DOLON

Nordic Rare Disease Summit - An Assessment of Alignment of P&R Systems with ORPH-VAL Principles

Final Report

March 2021

Report content

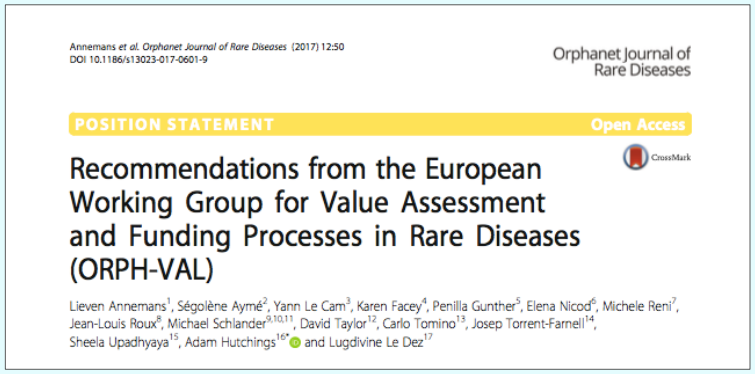
- Background & methodology
- Cross-country summary and recommendations
- Nordic countries summary and recommendations
- Baltic countries top-line summary
- Appendix – detailed country assessments

Project context

Background

- Takeda is planning a **Nordic Rare Disease Summit** to help improve patient access to rare disease treatments (RDTs)
- The Summit will bring together **patient associations, policy makers, physicians and payers/economists**
- As part of this Summit, Takeda would like to present an assessment of the alignment of Nordic P&R systems for RDTs with the ORPH-VAL principles, as a way of generating discussion on opportunities to improve access

ORPH-VAL initiative



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Orphanet Journal of Rare Diseases

POSITION STATEMENT — Open Access

Recommendations from the European Working Group for Value Assessment and Funding Processes in Rare Diseases (ORPH-VAL)

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- ✓ ORPH-VAL published in the Orphanet Journal of Rare Diseases in March 2017
- ✓ 9 Principles developed to improve patient access to RDTs through greater consistency in P&R processes in Europe

Project methodology

1 **Review (2018)**

In-depth review of ORPH-VAL principles vs. current P&R systems in:

- Sweden, Norway, Denmark & Finland
- Iceland and Baltics

2 **Validation (2018)**

Two-step validation of the assessment with:

- local P&R experts within the company
- payers in the individual Nordic countries

3 **Report**

High-level summaries of country assessments and recommendations that can be leveraged for the Summit

4 **2020 and 2021updates**

Report update with changes to current P&R systems in Sweden, Norway, Denmark and Finland via desk research, interviews and consultation with P&R experts – occurred in February 2020 and February 2021

5 **Summit**

Present the analysis at the Nordic Rare Disease Summit, with the involvement of a member of the ORPH-VAL Working Group

Possible future work

- Publication of findings to disseminate results to a broader audience
- Dissemination activities targeting key stakeholders (e.g. conferences, roundtables)
- Benchmark of principles with reimbursement decisions in individual countries

Project limitations

- In the 2018 assessment, insights were validated with external payers during the review phase, but payers were not asked to endorse final recommendations
- The application of the recommendations made for the Nordic countries are to be interpreted in their own context
- The abbreviated assessment performed for the Baltic countries relies on desk research only

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Overview of Nordic country pricing and reimbursement systems for RDTs

- The way RDTs are assessed depends whether they are delivered in the inpatient (hospital) vs outpatient setting
  - In **Denmark** and **Norway**, RDTs go through the hospital route only
  - In **Sweden**, and **Finland**, RDTs can be assessed through either route. The HTA process and responsible bodies differ depending on which route is used
- Regardless of the delivery setting, there is no formal distinction between RDT and non-RDT assessment in any of the Nordic countries. Denmark recognises that some medicines, such as RDTs, often have 'sparse evidence', but this recognition had little or no practical consequences
- P&R processes in **Sweden, Norway and Finland** all use a cost-effectiveness approach (cost/QALY) with no fixed threshold
  - **Sweden and Finland** are flexible in their willingness to pay (WTP) for ultra RDTs and may accept higher ICERs
  - **Norway** also has flexibility in WTP for RDTs, but in practice often rejects RDTs due to lack of cost-effectiveness
- As of Jan 1, 2021, the process in **Denmark** changed from a clinical benefit evaluation to a cost/QALY system
- In **Sweden**, **Finland** and **Denmark**, some aspects of rarity are indirectly considered, for example, product value is considered in light of disease severity and/or unmet need, which is often strongly correlated with rarity in those diseases
- In **Finland** and **Denmark**, RDTs are funded nationally, while in **Sweden** funding is national or regional depending on the route selected for assessment. In **Norway**, RDT funding has recently been shifted to hospitals

Possible areas for improvements in the Nordic countries

1

Value assessment processes should consider all RDT specificities in a consistent way

- More comprehensive decision-making framework including all relevant criteria for RDTs
- More formalised and consistent consideration of these criteria through separate RDT pathways or special criteria, including better guidance on weight of criteria on decisions
- Better documentation of processes including reasons for decisions (weight of criteria on decisions, deliberative processes)

2

More consistent disease-specific expertise should be incorporated in current processes

- Involvement of disease-specific expertise to provide knowledge on clinical data and pathways, and patient experiences, preferences, needs and values
- More formal and consistent integration of clinician and patient perspectives in the appraisal and decision-making

3

RDT assessment processes should be adaptive and subject to the need and availability of information over time

- Processes should allow review of decisions over time
- Decisions should be able to move up and down with new evidence
- Use of real-world evidence when reviewing decisions, preferably via supra-national registries
- Clarity around roles and responsibilities of all parties involved in the pathway

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Country deep dive - Sweden

- P&R process for rare diseases treatments in Sweden
- Overview of country alignment with 9 principles
- Area of improvements & recommendations

P&R processes in Sweden

OUTPATIENT	INPATIENT
• TLV is the HTA body that makes reimbursement decisions for outpatient drugs (national positive list), which are to be implemented across the 21 regions • Value-based pricing system (human value, needs & solidarity, cost-effectiveness) is in place. There is no fixed threshold; willingness to pay (WTP) increases with disease severity • No special status for RDTs, except for new criteria for ultra-RDTs (very effective, very severe, very rare), where a higher WTP would be accepted	• Most inpatient drugs are procured by the regions (through tenders), no national list or prices exist as this is done at a regional level • Council for New Therapies (NT Council) supports health authorities in making informed decisions. They may request TLV to conduct HTA for a drug. The same methods are used as for outpatient. The NT Council then evaluates the assessment and makes recommendations to the regions • Some drugs undergo three-party negotiations, where negotiations take place between the manufacturer and NT Council, resulting in recommendations at different price levels or a side agreement (e.g. discount)

Key takeaways for rare disease treatments

- RDTs are prescribed both outpatient and inpatient
- Increasingly, TLV is conducting HTA for NT Council to inform inpatient drug reimbursement recommendations (80% oncology treatments)
- TLV's HTA process is increasingly more central to reimbursement decisions for inpatient and outpatient drugs

9 PRINCIPLES – ALIGNMENT IN SWEDEN	Outpatient	Inpatient
Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework	✓✓	✓ - ✓✓*
Principle 2: Pricing and reimbursement decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value	✓✓✓	✓ - ✓✓✓*
Principle 3: All official regulatory and health technology assessments of OMPs undertaken at the European level should be acknowledged by national health authorities	✓✓✓	✓✓
Principle 4: The assessment and appraisal of OMPs in Europe should incorporate rare disease expertise including both the healthcare professionals' and patients' perspectives	✓✓	✓✓
Principle 5: To accommodate uncertainty, value assessment and pricing and reimbursement decisions should be adaptive subject to the need and availability of information over time.	✓✓	NA
Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations	✓✓✓	✓✓✓
Principle 7: Funding should be provided at the national level to ensure patient access to OMPs	✓✓ - ✓✓✓	✓ - ✓✓*
Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability	✓✓	✓✓
Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level	✓	NA

