Improving patient access to gene and cell therapies for rare diseases in Europe

A review of the challenges and proposals for improving patient access to advanced therapeutic medicinal products in Denmark

V1

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Chaired by:

Secretariat support by:

Reader notes:

This document contains country-specific insights on challenges and potential solutions to patient access to advanced therapeutic medicinal products (ATMPs) for patients with rare diseases.

The purpose of the document is to provide a starting point for country-specific engagement and discussion within multi-stakeholder meetings.

The challenges and solutions were discussed and prioritised with members of the RARE IMPACT Working Group in meetings and WebEx's between September 2018 and September 2019. Country-specific challenges/solutions have drawn on global recommendations previously published by EUCOPE and ARM, both members of the Working Group.

The challenges and solutions contained within this document are those that have been proposed as priorities for discussion with local stakeholders by members of the Working Group – the report does not include all challenges identified during the secondary research or Working Group meetings.

Contents

Executive Summary

The RARE IMPACT initiative was launched at the European Conference on Rare Diseases and Orphan Products in 2018. It is a multi-stakeholder initiative working to improve patient access to gene and cell therapies (or advanced therapy medicinal products [ATMPs])[1]. This patient-focused initiative aims to both assess challenges and propose actionable solutions to concerns regarding patient access to these transformative rare disease treatments in Europe. Through engagement with health technology assessment (HTA) agencies, regulatory bodies, payers, patient groups, clinicians, manufacturers and other experts across Europe, RARE IMPACT partners have proposed ideas to provide better access to ATMPs in Europe.

In recognition of the pipeline of ATMPs and the difficulty in providing patient access to these innovative therapies in a sustainable way with existing pathways, Denmark has begun to implement changes in the assessment system for ATMPs. Within the existing assessment frameworks there are evidence criteria challenges for ATMPs that are very similar to the challenges faced by orphan drugs; the evidence itself often contains many uncertainties, and the long-term clinical benefit is regularly uncertain. Although there are clearly outlined assessment requirements that ATMPs must meet, it may be difficult for them to fulfil these requirements. Recognition that the standard assessment process does not fit well for ATMPs, along with a willingness to accept different methods/evidence levels that can more realistically be fulfilled, may contribute to making the process more conducive to the nature of these innovative products. It appears that this willingness is present in Denmark, as changes to the assessment process are planned for 2020. It is expected that these changes will likely address many of the existing assessment challenges which have resulted in challenging patient access for existing ATMPs.

While affordability is not an issue in Denmark, an emphasis on a need for socioeconomic responsibility places high scrutiny on high-cost medicines. Affordability issues specific to ATMPs arise when individual hospitals are responsible for delivering specialist treatment; specialist prescribed products are funded by hospitals, and the use of such products is likely to be restricted to a single hospital. The potential availability of specialist funds for ATMPs is uncertain, which leaves hospitals and health insurers to cover treatment costs. In addition to product costs, the logistical demands associated with ATMP delivery add further costs and budget impact. Solutions such as innovative payment plans, early access programmes and better security for specialist funds may help alleviate some of these challenges.

Denmark has a network of specialist centres that are capable of treating patients with ATMPs. There is, however, a burden of reconfiguring services for these treatments that will be felt by a small number of centres. Denmark is well-placed to configure its services to allow access to ATMPs. Having built-in service preparation requirements in a joint horizon scanning process at the Nordic level and identifying infrastructure and services that can be reconfigured for ATMPs, are two approaches to help ensure success and access for patients across regions.

[1] Medicines for human use developed from genes, cells or tissues are classified as advanced therapy medicinal products (ATMPs) by the European Medicines Agency (EMA)

An overview of challenges and proposals for improving patient access to ATMPs in Denmark

