that 81% of patients believe the Government should be doing more to improve access to the newest treatments
- Ms McKinlay also advised that, currently in England, only 56% of licensed combination treatments were routinely available to patients
- Ms McKinlay offered the view, that if the NHS is not able to routinely use the most advanced treatment options, then this could result in the attractiveness of the UK as a key market for early launch of new treatments and future clinical trials becoming eroded. In turn, this will have an impact on how early patients in the UK can access potentially beneficial combination treatments
- Ms McKinlay concluded by noting that it is therefore important that all relevant stakeholders come together to find a transactable and implementable solution that aligns with current NICE appraisal and NHSE commercial methods, and that this will help to ensure that patients have access to the latest licensed combination treatments

2. Takeda's approach to finding a solution: a presentation by Eric Low

Eric Low (Chair of Takeda UK's Combination Treatments Project Advisory Group) provided attendees with an overview of the background to Takeda's proposed solution, including the multi-stakeholder work that has underpinned its development so far, and the rationale behind Takeda's approach and philosophy.

During his presentation, Mr Low:

- Noted that from the outset it is clear from the Voluntary Scheme for Branded Medicines Pricing and Access (VPAS) agreement that overall responsibility for proposing a solution to NICE to overcome the associated challenges of combination treatments sits with the pharmaceutical industry
 - Mr Low further noted that this view has been corroborated through feedback from Takeda's Combination Treatment Project Advisory Group and the outputs of an international multi-stakeholder workshop hosted by the Bellberry Group in 2019 to discuss these challenges
- Advised attendees that Takeda has been looking into these challenges since 2016 and that there is international consensus that a fair, implementable and transactable solution needs to be found as shown in concurrent work being developed by other interested parties
- Noted that Takeda established a Combination Treatments Project Advisory Group – comprised of experts representing the patient, clinical, academic and competition law communities – that was tasked with clearly defining the issues faced and consequently designing solutions to the problem of assessing combination treatments
 - Mr Low advised that Takeda's multi-stakeholder approach ensured that the development of the solution was representative and that input on the challenges was also sought from representatives of NICE and NHS England
- Outlined that the work of the Combination Treatments Project Advisory Group has led to the development of two Whitepapers setting out a proposed solution for improving access to combination medicines which make up two distinct component "Frameworks" which are intended to be used together to address the cost-effectiveness and competition challenges (see chapter 3)
- Added that it has been developed in accordance with current NICE methods and practices and is intended to be future-proofed to any future changes to NICE or NHS England processes (e.g., the new NHS England Commercial Framework and potential changes adopted through the NICE methods and processes review)
- Concluded by noting that Takeda's proposed solution is just one of a tapestry of solutions being developed by industry and other stakeholders, which Takeda is supportive of, and that it will ultimately be for the Association of the British Pharmaceutical Industry (ABPI) to further develop and lead the implementation of a solution on behalf of the industry

Further detail on the background, rationale and development of Takeda's proposed solution can be found in the *An Attribution of Value Framework for Combination Therapies* Whitepaper and the *Voluntary Arbitration for Combination Therapies* Whitepaper.

3. Takeda's proposed solution: a presentation by Tanja Podkonjak

Following Mr Low's overview of the background, rationale and philosophy of Takeda's proposed solution, Tanja Podkonjak (Director of Access and Reimbursement Policy, EUCAN (Oncology)) provided attendees with an overview of the key requirements that an implementable solution must satisfy and presented an outline of the proposed Voluntary Arbitration Framework.

During her presentation, Ms Podkonjak noted that:

- Takeda's Combination Treatments Project Advisory Group has identified the following key requirements a solution must satisfy to address the issues from the ground up:
 - Deliver improved patient access to combination treatments
 - Be compatible with existing health technology assessment (HTA) methods and processes
 - Adhere to existing cost-effectiveness thresholds
 - Address competition law issues
 - Encourage manufacturers to work together
- With input and advice from the Advisory Group, and following robust scrutiny and debate, Takeda has developed two Whitepapers setting out a proposed solution for improving access to combination treatments
- The solution is treatment and disease agnostic and could be applied to any combination treatment
- Takeda's solution is made up of two component "Frameworks" – that are intended to be used together:

1. Attribution of Value Framework

The Attribution of Value Framework proposes an economic methodology that aims to define a fair division of value across the treatments in a combination by assigning a relative value to each treatment based on the health benefit. It takes into consideration health-economic methods used by NICE in making decisions about access to medicines.