** Greater alignment if P&R decision relies on an HTA by TLV*

Recommendation 1: Value assessment processes should consider all RDT specificities in a consistent way

CURRENT STATUS → **RECOMMENDATION**

Value based system which accounts for disease severity

- Value-based system with cost-effectiveness assessment based on cost/QALY, with no fixed threshold
- Willingness to pay (WTP) increases with disease severity
  - No special status for RDTs, but higher WTP accepted for ultra-RDTs (very effective, very severe, very rare)
- TLV's approach captures patient, healthcare and societal perspectives
- However, there is limited consideration of criteria that are not quantified or measured with reliable instruments,
  - e.g. treatment convenience requires strong evidence of value, or aspects such as family/carer burden are typically considered not reliable

Greater & consistent consideration of multiple criteria relevant for RDTs

- Steps are being taken via discussions between TLV, NT council and manufacturers to improve the deliberative processes, but more consistent consideration of relevant criteria is still needed for all RDTs
- Better documentation of deliberative processes and the influence of different criteria on decision are needed
- Development of a more comprehensive decision-making/appraisal framework is required for RDTs to ensure relevant criteria are considered **consistently**

Recommendation 2: Disease-specific expertise should be formally and consistently considered in pricing and reimbursement processes

CURRENT STATUS → **RECOMMENDATION**

Disease-specific expertise is consulted, but not consistently

- Feedback is collected from clinical experts and discussed during appraisal meetings
- Clinicians are consulted when needed to provide information about uncertainty, but are not given the possibility to provide their own perspective, including their preferences, values and needs
- There are initiatives aiming to increase patient involvement in decision making, but currently patient involvement is limited
- There are patient representatives on TLV board, but they are not disease specific

Formal & consistent consideration of disease-specific expertise

- Generally, better documentation of the influence and impact of clinicians' and patients' expertise on decisions is needed
- More formal and consistent process for patient input (e.g. patient submissions) is required
- Consideration of patient experiences, preferences, needs and values would be valuable

Recommendation 3: RDT assessment processes should be adaptive and subject to the need and availability of information over time

CURRENT STATUS → **RECOMMENDATION**

Little revision of decisions over time or when new evidence is available; only for limited cases

- Re-introduction by TLV of conditional approval processes, with 1-3 years re-assessments relying on real-world evidence, however, this is not preferred by TLV and is fairly uncommon
- Review of decisions done for limited cases, e.g. therapeutics areas with high a budget impact

More adaptive and continuous process

- More consistent review of P&R decisions over time and when new evidence becomes available
- Review of P&R decisions should allow movement up and down with new evidence on value
- Use of, preferably supra-national, real-world evidence

Country deep dive - Denmark

- P&R process for rare diseases treatments in Denmark
- Overview of country alignment with 9 principles
- Area of improvements & recommendations

P&R processes in Denmark

OUTPATIENT (primary care)	INPATIENT (hospital)
• Danish Medicines Agency (DMA) is in charge of outpatient (primary care sector) funding decisions • Criteria: Safe and valuable therapeutic effect in indication; reasonable price in relation to therapeutic value • Reimbursed products are included on a positive list • Manufacturer sets medicines prices, agreements are in place between LIF (industry association) and Danish Health Ministry to cap prices	• Danish Medicines Council (DMC) is in charge of inpatient and hospital outpatient funding decisions • DMC has full ability to decide on assessment process, then produces assessment report with recommendation following negotiation • Amgros negotiates prices and purchases pharmaceutical products on behalf of the 5 regions for public hospital products • All specialised/expensive drugs go through hospitals

Key takeaways for rare disease treatments

- All RDTs are assessed through the inpatient setting (hospital products) *(This analysis focuses on the DMC process)*
- Three-step process where DMC assesses the HTA submission, followed by a price negotiation with Amgros, and a final decision by DMC regarding whether or not to accept the price
- There is no difference between the assessment of RDTs and non-RDTs, although DMC includes the possibility to account for disease severity in its assessment. It also recognises that some treatments such as RDTs often have sparse evidence due to the nature of the disease, but the impact of this recognition is unclear

Alignment in Denmark

9 PRINCIPLES – ALIGNMENT IN DENMARK	Inpatient
Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework	✓✓
Principle 2: Pricing and reimbursement decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value	✓ - ✓✓
Principle 3: All official regulatory and health technology assessments of OMPs undertaken at the European level should be acknowledged by national health authorities	✓✓
Principle 4: The assessment and appraisal of OMPs in Europe should incorporate rare disease expertise including both the healthcare professionals' and patients' perspectives	✓✓✓
Principle 5: To accommodate uncertainty, value assessment and pricing and reimbursement decisions should be adaptive subject to the need and availability of information over time.	✓✓
Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations	✓✓- ✓✓✓
Principle 7: Funding should be provided at the national level to ensure patient access to OMPs	✓✓
Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability	✓✓ - ✓✓✓
Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level	✓

Recommendation 1: Value assessment processes should better account for RDT specificities

CURRENT STATUS → **RECOMMENDATION**

No formal distinction between RDTs and non-RDTs, but possibility for companies to argue that QALY procedure should not be followed

- RDTs may go through a QALY-based assessment, or a more analytical assessment if QALY is not appropriate – for this manufacturers need a good rationale for why QALY is not appropriate
- There is recognition of severity in assessment criteria, but lack of clarity on its importance for final decision
- Rarity is not formally accounted for, but severity is somewhat correlated to rarity
- The wider societal impact of RDs and RDTs are not considered

Adjustment of P&R decisions based on RDT specificities

- More clarity is still needed around what the analytical assessment entails, when the QALY assessment is not appropriate
- Consideration of uncertainty is recommended in light of disease prevalence and the level of existing knowledge and evidence about the disease
- There could be better recognition of higher QALY-level for RDTs
- There could be inclusion of specific criteria in decision making (rarity, severity alternative treatment options, productivity)

Recommendation 2: Value assessment process should be more transparent

CURRENT STATUS → **RECOMMENDATION**

New assessment process (QALY)for hospital products, but lack of clarity around weight of criteria on decisions/impact on pricing	More transparent and documented process still needed
• QALY system and alternative analytic path introduced in January 2021 • Possibility for company to argue that a product cannot be assessed through the QALY system, but limited description of what alternative assessment would entail • It is not clear how disease severity impacts the evaluation and final reimbursement decision • There is a lack of clarity around protocolled use of RDTs (i.e. Value based contracts)	• Transparent and clear documentation on definition of assessment criteria • Better guidance on the relative importance/weight of value elements in the assessment of RDTs • The changes to a QALY system call for transparency about case processing time, and better treatment guidelines. This could be extended to assessment criteria for RDTs

Recommendation 3: The requirements behind adaptive assessment processes should be clearly documented

CURRENT STATUS → **RECOMMENDATION**

Coverage with further evidence Informal and unclear process

- Conditional reimbursement is possible provided new data is submitted
- Review of new evidence is done on a case-by-case basis
- There is no formal guidance on the process or the requirements behind conditional reimbursement
- RWE is not consistently used in assessment processes

Transparent and documented adaptive process

- Clear guidance is needed on the requirements for new evidence generation and how this will be used in and impact funding decisions
- There is a need to support early access to RDTs through a well-defined, formal approach to protocolled use or managed entry, in which all parties understand their role and responsibilities
- As the DMC now has full competence to decide on the assessment process, such guidance could be a point of consideration

Country deep dive - Norway

- P&R process for rare diseases treatments in Norway
- Overview of country alignment with 9 principles
- Area of improvements & recommendations

P&R processes in Norway

NATIONAL FUNDING

- NOMA makes decisions on reimbursement by the National Insurance Scheme (NIS)
- Decision-making prioritisation criteria: severity, utility, resources use + modifiers (budget impact and certainty)
- No fixed ICER threshold, WTP increases with disease severity and modifiers
- Price: max reimbursement price set by NOMA based on IRP (= official price). Actual price may include a confidential discount after price negotiations, same negotiator as inpatient (CEA recalculated with new price)
- NOMA cannot decide for drugs with a greater budget impact of NOK 100 million, in which case decision is to be made by the Parliament