Impact*	Challenges		Proposed solutions		Feasibility**
Assessment 	**AS1.**	The Danish Medicines Council (DMC) is willing to accept surrogate outcomes, but evidence is graded lower than conventional endpoints	**AS1.**	Key changes to assessment in Denmark are planned for the near future to address ATMP assessment	+++
	AS2.	DMC evidence requirements are clearly outlined, but a product achieves added clinical value only if a minimal clinically important difference is demonstrated	**AS2.**	Adjust evidence requirements and include patient perspectives when defining minimal clinically important differences for ATMPs - this may be taken into account in the upcoming changes	++
	AS3.	Clarity is still needed on the assessment changes in terms of how they will be implemented and what will actually change	**AS3.**	Clarity should be requested on anticipated amendment and the implications of *not* changing should be communicated, to ensure changes are successfully made	+++
Affordability 	**AF1.**	Affordability issues arise when individual hospitals are responsible for delivering specialist treatment	**AF1a.** **AF1b.**	Innovative payment models could alleviate the burden of up-front payments A secure specialist fund for ATMPs to reduce burden on individual hospitals	+ +
	AF2.	Higher logistical demands associated with ATMP administration: patients require additional outpatient appointments which adds costs and affects budget impact	**AF2.**	Collect data from early access programme to determine what should be included in the model for assessment	++
Availability 	**AV1.**	The outlook of physicians in Denmark emphasises a need for socioeconomic responsibility beyond advice from AMGROS	**AV1.**	Early communication with physicians around benefit of ATMPs	+++
	AV2.	Patients have received access to treatment via cross-border initiatives – it is uncertain if patients will receive the same level of cross-border access to ATMPs	**AV2.**	Denmark is involved in cross-border agreements which are not a challenge; but rationale for cross-border treatment will be required	+++
Accessibility 	**AC1.**	Denmark has a network of specialist centres that are capable of treating patients with ATMPs; however, there will be a burden of reconfiguring services for these treatments	**AC1.**	Configure services for ATMPs by identifying infrastructure/services that can be reconfigured, and having built-in service preparation requirements in a joint horizon scanning process	++

Notes: *The working group assessment of the relative impact of the challenge of each domain on patient access is represented by Harvey balls from highest (represented by a full blue Harvey ball) to lowest (represented by an empty, white Harvey ball); **Feasibility: Working Group assessment of feasibility of solutions to be implemented. + low feasibility, ++ medium feasibility, +++ high feasibility.

The collaboration

RARE IMPACT is a collaboration of three not-for-profit organisations, two trade associations and 18 manufacturers of ATMPs brought together by EURORDIS, a non-governmental patient driven alliance of patient organisations. The overarching objective of the collaboration is to ensure European patients with rare diseases obtain quick access to gene and cell therapies and to create a sustainable model for manufacturers and payers to maintain patient access and innovation. To achieve this objective, the collaboration has established the following goals:

- Identify challenges that are preventing rare disease patients accessing ATMPs
- Propose actionable solutions to address these challenges
- Utilise these ideas within multi-stakeholder discussions within individual countries and in pan-regional forums

The approach

A framework for categorising barriers to patient access was developed and validated by the collaboration. The framework includes four categories, described in Table 1 below.

Table 1. Framework applied to structuring identified challenges

Category	Description
Assessment (magnitude of benefit)	Challenges related to the assessment of the benefit of ATMPs within pricing and reimbursement processes. This includes topics such as evidence uncertainty, generating comparative data, use of surrogate endpoints and assessment pathways
Affordability (price, cost and funding	Challenges concerning the pricing, funding and affordability of ATMPs, including the application of innovative payment models
Availability (legally available)	Non-regulatory challenges to the product being available within countries, such as those related to cross-border healthcare and hospital exemptions
Accessibility (accessible by patients)	Administrative, service capacity and geographic challenges that delay or prevent patient access to ATMPs

Identification of challenges and proposals for improving patient access

Primary and secondary research was conducted to identify challenges to patient access to ATMPs and potential solutions. Initially, secondary research was conducted to create a database of conceptual and country-specific challenges. This research included:

- A targeted literature search
- Reviewing outputs from other initiatives (e.g., ARM's "Recommendations for Timely Access to ATMPs in Europe" and EUCOPE's "Gene & Cell Therapy – Pioneering Access for Ground-Breaking Treatments")
- Assessing pathways through which patients access ATMPs in the countries of interest
- Reviewing HTA and P&R decisions for existing ATMPs

Challenges and potential solutions were supplemented, assessed and prioritised through a review process including:

- Members of the Working Group (including EURORDIS, trade associations, affiliated NGOs and 18 member companies)
- Country-specific patient associations
- Country level decision makers, such as policymakers, HTA bodies and budget holders
- Experts and advisors, such as healthcare professionals, patient representatives, P&R system experts, ATMP technical experts, economists and academics

Following stakeholder engagement, the challenges and solutions were refined and prioritised to reflect the perceived importance in improving patient access and feasibility of implementation. Therefore, the challenges in this report are not exhaustive of all identified through primary and secondary research but represent the most important issues as determined by stakeholders.