2. Voluntary Arbitration Framework

The Voluntary Arbitration Framework proposes a standard operating procedure to support compliant dialogue and agreement between pharmaceutical companies on the value attributed to each treatment within a combination. It takes into consideration competition law and the current NICE processes in making decisions on access to medicines.

- For the subsequent discussion, the focus was the Voluntary Arbitration Framework. With this in mind, Ms Podkonjak provided a summary of the following four elements (which were discussed in greater detail in chapter 4):
 - 'Clean teams'
 - Combination-based discounting
 - A long-term commitment to participate
 - The option of adjudicator oversight

Further detail on Takeda's proposed solution and these two components can be found in the *A Attribution of Value Framework for Combination Therapies* Whitepaper and the *Voluntary Arbitration Framework for Combination Therapies* Whitepaper.

4. Refining the proposals and gathering feedback: group discussion

After listening to the presentations on the cost-effectiveness and competition challenges associated with combination medicines, Takeda's approach to developing a solution and the key elements that comprise Takeda's solution, the Chair opened the discussion to attendees. Specifically, he asked attendees to provide their reflections on the principles and concepts underpinning the solution, as well as how it could be applied within the context of the UK HTA process. Whilst facilitating the discussion, the Chair also encouraged participants to stress-test and refine the proposals.

Overall, participants welcomed Takeda's commitment to driving the agenda by putting forward a potential solution. However, they also posed a series of questions and challenges about the proposed solution, including suggestions on how it could be developed further. Takeda colleagues sought to provide clarity on these points and noted that they are committed to finding a solution and open to working collaboratively with all relevant stakeholders to do so. The challenges and queries discussed can be broadly split into eight key themes, as follows:

A single company initiative

- Participants noted that the proposals presented represent a single company solution to the challenges of accessing combination therapies and queried whether this would achieve sufficient buy-in with the rest of industry and, ultimately, NICE and NHS England
 - Takeda responded by confirming that this solution is one of a tapestry being developed by the pharmaceutical industry and work was underway through the ABPI to bring the cross-industry proposals together. It was added that it would ultimately be the ABPI proposing a solution to NICE and NHS England, rather than Takeda or any other single company, raising the prospect of ensuring a consensus solution is adopted

Patient organisation involvement and engagement

- Participants noted that there is little mention of patient organisation involvement within the proposed solution and that there is an opportunity to take account of the patient perspective
 - Takeda welcomed patient and patient organisation engagement in the solution and asked for input from patient organisations in co-creating the involvement of patients and patient organisations in the solution
 - Takeda suggested that a key role for patient organisations' will be in their horizon scanning to ensure that potential combination treatments are signposted to the solution at the earliest possible stage
- Participants suggested that there could be an opportunity for qualitative patient benefits to be included in the Value Attribution methodology – though they also noted that this may already be fulfilled within current NICE processes
- It was noted that in the rare disease space, qualitative data is an important part of driving successful cost-effectiveness cases and lessons could be learnt from this
- The group agreed that further work was needed in partnership with patient organisations and patients to define their involvement in the process

Mandatory vs voluntary nature

- Participants asked about the role of the adjudicator and queried why the adjudicator's decision was not binding given that multi-indication discounting would mean that the value attribution would only be applicable to the specific combination
 - Takeda noted that mandatory arbitration could risk undermining industry uptake of the solution and therefore this may impact its long-term viability
 - Takeda advised that, at this stage, the solution needs to be disseminated further before considering this proposal, although they would give due consideration to this feedback

Transparency in the solution

- A number of participants advised that transparency in the operation of the solution is of high importance to patient organisations
- Participants clarified that they appreciate that specific details of inter-company negotiations cannot be disclosed, such as confidential information on pricing or discounting, but they would value being informed of which combination treatments are going through the solution and when the different stages of the solution are taking place
- It was noted that patients and patient organisations can feel frustrated when they do not receive updates on the timelines for commercial discussions in the NICE process and asked that due consideration is taken to ensure that any proposed solution does not further add to these frustrations
 - Takeda welcomed the views of patient organisations on how they could be involved in the proposed Voluntary Arbitration Framework. Takeda noted that they are keen to ensure the process of engagement and communication to relevant external stakeholders is clear throughout and that updates are provided in a timely manner to stakeholders
 - Takeda also encouraged efforts by patient organisations to horizon scan and implement programmes to ensure they are routinely in the loop with clinical development and combination treatments that could be candidates for the solution