HOSPITAL FUNDING

- As of 01.02.2019: all RDTs undergo the hospital route, covered by hospital budgets. The ministry of health allocates funds to regional health authorities (RHAs), which fund hospitals; hospitals are responsible for managing their budgets
- NOMA makes recommendations to the Decision Forum, who decide for the whole country
- Recommendation for tender (if existing national tenders, no CEA) or price negotiations
- Price negotiation is not required and price setting process is not clear. If price negotiation is undertaken, CEA is recalculated with new price and negotiators include note to decision forum
- Decision forum decides (and can go against NOMA's recommendation, if e.g. budget insufficient)

Key takeaways for rare disease treatments

- Within the hospital funding route, RDTs are prescribed for both outpatient and inpatient
- HTA by NOMA is central to reimbursement as it informs the hospital funding processes, and makes recommendations to the Decision Forum

9 PRINCIPLES – ALIGNMENT IN NORWAY	HOSPITAL FUNDING
Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework	✓
Principle 2: Pricing and reimbursement decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value	✓
Principle 3: All official regulatory and health technology assessments of OMPs undertaken at the European level should be acknowledged by national health authorities	✓✓
Principle 4: The assessment and appraisal of OMPs in Europe should incorporate rare disease expertise including both the healthcare professionals' and patients' perspectives	✓✓
Principle 5: To accommodate uncertainty, value assessment and pricing and reimbursement decisions should be adaptive subject to the need and availability of information over time.	✓
Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although decisions on access may apply to different sub-populations	✓✓✓
Principle 7: Funding should be provided at the national level to ensure patient access to OMPs	✓✓
Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability.	✓
Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level	✓✓

✓ Limited alignment ✓✓ Somewhat aligned ✓✓✓ Mostly aligned

Recommendation 1: Value assessment processes should consider all relevant elements to account for RDT specificities

CURRENT STATUS → **RECOMMENDATION**

No special RDT path in HTA or systematic consideration of additional criteria for RDTs

- There is no specific appraisal process for RDTs
- HTA approach captures healthcare perspectives in terms of direct costs, using the same appraisal process as for conventional medicines
- Limited consideration of societal and other perspectives, or additional criteria that may be particularly relevant for RDT specificities
- Recognition of high uncertainty around RDTs and greater WTP officially, but often not seen in practice
- Cost-effectiveness model often rejected because typical RDT challenges make it inappropriate

Special RDT process with consistent consideration of multiple criteria

- There is a need for a separate assessment process if possible, or process enabling consideration of RDT specificities
- Process should include a more comprehensive decision-making/appraisal framework for RDTs to ensure relevant criteria are considered consistently
- Including adaptive processes (e.g. outcome-based agreements) can help manage RDT specificities

Recommendation 2: Disease-specific expertise should be formally and consistently considered and documented in P&R processes

CURRENT STATUS → **RECOMMENDATION**

Disease-specific expertise is consulted to some extent, but no formal process for patient input

- Clinical experts are consulted by NOMA during the appraisal process, but they are not substantially involved in the decision-making process
- NOMA accepts patient submissions and does consult patients, but not formally
- NOMA started an internal working group about how to use patient evidence in the decision processes

Formal and consistent consideration of disease-specific expertise

- Better documentation of the influence of expertise on decision, and involvement of experts in the decision-making process is needed
- More formal and consistent process for patient input (e.g. patient submissions), including consideration of patient experiences, preferences, needs and values

Recommendation 3: A national funding system for RDTs can better ensure equal patient access

CURRENT STATUS → **RECOMMENDATION**

All RDTs go through hospital route, but RDT access may be at risk with regional funding

- National funding is distributed among regions; decision is made nationally, but funding is at regional level (hospitals)
- Hospitals are responsible for their own budgets; mainly based on budget impact and previous year expenditure. Not earmarked for RDTs
- Equal patient access across regions is not guaranteed

Arrangement of a national funding system for RDTs

- Coordination of funding at the national level can avoid disparate access across regions
- Coordination of national funding for RDTs from a normal healthcare budget is recommended (not earmarked) to better ensure long-term sustainability

Country deep dive – Finland

- P&R process for rare diseases treatments in Finland
- Overview of country alignment with 9 principles
- Area of improvements & recommendations

P&R processes in Finland

OUTPATIENT

- HILA grants reimbursement and a reasonable wholesale price of medicinal products under the Health Insurance Act for outpatient products (usually oral products)
- HILA grants national reimbursement, hence products can be used all over Finland
- Assessment of cost-effectiveness but no formal ICER threshold
- Continuing legislation that began three years ago has allowed the option of confidential mid level discussions/risk sharing agreements. Manufacturer can request this option if considerable uncertainty exists, pricing board decides whether or not to accept. No clear criteria for acceptance, can depend, e.g., on unmet need

INPATIENT

- Fimea, the Finnish medicines agency conducts HTA for hospital only products (usually IV products)
- Rapid HTA assessment: starts at the time of CHMP approval and Fimea's recommendation (not binding) is typically provided at the time of marketing authorisation by the European Commission
- Hospitals make their own decisions to fund products
- Local assessment bodies within university hospitals do mini HTAs; this is relevant for permission to start using product in a hospital
- COHERE is a national body that was making recommendations to include or exclude products in the range of public health services, but mandate is currently not that clear
- There has been some movement in recent years to re-consider which agencies conduct assessments on which products

Key takeaways for rare disease treatments

- Overall, there is no differentiation in the assessment process between RDTs and non RDTs
- HILA and Fimea are independent bodies. RDTs can be assessed through either the outpatient or inpatient route; it is not clear beforehand which route they will go through or which body will assess the product

9 PRINCIPLES – ALIGNMENT IN FINLAND	Outpatient	Inpatient
Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework	✓✓	✓✓
Principle 2: Pricing and reimbursement decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value	✓✓	✓✓
Principle 3: All official regulatory and health technology assessments of OMPs undertaken at the European level should be acknowledged by national health authorities	✓✓✓	✓✓✓
Principle 4: The assessment and appraisal of OMPs in Europe should incorporate rare disease expertise including both the healthcare professionals' and patients' perspectives	✓✓✓	✓✓
Principle 5: To accommodate uncertainty, value assessment and pricing and reimbursement decisions should be adaptive subject to the need and availability of information over time.	✓✓	✓✓
Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations	✓✓✓	✓✓
Principle 7: Funding should be provided at the national level to ensure patient access to OMPs	✓✓✓	✓✓
Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability	✓✓	✓✓
Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level	✓✓	✓✓

Recommendation 1: Value assessment processes should consider all RDT specificities in a consistent way

CURRENT STATUS → **RECOMMENDATION**

Rare disease specificities accounted for informally, but not all relevant elements of value may be considered

- Overall product value is considered in light of disease severity and prevalence by Fimea
- Rarity not explicitly considered, but other elements of value beyond patient and healthcare perspective are considered if they pose a challenge or have significant impact (e.g. unmet medical need)
- A higher willingness to pay may be considered for RDTs

Greater and consistent consideration of multiple criteria relevant for RDTs

- Development of a more comprehensive decision-making framework for RDTs to ensure relevant criteria are considered consistently within the standard assessment pathway, e.g having special criteria for RDTs
- Good documentation of the deliberative process and influence of different criteria (i.e. severity) on decision is needed

Recommendation 2: Both clinician and patient expertise should be integrated in product assessments

CURRENT STATUS → **RECOMMENDATION**

Disease-specific expertise is consulted to some extent, but patient input is limited and not integrated in assessment	Integration of patients' input in product assessments
• There is a strong integration of clinicians' perspective in Fimea's assessment • Patients are not consulted by Fimea in product assessments • Patient voice is generally not sufficiently incorporated	• Both clinicians' and patients' perspectives should be collected consistently and reviewed during product assessments • Formal and consistent process for patient input could supplement clinicians' input (e.g. patient submissions)