The outputs from this process have been summarised in this report as a basis for discussion within multi-stakeholder meetings in each country and at the European level.

ASSESSMENT

Impact: 

Challenge		Proposed solution		Feasibility
AS1.	The Danish Medicines Council (DMC) is willing to accept surrogate outcomes, but evidence is graded lower than conventional endpoints	**AS1.**	Key changes to assessment in Denmark are planned for the near future to address ATMP assessment	**+++**
AS2.	DMC evidence requirements are clearly outlined, but a product achieves added clinical value only if a minimal clinically important difference is demonstrated	**AS2.**	Adjust evidence requirements and include patients when defining minimal clinically important differences for ATMPs - these may be taken into account in the upcoming changes	**++**
AS3.	Clarity is still needed on the assessment changes in terms how they will be implemented and what will actually change	**AS3.**	Clarity should be requested on anticipated amendment and the implications of *not* changing should be communicated, to ensure changes are successfully made	**+++**

The Working Group assessment of the **impact** of the challenge relate to all challenges in each domain. The Working Group assessment of **feasibility** relates to the individual or groups of proposed solutions.

Working group identified challenges:

Challenge AS1.

The Danish Medicines Council (DMC) is willing to accept surrogate outcomes, but evidence is graded lower than conventional endpoints.

Evidence challenges that are inherent for ATMPs are very similar to the challenges faced by orphan drugs; the evidence itself often contains many uncertainties, and the long-term clinical benefit is regularly uncertain. DMC is willing to accept surrogate outcomes if a clinically important outcome is not available; however, confidence in the evidence is graded lower than conventional endpoints. According to DMC, "*the reason for this is that the evidence is indirect and it is not 100% certain that the surrogate effect predicts the clinical effect.*" This puts ATMPs at a disadvantage in the assessment process and leaves little flexibility for the evidence that ATMPs can generate.

Proposed solution AS1:

Key changes to assessment in Denmark are planned for the near future to address ATMP assessment.

There are three key changes currently planned for the assessment process in Denmark to take effect from the second quarter of 2020 that will impact ATMPs:

- Better acceptance of non-published data
- Implementation of QALYs as an assessment measure
- A clear assessment process for ATMPs to undergo

While these proposed changes signal an intention to improve patient access to ATMPs, there are uncertainties over how these reforms will work in practice. The existing process of the DMC will be

amended to consider the evidence that can be generated with ATMPs at launch. As the assessment methods stand, the confidence level in surrogate endpoints for ATMPs must be downgraded, which impacts the overall assessment of added clinical value. In cases of high unmet need, severe disease, lack of comparators, etc., allowances should be developed for assessment outside of conventional methods, which may occur when the expected changes are implemented. Acceptance of alternative methods and evidence for ATMPs has been successfully applied in other countries. It primarily requires political will to make amendments to the assessment process to account for the required flexibility, which Denmark appears to currently be in the process of.

Feasibility: +++
Stakeholders: DMC
Timeframe: Immediate

Challenge AS2.

DMC evidence requirements are clearly outlined, but a product achieves added clinical value only if a minimal clinically important difference is demonstrated.

DMC evidence requirements are clearly outlined. For a positive recommendation, products must achieve category 1-3 (added clinical value). This is only possible if a minimal clinically important difference (pre-defined by the DMC in the protocol) is demonstrated. This can be a difficult goal for ATMPs to reach, as clinically relevant outcomes are not always available and surrogate outcomes are often relied upon. The challenges this poses for ATMPs has been seen, for instance, in the case of CAR-T for lymphoma indications, which were both rejected because of a failure to meet the DMC evidence requirements.

Proposed solution AS2.

Adjust evidence requirements and include patients when defining minimal clinically important differences for ATMPs - these may be taken into account in the upcoming changes.

The minimum requirement of a 'clinically importance difference' should be adjusted for ATMPs, to better reflect what they can demonstrate at the time of assessment. It is understood that defining a clinically important difference is a difficult process and no universally accepted method exists. If the DMC intend to keep this as part of the process for ATMPs, early and routine discussion with patients, specialist physicians and manufacturers will be required to aid ATMPs in achieving an added clinical value (category 1-3) and be made available to patients. It is possible that this may be taken into account within the expected assessment changes.