Timescales for the Voluntary Arbitration Framework

- Participants raised concern about whether the Voluntary Arbitration Framework may increase the time that combination treatments take to complete the NICE process
 - Takeda advised that the solution has been designed to interact and align with the NICE appraisal processes and applicable timelines to avoid delaying patient access. The Framework proposes early initiation of the process during horizon scanning, with initial 'clean team' dialogue taking place prior to the NICE Single Technology Appraisal (STA) submission, both in hope of building common ground and resolving issues early to prevent delays
 - It was also suggested that a maximum timeframe for company negotiations as a part of the Voluntary Arbitration Framework could be agreed at the outset to avoid any delays, potentially via a 'terms of engagement' agreement
 - Additionally, Takeda advised that combination treatments are already experiencing longer timeframes within the current system due to ongoing cost-effectiveness and competition law challenges. Therefore, rather than increasing the appraisal timeline for combination treatments, this proposed solution could in fact decrease the timescale for approving combination treatments compared to the norm

Achieving widespread industry involvement in the solution

- Participants raised concern about the non-mandatory nature of industry participation in the proposed solution and noted a preference for it to be mandatory for manufacturers of combination medicines to part take in the solution and agree with its outcome, when submitting to NICE
 - In response, Takeda clarified that the proposed solution could form part of the VPAS and therefore signing up to the principles of the solution would be obligatory for scheme members. Acceptance of the outcome is non-binding, and it was noted that greater clarity was required in the proposed solution about this
 - However, as with existing commercial negotiations and NICE processes, a company must retain the ability to withdraw from negotiations, and as such the outcome of the solution should remain voluntary
 - It should also be noted that not all combination treatments would be deemed suitable to initiate the proposed solution

The role of the adjudicator

- Participants queried whether it was accurate to refer to the arbitrator as an ‘adjudicator’ if the decision was not binding and suggested that the role should be renamed to reflect that of a ‘mediator’ role
 - Takeda noted that there is potential that the solution could evolve as it becomes more socialised and, consequently, there is a possibility that the decisions made by the adjudicator could also evolve to become mandatory
 - On the renaming of the ‘adjudicator’, Takeda committed to exploring this issue with the authors of Takeda’s proposed solution and wider experts as necessary
- Participants asked for further information on who would fulfil the role of the adjudicator, how the solution would be governed and whether the solution would be applicable to other parts of the UK
 - Takeda advised that they envisage that the role of adjudicator would be fulfilled by an independent organisation that would work in a similar way to the Prescription Medicines Code of Practice Authority (PMCPA), whereby it is a self-governed model, run by industry. The PMCPA model begins with inter-company dialogue and only goes to the independent body for arbitration if the inter-company dialogue breaks down
 - Takeda clarified that the proposed solution has been based on HTA processes in England and has been built to sit alongside the NICE and NHSE process, however they believe that the principles outlined in the proposed solution could be adapted to align with other country HTA processes that use cost-effectiveness analyses
- Participants asked where accountability for the solution should sit within the wider HTA system and how the solution would be reviewed, to measure its impact and success, against its objectives
 - Takeda noted that this would be a topic for further exploration with all stakeholders through planned ongoing one-to-one engagement

The role of ‘clean teams’

- Participants queried if smaller manufacturers would be able to afford external ‘clean teams’, as proposed within the Voluntary Arbitration Framework

- Takeda advised that they are mindful of this issue and agreed that further work is required to determine suitable criteria for 'clean teams'. Takeda suggested that market access agencies – rather than more expensive legal teams – could fulfil the role of external 'clean teams' as they would have a good understanding of HTA processes and methods
- Takeda also noted that criteria/ a job role specification for 'clean teams' (including the qualifications required) would form part of considerations during the next stage of the proposed solution's development and hope further feedback from external stakeholders could help inform this
- Additionally, Takeda noted that as a proportion of the overall research and development and market authorisation costs, the cost of 'clean teams' is likely to be relatively modest. Additionally, it is also important to consider the cost-benefit factors if a 'clean team' model can help to overcome the challenges that currently exist in the system for combination treatments