Recommendation 3: RDT assessment processes should be adaptive and subject to the need and availability of information over time

CURRENT STATUS → **RECOMMENDATION**

Product re-assessments sometimes occur, but generally few adaptive processes exist to manage evidentiary uncertainty

- On rare occasions, a new application can be submitted for product re-evaluation if significant change in usage or new evidence is provided
- Fimea's guidelines refer to better collection and use of RWE
- Uncertainty around certain clinical outcomes is considered informally in product assessments
- Outcome-based agreements are being used, but still face a learning curve for how and when to best implement them

More adaptive and continuous process

- Adaptive and continuous processes over time should be consistently applied in FIMEA's HTA for RDTs
- Better collection and integration of RWE, (not necessarily formalised), could be more often incorporated in HTA process
- Good collaboration between manufacturers and payers can enable high quality communication for successful adaptive processes

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The Baltic countries

- Latvia
- Estonia
- Lithuania
- Iceland

P&R processes in Latvia

OUTPATIENT	INPATIENT
• NHS is responsible for P&R decisions, HTA, and implementing reimbursement decisions of drugs through inclusion on a positive list for outpatient care and definition of positive lists for inpatient use • Appraisal criteria: burden of disease, added benefit, correspondence to treatment schemes, cost-effectiveness, budget impact • Different reimbursement categories depending on disease area (nature of disease and severity) • No ICER threshold. The ICER (cost/additional life-year gained) should not exceed the ICER for other drugs and devices already included in positive list • Price negotiation between NHS and manufacturer, criteria include prices in other countries and cost-effectiveness	• Inpatient drugs are included in the cost of inpatient services and are provided free of charge • The positive list and price of inpatient drugs are determined by the NHS • Hospitals purchase medicines from wholesalers or pharmacies. Large purchases of pharmaceuticals are put out to tender • Hospitals requiring a broader or more specific range of the medicines must elaborate the list of additionally usable medicines to be examined by the NHS. These may be included in the Additional List if they have costs of treatment commensurable with the state budget funding for the in-patient services of the hospital, and has a lower price compared to other medicines with equal therapeutic efficacy and side effects

Key takeaway for rare disease treatments

- No special processes nor differentiated HTA approaches for rare disease treatments
- Rare disease treatments are provided through the standard inpatient and outpatient reimbursement process (positive lists), named-patient requests if the drug is necessary to save a patient's life, or through a special state funded program for the treatment of children with rare diseases

P&R processes in Estonia

OUTPATIENT	INPATIENT
• Positive list of drugs reimbursed by the Estonian Health Insurance Fund (EHIF) • Reimbursement: State Medicines Agency (SAM) assess clinical data, EHIF economic data. Ministry of Social Affairs (MOSA) decides reimbursement • Clinical benefit: disease nature and prevalence, alternative treatments, safety profile, optimal dosage, potential misuse, necessity for restrictions • Economic data: pharmacoeconomic analysis, budget impact • Price-volume agreements of drugs with positive opinion are negotiated between manufacturer and MOSA (reference pricing for off patent drugs) • Rare disease experts may be consulted	• Inpatient drugs covered as part of the price of health services paid by the EHIF • Some selected groups of drugs (chemotherapy, dialysis products) are included in list of health services as separate entities of pharmaceutical care and are paid for by EHIF in addition to health services • EHIF yearly approves budget and modifications of health services. Proposals of new health services are coming from physicians (specialist societies), Estonian Association of Hospitals and EHIF (and not manufacturers) • Criteria for evaluation of new services: added benefit compared to existing alternatives, cost-effectiveness (done by EHIF), budget impact (by EHIF), impact of healthcare system organization • Prices are determined by EHIF. Manufacturers can propose innovative cost-sharing solutions

Key takeaway for rare disease treatments

- No special processes nor differentiated HTA approaches for rare disease treatments
- Exemptions for orphan medicinal product dossier requirements (outpatient): dossier may be in English, no need to adapt pharmacoeconomic analysis to Estonian context
- Estonia contributes to European registries, e.g. EUROCARE CF

P&R processes in Lithuania

OUTPATIENT	INPATIENT
• Final reimbursement decision made by the Ministry of Health, supported by technical evaluations from the Pharmaceutical Reimbursement Commission (representatives of Ministry of Health, States Medicines Agency and NHIF) and National Health Insurance Fund (NHIF) • New evaluation criteria (since 2007): medical benefit (effectiveness, safety, severity), pharmacoeconomic evaluation, budget impact • Positive list, covered by the NHIF • Pricing: price negotiations, international reference pricing, reference price system (ATC5 & 4 levels) • Co-payment (0% 10%, 20%, 50%) depends on disease severity. 100% reimbursement for vulnerable groups, children and disabled patients	• List of Centrally Procured Medicines and Medical Devices, yearly revised, covered by hospital budgets and NHIF • Outpatient list relevant for the inpatient sector • Each hospital has its own formulary, no co-payments, medicines are integrated in the reimbursement lump sum (with some exceptions) • Price negotiations when manufacturers and wholesalers for the acquisition of patented expensive drugs • Named-patient reimbursement requests for expensive pharmaceuticals for rare diseases. Application from university hospital is discussed by the Committee of Rare Diseases in NHIF. Same pricing rules as other pharmaceuticals.

Key takeaway for rare disease treatments

- No special processes for rare disease treatments, with the exception of named-patient reimbursement for inpatient pharmaceuticals for rare diseases
- 100% reimbursement for vulnerable groups, children and disabled patients. Severity also accounted for. These may benefit rare disease patients

P&R processes in Iceland

OUTPATIENT	INPATIENT
• Pricing and reimbursement decisions are made by the Icelandic Medicines Pricing and Reimbursement Committee for both outpatient and inpatient • Positive list under the responsibility of the Medicines Pricing and Reimbursement Committee, covered by the Icelandic NHS • Different reimbursement rates • Criteria for reimbursement: Safety, budget impact, price in relation to efficacy in comparison to already reimbursed medicines, reimbursement status in Denmark, Norway, Sweden and Finland (e.g. consideration of their HTAs) • Pricing: international reference pricing (Denmark, Finland, Norway, Sweden) set by the Medicines P&R Committee	• Inpatient pharmaceuticals covered by Icelandic NHS • Two categories: (a) low-priced products restricted by annual budget, overseen by NHS; (b) high-priced products that undergo the Icelandic Medicines Pricing and Reimbursement Committee process, covered by special annual budget of the NHS • Criteria for high-cost specialty products: costly, challenging to administer, used as per clinical guidelines • Clinical and economic evaluations for high-priced medicines are done in cooperation between University Hospital and Icelandic NHS. • Decentralised procurement system by individual hospitals through tenders. Hospitals may also be in direct contact with manufacturers and negotiate individual prices. • Pricing: international reference pricing (Denmark, Finland, Norway, Sweden) set by the Medicines P&R Committee

Key takeaway for rare disease treatments

- No differentiated processes for rare disease treatments
- Rare disease treatments likely to be eligible as high-cost specialty treatments
- Reimbursement decisions and pricing account for reimbursement status and price in Nordic countries, respectively

Report content

- Background & methodology
- Cross-country summary and recommendations
- Nordic countries summary and recommendations
- Baltic countries top-line summary
- Appendix – detailed country assessments

Appendix 1

- Detailed assessment for Sweden

Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework

Subprinciples	Outpatient	Inpatient
Decision-makers should consider OMP value from the perspective of patients, the healthcare system and wider society	✓✓✓	✓✓ - ✓✓✓*
Core elements of value and other considerations (see next slide)	✓✓	✓✓
Societal values underpinning value assessment are explicit	✓✓	✓ - ✓✓*
Use of multi-criteria decision analytic (MCDA) frameworks approach	✓✓	✓ - ✓✓*

OUTPATIENT

- Some elements of value may not be captured
- Criteria do not prioritise orphan drugs (except for criteria for very severe diseases), although they may be considered severe; TLV may accept a higher WTP threshold for severe orphan conditions.
- Multiple criteria are accounted for