Feasibility: **++**
Stakeholders: DMC, patient associations and clinical experts
Timeframe: Immediate

Challenge AS3.

Clarity is still needed on the assessment changes in terms how they will be implemented and what will actually change.

There remains a need for clarity regarding the planned assessment changes for ATMPs in Denmark. That is, how these changes will look and how they will be implemented is still unclear.

Proposed solution AS3.

Clarity should be requested on anticipated amendment and the implications of not changing should be communicated, to ensure changes are successfully made.

Requests should be made to provide information and clarity on the planned changes in terms of what the framework will look like, within what timelines the changes will be carried out, what will actually change and how. To better ensure successful implementation and uptake of the planned changes, future implications of *not* making such changes should be communicated.

Feasibility: **+++**
Stakeholders: DMC, trade association
Timeframe: Immediate

AFFORDABILITY

Impact: 

Challenge		Proposed solution		Feasibility
AF1.	Affordability issues arise when individual hospitals are responsible for delivering specialist treatment	**AF1a.**	Innovative payment models could alleviate the burden of up-front payments	+
		AF1b.	A secure specialist fund for ATMPs to reduce burden on individual hospitals	+
AF2.	Higher logistical demands associated with ATMP administration: patients require additional outpatient appointments which adds costs and affects budget impact	**AF2.**	Collect data from early access programme to determine what should be included in the model for assessment	++

The Working Group assessment of the **impact** of the challenge relate to all challenges in each domain. The Working Group assessment of **feasibility** relates to the individual or groups of proposed solutions.

Working group identified challenges:

Challenge AF1.

Affordability issues arise when individual hospitals are responsible for delivering specialist treatment.

Affordability issues arise when individual hospitals are responsible for delivering specialist treatment. Specialist prescribed products such as ATMPs are funded by hospitals, and the use of such products is likely to be restricted to a single hospital, meaning affordability will be a significant challenge for these individual hospitals.

Proposed solution AF1a.

Innovative payment models could alleviate the burden of up-front payments.

The reimbursement environment needs to be managed to ensure expenditure is sustainable. Barriers to annuity payments (a series of periodic payments) due to legislative or accounting standards need to be confirmed. By addressing these barriers, it is easier for payers to allocate investment over a patient's life. For instance, annuity payments could help spread the cost of ATMPs over multiple years and better align expenditure and health gain.

Modifying annuity payment models to account for evidential uncertainty could be part of a risk-sharing programme with manufacturers. Outcome-based schemes could be established as a type of innovative funding scheme. Schemes used in other member states could provide examples of how ATMPs could be reimbursed in Denmark. For example, in countries such as Italy, Germany and Spain, Kymriah is reimbursed using an innovative 'payment at result' model. This model also looks to manage clinical uncertainty by requiring the manufacturer to repay treatment costs for patients who do not respond to treatment. Proposing solutions such as these may help in overcoming affordability issues at the hospital level.

Feasibility: +
Stakeholders: DMC, trade associations, individual companies
Timeframe: Immediate

Proposed solution AF1b.

A secure specialist fund for ATMPs to reduce burden on individual hospitals.

Although historically in Denmark financial agreements have focused on budget caps and tenders, there is now a preference for financially innovative solutions. An additional possible solution is to establish a specialist fund for ATMPs. This has been done in other countries and although the sustainability of a specialist fund is uncertain, it may offer a possibility for managing the affordability burden on individual hospitals, particularly if innovative arrangements can be made to better ensure the security of such a fund.

Feasibility: **+**
Stakeholders: DMC, trade association
Timeframe: Immediate

Challenge AF2.

Higher logistical demands associated with ATMP administration: patients require additional outpatient appointments which adds costs and affects budget impact.

ATMP administration poses logistical and cost demands on its own. Patients require additional outpatient appointments, which both adds costs and affects the budget impact (including extended and uncertain treatment costs). There is also a lack of clarity about exactly what additional costs the treatment might incur and how these might be paid for.

Proposed solution AF2.

Collect data from early access programme to determine what should be included in the model for assessment.

ATMPs could be made available through early access programmes that are already in place in Denmark. These programmes will provide greater insight into the associated administration costs that can be factored into reimbursement decisions.

Furthermore, in the assessment of Kymriah, administration, hospitalisation, and all tariffs for surgical procedures and monthly follow-up costs were included in the assessment. Including as much detail as possible in the model to be assessed by AMGROS can help make a better-informed decision.