Implementation of combination-based discounts

- Participants asked how likely it is that combination-specific discounts are taken forward by NHS England (NHSE)
 - Takeda noted that the NHSE commercial framework has provisions for non-uniform pricing in certain circumstances, so any such discounts would need to be implemented by NHSE
 - Takeda advised that as part of their engagement with the external experts during the development of the Voluntary Arbitration Framework, NHSE advised that they may be open to discussions around discounts for individual indications of medicines included in a combination, aligned to the Commercial Framework; particularly if it meant improved patient access to combination treatments that demonstrate a clear clinical benefit
 - Takeda reiterated that this component is also integral to ensure compliance with competition law and a fundamental principle within the wider tapestry of solutions being developed by industry and other stakeholders

5. Takeda's engagement strategy and involvement of the patient community in the solution: a presentation by Danielle Smith and Jerome Penn followed by a group discussion

Danielle Smith and Jerome Penn (Takeda) briefly outlined Takeda's planned engagement strategy to generate continued feedback and debate on the solution to support adoption.

Ms Smith and Mr Penn noted that Takeda's engagement strategy aims to build awareness of the combination treatment challenge, generate platforms for discussion and debate to secure critical feedback on the proposed solution. Takeda also noted their intention to employ a considered and targeted approach to stakeholder engagement to secure support and action for solutions to be implemented.

They outlined Takeda's planned engagement activities for 2021, including:

- Hosting closed pan-disease roundtables to gather feedback on the combination treatment challenge and Takeda's proposed solution with:
 - Patient organisations
 - Clinical stakeholders
 - Health economic experts
 - Competition law experts
- A multi-stakeholder panel discussion to highlight current thinking around the combination treatment challenge and the need for implementable and transactional solutions
- A phased 1:1 engagement programme to provide early sight of the solution to core stakeholders, across industry, academia and other relevant stakeholders who have an interest in this topic

The Chair opened a group discussion and participants were invited to provide feedback on Takeda's approach to engagement, particularly around the target stakeholders and the role of patient organisations to inform and strengthen next steps.

- Participants recommended that Takeda engage with larger patient organisations and coalitions – especially those beyond oncology (e.g., members of The Richmond group)
 - Takeda confirmed that they are keen to engage more widely with patient organisation coalitions and non-oncology patient organisations and requested that participants to inform them of any specific organisations outside of oncology that Takeda could engage
- Participants asked for an overview of the response to date from health economists, noting that their support is key to ensuring the adoption of any proposed solution to this challenge
 - Takeda advised that the problem has been discussed at length by the health economic community, such as the discussions led by the Bellberry Group, and there is therefore widespread interest in finding a solution
 - It was added that in addition to being supported by health economists, there is interest from HTA agencies to resolve the issue as indicated by their participation at the Bellberry Group conference

- Participants welcomed the planned multi-stakeholder panel discussion and asked Takeda to consider other potential avenues for multi-stakeholder events to discuss the issues and solutions, e.g., at annual HTA conferences
- Some participants were interested in Takeda presenting the proposed solution, once both Whitepapers have been published, to their organisations (e.g., Cancer52 members) and to continue the discussions around patient/patient organisation engagement in the solution, which they felt was of high importance

6. Agreed actions and next steps

The Chair closed the meeting by summarising the key themes of discussion that arose during the meeting. Helen Taylor (Takeda) then briefly outlined Takeda's planned next steps.

Next steps

Ms Taylor noted that further feedback from those in attendance would be welcome throughout 2021 and beyond.

Once published on the Takeda UK website, a link to the Voluntary Arbitration Whitepaper will be shared with patient organisations and continued engagement with interested parties will also take place throughout the year. Attendees were asked to inform Takeda if they wished to continue to engage on the proposed solution.

In early 2022, all feedback from across Takeda's stakeholder discussions will be reviewed and, if deemed necessary, there is the potential to publish an addendum to the proposed solution.

Materials developed throughout Takeda's stakeholder discussions, including this summary report, will be made accessible on the Takeda UK website: <https://www.takeda.com/en-gb/what-we-do/combination-treatments/>.