INPATIENT

- Inpatient drugs undergo public procurement. Product value is not accounted for except if HTA requested or an outpatient price exists
- Value may be accounted for in three-party conversations

** Greater alignment if P&R decision relies on an HTA by TLV*

Guide to core elements of value

	OMP value	
	Impact of disease on	Impact of treatment on
Patient level	✓ Survival/life expectancy ✓ Morbidity ✓ Patient experience and quality of life ✓ Patient economic burden	
	✓ Existing treatment options	✓ Side effects ✗ Treatment convenience
Healthcare system level	✓ Healthcare system resources and budget ✓ Healthcare system organisation	
Societal level	✗ Family/Carer quality of life ✓ Family/carer economic burden ✓ Societal economic burden	

OUTPATIENT

- Patient's productivity gains/losses not considered (carer's considered)
- Preference for cost/QALY (EQ-5D). Non-utility QoL accounted during deliberation
- Family/carer QoL often not reliable or reasonable
- Societal economic burden: costs outside healthcare system, e.g. due to a disability, captured
- Consideration of treatment convenience if impact on QoL, limited weight in past decisions. Often a lack of evidence for the value of convenience; convenience alone not sufficient for importance

INPATIENT

- Similar as outpatient if HTA by TLV

✓ Accounted for
✗ Not accounted for

Principle 2: P&R decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value

Subprinciples	Outpatient	Inpatient
Reimbursement decisions should be based on product value	✓✓✓	✓ - ✓✓✓*
Price should be informed by price-value precedents for other specialist medicines	✓✓✓	✓ - ✓✓✓*
Beyond product value, price and reimbursement status should be modulated to reflect other considerations, such as societal preferences, rarity, budget impact and sustainability of innovation in rare diseases (see next slide)	✓✓	✓✓
If cost-effectiveness is applied, ICER thresholds should be modulated to reflect specificities of rare diseases	✓✓	✓✓
Balances incentives for new research investment in rare diseases while maximising value for money for healthcare systems	✓✓	✓

OUTPATIENT

- Costs/effects compared to most used alternative, price levels between specialist areas not compared
- ICERs not modulated for RDTs, unless it falls under the ultra-orphan criteria
- Incentives for R&D not considered per se, but captured indirectly in added benefit of treatment

INPATIENT

- Value accounted for if HTA by TLV
- If available for outpatient use, its price would be accounted for in procurement

** Greater alignment if P&R decision relies on an HTA by TLV*

Considerations beyond product value & uncertainty of rare disease treatments

Considerations beyond OMP value

- ✓ Rarity
  - ✗ Sustainability of innovation in rare diseases
  - ✗ Small budget impact
- ✗ Societal preferences

Uncertainty of OMP value

- ✓ Quality of evidence
- ✓ Uncertainty around value parameters

OUTPATIENT

- Greater flexibility for ultra-rare diseases with the new criteria (and higher ICERs). Not applicable for RDTs
- Sustainability of innovation not directly accounted for, but indirectly in the added benefit of the treatment
- Budget impact not considered
- Lower demands on quality of evidence for very rare diseases, specificities of rare diseases accounted for (not explicitly as hard to quantify)

INPATIENT

- Similar as outpatient if HTA by TLV

✓ Accounted for
✗ Not accounted for

Principle 3: All official regulatory and HTA of OMPs undertaken at the European level should be acknowledged by national health authorities

Subprinciples	Outpatient	Inpatient
Assessment builds on the decisions and recommendations at a European level	✓✓✓	✓✓

OUTPATIENT

- Best available evidence expected, includes consideration of pivotal studies & local data (often not available for rare diseases)
- Consideration of other HTA decisions, if available
- Consideration of list prices in other countries

INPATIENT

- Consideration of list prices in other countries and of outpatient drugs

Principle 4: The assessment and appraisal of OMPs should incorporate rare disease expertise including healthcare professionals' and patients' perspectives

Subprinciples	Outpatient	Inpatient
Disease-specific expert physicians should be involved in the value assessment and provide direct input	✓✓	✓✓
Patients and their carers should be involved in the value assessment in the following ways: - Systematic representation of patient associations in meetings that assess and appraise OMPs - Disease-specific patient representatives should be involved throughout the process and given appropriate training and support to contribute fully	✓✓	✓✓

OUTPATIENT

- Clinical expert opinions collected and discussed during committee meetings
- Clinical expertise incorporated via written questions during assessments.
- Patient representative (non-disease specific) included in Pharmaceutical Benefits Board

INPATIENT

- Hospital doctors free to prescribe any drug procured
- Advice is provided by the Pharmaceutical and Therapeutic Committee composed of clinical experts
- Patient representatives sit on committee

Principle 5: To accommodate uncertainty, value assessment and P&R decisions should be adaptive subject to the need and availability of information over time

Subprinciples	Outpatient	Inpatient
Payers should consider uncertainty in light of disease prevalence, disease severity and unmet need, amount of prior research conducted in the disease, extent to which the manufacturer has taken reasonable steps to minimise uncertainty.	✓✓	✓ - ✓✓*
Value assessment processes should be adaptive and continuous	✓✓	NA
P&R decisions should allow movement both up and down with newly generated evidence on value	✓✓	NA
Where adaptive processes are required, all parties (payers, HTA agencies, involved HCP, patients and industry) need to agree on this iterative process	✓	NA
Where possible, the collection and analysis of RWE should be coordinated at EU or international level and should be integrated in disease level registries and databases	✓✓	NA

OUTPATIENT

- Consideration of disease severity and unmet need
- New ultra-RDTs criteria account for prevalence. Not considered for other RDTs
- Request for review of P&R by regions usually for a therapeutic area with high budget impact
- If new product has a lower price than an existing one, the existing one will be asked to provide new evidence to justify price
- Conditional approval for 1-3 years, after which RWE requested

INPATIENT

- Similar as outpatient if HTA by TLV
- Possibility to implement a managed introduction of new medicines scheme when tripartite negotiations with NT Councils take place
- Principle not applicable to standard procurement processes

** Greater alignment if P&R decision relies on an HTA by TLV*

Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations

Subprinciple	Outpatient	Inpatient
Wherever possible, reimbursement decisions should seek to ensure that all patients specified in the product license should receive access to treatment	✓✓✓	✓✓✓
Reimbursement may be reflective of situations where there is a broad spectrum of disease and clearly defined patient subgroups in which OMP value substantially differs	✓✓✓	✓✓✓

OUTPATIENT

- Application for reimbursement of an indication by manufacturers
- If no reimbursement requested, drug marketed with free pricing for that indication
- Possible request for a reimbursement application on an indication from TLV to a manufacturer
- For heterogeneous populations, possible variation of ICER across patient subgroups. TLV is often willing to look at subgroups and reimburse them if the full population is not cost-effective

INPATIENT

- Principle not applicable for inpatient drugs

Principle 7: Funding should be provided at the national level to ensure patient access to OMPs

Subprinciple	Outpatient	Inpatient
Funding for OMPs should be co-ordinated at a national level in order to avoid disparities in access between regions	✓	✓
It is preferable that funding for OMPs should come out of normal healthcare budgets rather than from ear-marked rare disease funds that do not allow for a long-term perspective	✓✓	✓✓

OUTPATIENT

- No distinction between funding for rare and non-rare disease treatments
- General subsidy of ~SEK 6 billion from Stockholm to other regions (not specific to rare diseases)
- National subsidy for HIV and Haemophilia (no other diseases to be included)

INPATIENT

- National coordination of certain highly specialised care where provision of care provided by one or two regions
- Inpatient funding from local hospitals

Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability

Subprinciples	Outpatient	Inpatient
Manufacturers, payers and HTA agencies should collaborate nationally to improve forecasting of expenditure and ensure adequate funding of OMPs	✓✓	✓✓
Early stage dialog between all stakeholders should be put in place to ensure long term sustainability of outcomes	✓✓	NA