Feasibility: **++**
Stakeholders: Individual companies. AMGROS, DMC
Timeframe: 6–18 months

AVAILABILITY

Impact: 

Challenge		Proposed solution		Feasibility
AV1.	The outlook of physicians in Denmark emphasises a need for socioeconomic responsibility beyond advice from AMGROS	**AV1.**	Early communication with physicians around benefit of ATMPs	+++
AV2.	Patients have received access to treatment via cross-border initiatives – it is uncertain if patients will receive the same level of cross-border access to ATMPs	**AV2.**	Denmark is involved in cross-border agreements which are not a challenge; but rationale for cross-border treatment will be required	+++

The working group assessment of the **impact** of the challenge relate to all challenges in each domain. The working group assessment of **feasibility** relates to the individual or groups of proposed solutions.

Working Group identified availability challenges

Challenge AV1.

The outlook of physicians in Denmark emphasises a need for socioeconomic responsibility beyond advice from AMGROS.

Although the availability of ATMP treatments for patients with rare diseases in Denmark does not pose a significant challenge, the outlook of physicians emphasises a need for socioeconomic responsibility beyond advice from AMGROS, to ensure that there is adequate support not just for product availability, but also for effective product administration and delivery.

Proposed solution AV1.

Early communication with physicians around benefit of ATMPs.

Early education and communication regarding ATMP benefit should be carried out with all stakeholders involved (patients, doctors, health insurance, etc.) in the assessment and administration of ATMPs. This could make the benefits of these treatments better understood. This education and communication should be provided through trade associations to avoid bias with speaking with a single manufacturer.

Since many health institutes may not be adequately equipped to deliver ATMPs, and health professionals may not have the required expertise, processes must be in place to ensure that the infrastructure and knowledge is present to sustain the ability to make ATMPs available in a safe and effective manner. Education is not innovative or especially costly, making it a feasible and necessary step in the process to ensure the benefit of ATMPs is understood and received.

Feasibility: +++
Stakeholders: DMC, clinical experts, patient associations, trade association
Timeframe: Immediate

Challenge AV2.

Patients have received access to treatment via cross-border initiatives – it is uncertain if patients will receive the same level of cross-border access to ATMPs.

Patients have received access to treatment via cross-border initiatives, but it is uncertain if patients will receive the same level of cross-border access to ATMPs.

Proposed solution AV2.

Denmark is involved in cross-border agreements which are not a challenge; but rationale for cross-border treatment will be required.

Denmark is actively participating in cross-border treatment agreements (e.g., Nordic Council) to share costs and to develop expertise in ATMPs which supports availability of ATMPs. Cross-border treatments are not seen as a challenge in and of themselves, but a rationale is required when cross-border treatment is sought, to ensure the choice of such treatment is valid and accepted within the regulations. Guidelines to standardise the approach to providing access specifically to ATMPs in cross border scenarios, included the details of the required rationale, would benefit patients and remove uncertainty over availability.

Feasibility: **+++**
Stakeholders: Ministry of Health, patient associations
Timeframe: Immediate

ACCESSIBILITY

Impact: 

Challenge		Proposed solution		Feasibility
AC1.	Denmark has a network of specialist centres that are capable of treating patients with ATMPs; however, there will be a burden of reconfiguring services for these treatments	**AC2.**	Configure services for ATMPs by identifying infrastructure/services that can be reconfigured and having built-in service preparation requirements in a joint horizon scanning process	++

The Working Group assessment of the **impact and importance** of the challenge relate to all challenges in each domain. The Working Group assessment of **feasibility** relates to the individual or groups of proposed solutions.

Working Group identified accessibility challenges

Challenge AC1.

Denmark has a network of specialist centres that are capable of treating patients with ATMPs; however, there will be a burden of reconfiguring services for these treatments.

Accessibility does not pose a large challenge, as Denmark has a network of specialist centres that are capable of treating patients with ATMPs. There is, however, a burden of reconfiguring services for ATMP treatments that will be felt by a small number of centres.

Proposed solution AC1.

Configure services for ATMPs by identifying infrastructure/services that can be reconfigured and having built-in service preparation requirements in a joint horizon scanning process.

Denmark is well-placed to configure its services to allow access to ATMPs. Built-in service preparation requirements in the horizon scanning process would better prepare centres for managing the delivery of ATMPs. Joint horizon scanning – if possible, at the Nordic level – should identify resource and infrastructure needs of future ATMPs treatments. The aim of such joint horizon scanning activity is to ensure strong preparation across regions.

A related process is to identify infrastructure and/or services that can be reconfigured for ATMPs. Existing infrastructure and services that are not yet configured for ATMP administration, but could be, should be systematically identified and evaluated in terms of the resources needed to reconfigure them to accommodate ATMP administration. Identifying the resource needs for ATMPs in advance may proactively ensure that patient access is not delayed at the time of launch.

Feasibility: ++
Stakeholders: DMC
Timeframe: Immediate

Bibliography

AMGROS. Joint Nordic Procurement (Denmark, Norway and Iceland). Information and dialogue meeting. Available from: https://www.landspitali.is/library/Sameiginlegar-skrar/Gagnasafn/Stodsvid/Fjarmalasvid/Innkaupadeild/Joint%20NordicTender-Information%20meeting%2028thofSeptember%202018.pdf

AMGROS. Implementing QALY is a natural next step. Available from: https://amgros.dk/en/knowledge-and-analyses/articles/implementing-qaly-is-a-natural-next-step/. Accessed: December 2019

AMGROS. Kymriah. Available from: https://www.amgros.dk/media/1862/afrapportering-kymriah-dlbcl.pdf

Balasubramanian G., et al. An overview of Compassionate Use Programs in the European Union member states. *Intractable & Rare disease Research.* 2016 Nov; 5(4): 244–254. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5116859/

Danish Medicines Council. Process and methods guide – how the Danish Medicines Council develops joint regional assessments of the added clinical value of new medicines and new indications. Version 1.1. Available from: https://medicinraadet.dk/media/5139/process-and-methods-guide-join-regional-assessment-of-the-clinical-added-value-of-new-medicines-and-indications-002.pdf

Joint Nordic Procurement. Available from: http://old.amgros.dk/en/areas/nordic-collaboration/joint-nordic-procurement/

Stoner, N. Are UK hospital pharmacy departments ready for the rise of gene therapy medicinal products? *Expert Opinion on Biological Therapy.* 2018 18(8): 837-840. Available from: https://www.tandfonline.com/doi/full/10.1080/14712598.2018.1495192

Sykehusinnkjop. Joint Nordic Procurement. Available from: https://sykehusinnkjop.no/joint-nordic-procurement

Two Scenarios. Update on the Danish Medicines Council and Nordic joint procurement. Slideshow presentation. June 2018.

Appendix

Country profile

Market type	Budget impact analysis
Position in launch sequence	Early
Previous experience with ATMPs	Unknown

	Status	Note
Strimvelis	Not evaluated	
Holoclar	Recommended[1]	
Zalmoxis	Not evaluated	
Glybera	Not evaluated	
Imlygic	Not evaluated	
Provenge	Not evaluated	
MACI	Not evaluated	
ChondroCelect	Not evaluated	
Yescarta	Not recommended in DLBCL[2]	
Kymriah	Recommended[3]	Alternative pricing agreement. Limited number of patients[3]
Alofisel	Not recommended[4]	
Luxturna	Not recommended[5]	
Zolgensma	Not evaluated	
Zynteglo	Not evaluated	

[1] DMC. Holoclar. Available from: https://medicinraadet.dk/media/10022/medicinraadets-anbefaling-vedroerende-holoclar-til-limbal-stamcellemangel_vers10.pdf

[2] DMC. Yescarta. Available from: https://medicinraadet.dk/media/11379/medicinraadets-anbefaling-vedr-axicabtagene-ciloleucel-til-diffust-storcellet-b-celle-lymfom-vers-10.pdf

[3] DMC. Kymriah. Available from: https://www.amgros.dk/media/1861/beslutningsgrundlag-dlbcl-kymriah.pdf

[4] DMC. Alofisel. Available from: https://medicinraadet.dk/media/12226/medicinraadets-anbefaling-vedr-voretigene-neparvovec-til-arvelig-rpe65-relateret-nethindedystrofi-vers-10.pdf

[5] DMC. Luxturna. Available from: https://medicinraadet.dk/media/12226/medicinraadets-anbefaling-vedr-voretigene-neparvovec-til-arvelig-rpe65-relateret-nethindedystrofi-vers-10.pdf