OUTPATIENT

- Horizon scanning by TLV to identify drugs for assessment
- Possible participation in advisory or EMA early scientific advice meetings

INPATIENT/OUTPATIENT

- Horizon scanning by West Region on behalf of all regions. Lack of clarity on how this activity helps better planning for regions
- Manufacturers invited to present 1-2 years pipeline during horizon scanning activities

Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level

Subprinciples	Outpatient	Inpatient
Collaborate with other European payers in regard to value assessment and data generation	✓	NA

OUTPATIENT

- TLV is an active participant of EUnetHTA JA3 and Finose HTA collaboration
- TLV has been the “rapporteur” in a number of joint relative effectiveness assessments.
- These are at early stages and have limited impact

Appendix 2

- Detailed assessment for Denmark

Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework

Subprinciples	Inpatient
Decision-makers should consider OMP value from the perspective of patients, the healthcare system and wider society (dynamic effects not included)	✓✓
Core elements of value and other considerations (see next slide)	✓✓✓
Societal values underpinning value assessment are explicit	✓
Use of multi-criteria decision analytic (MCDA) frameworks approach	✓✓

INPATIENT

- In the joint assessment, a restricted societal perspective is adopted and some other elements of value are not captured (see next slide for more details)
- No formal MCDA approach used in the overall decision making#
- ICER threshold: No, but cost/QALY is used as an indication of value
- No special rules for RDTs (although some elements are informally considered – see next slides)

Guide to core elements of value

	OMP value	
	Impact of disease on	Impact of treatment on
Patient level	✓ Survival/life expectancy ✓ Morbidity ✓ Patient experience and quality of life ✓ Patient economic burden	
	✓ Existing treatment options	✓ Side effects ✗ Treatment convenience
Healthcare system level	✓ Healthcare system resources and budget ✗ Healthcare system organisation	
Societal level	~ ✓ Family/Carer quality of life ~ ✓ Family/carer economic burden ✗ Societal economic burden	

INPATIENT
• Only direct costs are considered. Patient and carer time for treatment are also accounted for. A budget impact for the regions must be produced • The wider societal aspects are not included (e.g.: loss/gains of productivity) • Impact on family and carers can be provided, but it is unclear how these elements are weighted in the decision, informal conclusions may be inferred from them • Overall, there is no explicit documentation on how the different criteria should be weighted in the final decision

✓ Accounted for ✗ Not accounted for

Principle 2: P&R decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value

Subprinciples	Inpatient
Reimbursement decisions should be based on product value	✓✓✓
Price should be informed by price-value precedents for other specialist medicines	✓✓✓
Beyond product value, price and reimbursement status should be modulated to reflect other considerations, such as societal preferences, rarity, budget impact and sustainability of innovation in rare diseases (see next slide)	✓
If cost-effectiveness is applied, ICER thresholds should be modulated to reflect specificities of rare diseases	✓
Balances incentives for new research investment in rare diseases while maximising value for money for healthcare systems	✓

INPATIENT

- The assessment informs purchasing and negotiations by Amgros
- Price of other rare disease products in other therapeutic areas may be reviewed
- Tendering process for hospital products is carried out by Amgros (tenders occur when several products are on the market, less likely for RDTs)
- Cost/QALY approach used as of January 1, 2021

Considerations beyond product value & uncertainty of rare disease treatments

Considerations beyond OMP value

- ✗ Rarity
  - ✗ Sustainability of innovation in rare diseases
  - ~✓ Small budget impact
- ✗ Societal preferences

Uncertainty of OMP value

- ✓ Quality of evidence (via PICO)
- ~✓ Uncertainty around value parameters

INPATIENT

- There is no systematic validation of the evidence against real-world evidence in the Danish setting, although DMC can ask for follow-up data
- No transparency on how uncertainty is accounted or quantified for in the overall process but may impact price negotiation
- Severity of the disease may have an impact on how the different criteria are weighted in the final decision. However, this is not structured and it is more a political statement to accommodate for the challenges associated with rare diseases.
- Rarity not formally accounted for but because of the correlation between rarity and severity, this is somewhat indirectly accounted for → No transparency on how severity is assessed

✓ Accounted for ✗ Not accounted for

Principle 3: All official regulatory and HTA of OMPs undertaken at the European level should be acknowledged by national health authorities

Subprinciples	Inpatient
Assessment builds on the decisions and recommendations at a European level	✓✓

INPATIENT
• EPAR document from EMA is included while EUnetHTA is not included • Denmark has historically been very fast and often one of the first to have a recommendation

Principle 4: The assessment and appraisal of OMPs should incorporate rare disease expertise including healthcare professionals' and patients' perspectives

Subprinciples	Inpatient
Disease-specific expert physicians should be involved in the value assessment and provide direct input	✓✓✓
Patients and their carers should be involved in the value assessment in the following ways: - Systematic representation of patient associations in meetings that assess and appraise OMPs - Disease-specific patient representatives should be involved throughout the process and given appropriate training and support to contribute fully	✓✓✓

INPATIENT

- The Danish Medicines Council can use existing expert committees or set up new expert committees to assess the new medicines and indications
- Disease-specific experts are involved in product assessments
- Strict conflict of interest policy in Denmark where many experts are disqualified (challenging for RDTs)
- Disease-specific patient representative participate in a large part of the assessment. In the actual Appraisal Committee, there is a representative from a patient umbrella organisation (2 mandates in the Council)
- Clinical expert assessment may be included to a greater extent for treatments with sparse evidence (e.g. RDTs)
- Approach to incorporating clinicians and patients in Denmark is very well structured
- Nurses are part of the clinical expert committees

Principle 5: To accommodate uncertainty, value assessment and P&R decisions should be adaptive subject to the need and availability of information over time

Subprinciples	Inpatient
Payers should consider uncertainty in light of disease prevalence, disease severity and unmet need, amount of prior research conducted in the disease, extent to which the manufacturer has taken reasonable steps to minimise uncertainty.	✓✓
Value assessment processes should be adaptive and continuous	✓✓
P&R decisions should allow movement both up and down with newly generated evidence on value	✓✓
Where adaptive processes are required, all parties (payers, HTA agencies, involved HCP, patients and industry) need to agree on this iterative process	✓
Where possible, the collection and analysis of RWE should be coordinated at EU or international level and should be integrated in disease level registries and databases	✓

INPATIENT

- Amgros does not take severity into account, only DMC accounts for it in the assessment
- DMC may decide to reimburse a product despite Amgros not recommending a product due to high costs, and conversely may decide not to reimburse a product despite Amgros making a positive recommendation
- No formal adaptive processes, and there are no instructions in methods guideline
- Re-evaluation possible with new evidence, only few examples to date but the effects of such decision have not been seen yet
- RWE not consistently used in assessment processes, typically published evidence has more impact
- Nordic collaboration on RWE collection, willingness to use the data in the future, might be used to validate a decision
- When cost-utility analysis is not possible, manufacturers must justify why, and have the opportunity to submit alternative analyses, as well as unpublished data

Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations

Subprinciple	Inpatient
Wherever possible, reimbursement decisions should seek to ensure that all patients specified in the product license should receive access to treatment	✓✓✓
Reimbursement may be reflective of situations where there is a broad spectrum of disease and clearly defined patient subgroups in which OMP value substantially differs	✓✓✓

INPATIENT

- Manufacturers make a proposition on the reimbursement population in their submission and/or are asked to make a submission for any sub-population(s)
- The DMC then reviews and decides which population should get reimbursement; this is based on the manufacturer's submission within the product license

Principle 7: Funding should be provided at the national level to ensure patient access to OMPs

Subprinciple	Inpatient
Funding for OMPs should be co-ordinated at a national level in order to avoid disparities in access between regions	✓✓
It is preferable that funding for OMPs should come out of normal healthcare budgets rather than from ear-marked rare disease funds that do not allow for a long-term perspective	✓✓✓

INPATIENT

- Although DMC grants reimbursement for RDTs nationally, they have no mandate to force regions to use RDTs. Regions decide, and most often follow the recommendation. If they don't have enough finance, they may not be able to reimburse RDTs
- Price negotiations by Amgros apply nationally
- Products are procured centrally by Amgros

Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability

Subprinciples	Inpatient
Manufacturers, payers and HTA agencies should collaborate nationally to improve forecasting of expenditure and ensure adequate funding of OMPs	✓✓ - ✓✓✓
Early stage dialog between all stakeholders should be put in place to ensure long term sustainability of outcomes	✓✓

INPATIENT

- Horizon scanning is conducted for planning purposes by DMC and Amgros and for budgetary reasons by the regions
- Informal dialogue with the Council can happen, near the submission date to discuss the kind of data to include in the dossier
- There is opportunity for early dialogue between manufacturer and DMC

Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level

Subprinciples	Inpatient
Collaborate with other European payers in regard to value assessment and data generation	✓

INPATIENT
• Nordic collaborations and EUnetHTA are different institutions from the DMC, hence what they do does not have any impact on product assessments

Appendix 1

- Detailed assessment for Norway

Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework

Subprinciples	Hospital Funding
Decision-makers should consider OMP value from the perspective of patients, the healthcare system and wider society	✓
Core elements of value and other considerations (see next slide)	✓
Societal values underpinning value assessment are explicit	✓✓✓
Use of multi-criteria decision analytic (MCDA) frameworks approach	✓✓

HOSPITAL FUNDING

- Decision accounts for NOMA's recommendation
- Decision also depends on if sufficient funds or if organisational changes are required
- Cost containment may have more weight for in the decision by the Decision Forum, if there is insufficient budget
- Societal perspective and additional considerations are not accounted for; focus of assessment is on economic effectiveness and direct health care perspective (costs)

Guide to core elements of value

	OMP value	
	Impact of disease on	Impact of treatment on
Patient level	✓ Survival/life expectancy ✓ Morbidity ✓ Patient experience and quality of life ✓ Patient economic burden	
	✓ Existing treatment options	✓ Side effects ~x Treatment convenience
Healthcare system level	✓ Healthcare system resources and budget ~x Healthcare system organisation	
Societal level	~x Family/Carer quality of life ✓ Family/carer economic burden ~x Societal economic burden	

HOSPITAL FUNDING

- The ICER (preferably cost/QALY) captures survival and QOL impact (EQ-5D). The rest would be accounted for during discussions
- Treatment convenience: not often used, but would be if main advantage
- Healthcare system organisation: not considered by NOMA, but could be included by hospitals in their recommendations to the Decision Forum
- Family/carer quality of life: considered as a modifier, as difficult to quantify

Principle 2: P&R decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value

Subprinciples	Hospital Funding
Reimbursement decisions should be based on product value	✓✓✓
Price should be informed by price-value precedents for other specialist medicines	✓✓✓
Beyond product value, price and reimbursement status should be modulated to reflect other considerations, such as societal preferences, rarity, budget impact and sustainability of innovation in rare diseases (see next slide)	✓
If cost-effectiveness is applied, ICER thresholds should be modulated to reflect specificities of rare diseases	✓
Balances incentives for new research investment in rare diseases while maximising value for money for healthcare systems	✓✓

HOSPITAL FUNDING

- The Decision Forum may decide not to follow NOMA's recommendation, and focus on cost-containment
- Other considerations, like rarity, not made; there is recognition of high uncertainty around RDTs and greater WTP officially, but often not seen in practice

Considerations beyond product value & uncertainty of rare disease treatments

Considerations beyond OMP value

- ✗ Rarity
  - ✗ Sustainability of innovation in rare diseases
  - ✓ Small budget impact
- ✗ Societal preferences

Uncertainty of OMP value

- ✓ Quality of evidence
- ✓ Uncertainty around value parameters

HOSPITAL FUNDING
• Criteria for ultra-rare diseases would give more flexibility (and accept higher ICERs) for very small patient populations. For the other rare diseases, their rare nature would not be considered • Sustainability: higher WTP through new criteria for ultra-RDTs (captured indirectly, also in the added benefit of the drug) • Quality of the evidence: modifier + for RDTs may expected more uncertainty & lower quality evidence

✓ Accounted for
✗ Not accounted for

Principle 3: All official regulatory and HTA of OMPs undertaken at the European level should be acknowledged by national health authorities

Subprinciples	Hospital Funding
Assessment builds on the decisions and recommendations at a European level	✓

HOSPITAL FUNDING
• EMA EPAR and assessment reports frequently used (particularly for RDTs) • Don't necessarily adopt their conclusions • Don't look at HTA body decisions in other countries

Principle 4: The assessment and appraisal of OMPs should incorporate rare disease expertise including healthcare professionals' and patients' perspectives

Subprinciples	Hospital Funding
Disease-specific expert physicians should be involved in the value assessment and provide direct input	✓✓
Patients and their carers should be involved in the value assessment in the following ways: - Systematic representation of patient associations in meetings that assess and appraise OMPs - Disease-specific patient representatives should be involved throughout the process and given appropriate training and support to contribute fully	✓

HOSPITAL FUNDING

- No disease-specific experts in the Decision Forum. Medical experts from each health region are included earlier in the process. One patient representative in the Decision Forum, does not have formal vote, but can possibly influence the process
- Hospitals include a report with NOMA's report with their input, including input from clinical experts

Principle 5: To accommodate uncertainty, value assessment and P&R decisions should be adaptive subject to the need and availability of information over time

Subprinciples	Hospital Funding
Payers should consider uncertainty in light of disease prevalence, disease severity and unmet need, amount of prior research conducted in the disease, extent to which the manufacturer has taken reasonable steps to minimise uncertainty.	✓✓
Value assessment processes should be adaptive and continuous	✓
P&R decisions should allow movement both up and down with newly generated evidence on value	✓
Where adaptive processes are required, all parties (payers, HTA agencies, involved HCP, patients and industry) need to agree on this iterative process	✓
Where possible, the collection and analysis of RWE should be coordinated at EU or international level and should be integrated in disease level registries and databases	✓

HOSPITAL FUNDING

- The Decision Forum does not consider outcome-based MEAs
- All points raised about the assessment by NOMA are applicable for hospital funding
- Decisions are not adapted once made
- NOMA recognises difficulty coping with RDTs

Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations

Subprinciple	Hospital Funding
Wherever possible, reimbursement decisions should seek to ensure that all patients specified in the product license should receive access to treatment	✓✓✓
Reimbursement may be reflective of situations where there is a broad spectrum of disease and clearly defined patient subgroups in which OMP value substantially differs	✓✓✓

HOSPITAL FUNDING

- Manufacturers are invited to apply for reimbursement of an indication
- All new drugs and indications undergo the reimbursement process
- NOMA prefers not to use subpopulations; uses ITT population, but may recommend reimbursement to certain subgroups

Principle 7: Funding should be provided at the national level to ensure patient access to OMPs

Subprinciple	Hospital Funding
Funding for OMPs should be co-ordinated at a national level in order to avoid disparities in access between regions	✓✓
It is preferable that funding for OMPs should come out of normal healthcare budgets rather than from ear-marked rare disease funds that do not allow for a long-term perspective	✓✓✓

HOSPITAL FUNDING
• The Decision Forum makes national decisions, which are to be covered by hospital budgets • National funding is distributed among regions. Decision is made nationally, but funding is regional (hospitals; mainly based on budget impact and previous year expenditure, not earmarked) • Regional funding may put access to RDTs at risk.

Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability

Subprinciples	Hospital Funding
Manufacturers, payers and HTA agencies should collaborate nationally to improve forecasting of expenditure and ensure adequate funding of OMPs	✓✓
Early stage dialog between all stakeholders should be put in place to ensure long term sustainability of outcomes	✓✓

HOSPITAL FUNDING

- NoMA has access to information from EMA, then ask for information to conduct HTA before market authorisation is obtained in order to start the assessment early.
- Early scientific advice: it is possible to have pre-meetings before submitted the dossier. This would be the first contact with NOMA
- Limited early dialogue except between manufacturer and trade organisation

Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level

Subprinciples	Hospital Funding
Collaborate with other European payers in regard to value assessment and data generation	✓✓

HOSPITAL FUNDING
• NOMA is a participant of EUnetHTA JA3 and Finose HTA collaboration, though engagement is difficult when it comes to RDTs

Appendix 1

- Detailed assessment for Finland

Principle 1: OMP assessment should consider all relevant elements of product value for OMPs in an appropriate multi-dimensional framework

Subprinciples	Outpatient	Inpatient
Decision-makers should consider OMP value from the perspective of patients, the healthcare system and wider society	✓✓✓	✓✓
Core elements of value and other considerations (see next slide)	✓✓ - ✓✓✓	✓✓
Societal values underpinning value assessment are explicit	✓	✓
Use of multi-criteria decision analytic (MCDA) frameworks approach	✓	✓

OUTPATIENT

- Most elements of value are captured (see next slide)
- No specification or prioritisation of orphan drugs, although some drugs receive a higher reimbursement level, this does not depend on rare disease status. Higher ICER may rather be permitted due to other considerations like high societal value, paediatric indications, unmet need
- Multiple criteria are accounted for but no formal MCDA approach

INPATIENT

- The wider societal perspective is no considered (see next slide)
- Societal values are not explicitly considered but my be reflected by assessing severity of the disease
- PICO approach used to assess the clinical benefit but no formal MCDA approach is used to review of elements ff value

Guide to core elements of value

	OMP value (HILA)		OMP value (Fimea)	
	Impact of disease on	Impact of treatment on	Impact of disease on	Impact of treatment on
Patient level	✓ Survival/life expectancy ✓ Morbidity ✓ Patient experience and quality of life ✓ Patient economic burden		✓ Survival/life expectancy ✓ Morbidity ✓ Patient experience and quality of life ✗ Patient economic burden	
	✓ Existing treatment options	✓ Side effects ✗ Treatment convenience	✓ Existing treatment options	✓ Side effects ✗ Treatment convenience
Healthcare system level	✓ Healthcare system resources and budget ✗ Healthcare system organisation		✓ Healthcare system resources and budget ✗ Healthcare system organisation	
Societal level	✓ Family/Carer quality of life ✓ Family/carer economic burden ✓ Societal economic burden		✗ Family/Carer quality of life ✗ Family/carer economic burden ✗ Societal economic burden	

OUTPATIENT

- Indirect costs are assessed but they are not mandatory
- CEA is compulsory (but no ICER threshold)

INPATIENT

- Clinical assessment, cost and budget impact are conducted
- Optionally, cost-effectiveness data can be provided, but this is typically seen as less important by hospitals
- Aspects such as treatment convenience or healthcare system organisation are discussed only if there is a specific setting or issue in relation to these
- Societal impact of the disease and the treatment are not considered by Fimea

Principle 2: P&R decisions should be founded on the assessment of OMP value for money and adjusted to reflect other considerations beyond product value

Subprinciples	Outpatient	Inpatient
Reimbursement decisions should be based on product value	✓✓ - ✓✓✓	✓✓
Price should be informed by price-value precedents for other specialist medicines	✓✓✓	✓ - ✓✓
Beyond product value, price and reimbursement status should be modulated to reflect other considerations, such as societal preferences, rarity, budget impact and sustainability of innovation in rare diseases (see next slide)	✓✓	✓✓
If cost-effectiveness is applied, ICER thresholds should be modulated to reflect specificities of rare diseases	N/A	N/A
Balances incentives for new research investment in rare diseases while maximising value for money for healthcare systems	✓✓	✓

OUTPATIENT

- Price is a key driver of reimbursement
- Funds available for special reimbursement
- Higher reimbursement rates (65-100%) for severe and chronic disorders
- No formal CE threshold
- Additional value can be based on unmet medical need, but not on rarity alone

INPATIENT

- Economic evaluation not conducted for inpatient products by Fimea
- Free pricing based on competitive bidding

Considerations beyond product value & uncertainty of rare disease treatments

Outpatient	*Hospital-only*
Considerations beyond OMP value	**Considerations beyond OMP value**
• ✓Rarity – ✓Sustainability of innovation in rare diseases – ✓Small budget impact • ✗ Societal preferences	• ✗ Rarity – ✗ Sustainability of innovation in rare diseases – ✓Small budget impact • ✗ Societal preferences
Uncertainty of OMP value	**Uncertainty of OMP value**
• ✗ Quality of evidence • ✗ Uncertainty around value parameters	• ✓ Quality of evidence • ✓ Uncertainty around value parameters

OUTPATIENT

- Rarity may be considered in certain cases, but additional value can only be based on other elements such as unmet medical need
- Reimbursement application can include manufacturing and R&D costs

INPATIENT

- No formal procedure for accounting for rarity and uncertainty
- Rarity is not explicitly considered but severity of the disease is reviewed
- Requirements for rare diseases are implicitly not the same, and uncertainty around certain clinical outcomes is considered

✓ Accounted for
✗ Not accounted for

Outpatient setting findings were not validated by an external country representative

Principle 3: All official regulatory and HTA of OMPs undertaken at the European level should be acknowledged by national health authorities

Subprinciples	Outpatient	Inpatient
Assessment builds on the decisions and recommendations at a European level	✓✓✓	✓✓✓

OUTPATIENT

- Manufacturer submission to include EPAR
- Reference to other countries' HTA decisions
- Evidence used in applications can come from other countries with exception of costs

INPATIENT

- Various sources are used, this includes EMA's assessment and broader evidence from the literature and the manufacturer submission

Principle 4: The assessment and appraisal of OMPs should incorporate rare disease expertise including healthcare professionals' and patients' perspectives

Subprinciples	Outpatient	Inpatient
Disease-specific expert physicians should be involved in the value assessment and provide direct input	✓✓✓	✓✓✓
Patients and their carers should be involved in the value assessment in the following ways: - Systematic representation of patient associations in meetings that assess and appraise OMPs - Disease-specific patient representatives should be involved throughout the process and given appropriate training and support to contribute fully	✓✓	✓

OUTPATIENT

- P&R board appointed for 3 years. Usually use same group of disease experts for different diseases, sometimes (not always) reach out for specific disease expertise
- Patient associations can provide an opinion on the assessment, although information is not public and do not know the content of the submission
- In general patient voice not heard as much and input that is contributed needs could be better accepted. Some changes in that patient groups are now proactively sending own statements more often

INPATIENT

- Clinical experts assist in definition of PICOs and comment on material produced by the assessment team, they are also solicited to answer specific clinical questions
- Patient associations are not consulted during the assessment by FIMEA
- The assessments are public and anyone can comment within a specific time frame, comments are published and delivered to the decision-maker
- Submissions can include experts' opinions. Usually same group for different diseases, but sometimes reach out for specific disease expertise

Principle 5: To accommodate uncertainty, value assessment and P&R decisions should be adaptive subject to the need and availability of information over time

Subprinciples	Outpatient	Inpatient
Payers should consider uncertainty in light of disease prevalence, disease severity and unmet need, amount of prior research conducted in the disease, extent to which the manufacturer has taken reasonable steps to minimise uncertainty.	✓✓	✓✓
Value assessment processes should be adaptive and continuous	✓✓	✓✓
P&R decisions should allow movement both up and down with newly generated evidence on value	✓ - ✓✓	✓
Where adaptive processes are required, all parties (payers, HTA agencies, involved HCP, patients and industry) need to agree on this iterative process	✓	✓
Where possible, the collection and analysis of RWE should be coordinated at EU or international level and should be integrated in disease level registries and databases	✓✓	✓✓

OUTPATIENT

- Unmet need accounted for (100% reimbursement. status)
- New system to reduce uncertainty related to P&R decisions launched in 2017, “conditional reimbursement” has now been used in 30 cases, both big and small products. MAH submits request for this option, deciding factor for acceptance is often unmet need. Current learning curve regarding how to best collect data

INPATIENT

- Uncertainty not accounted for explicitly but the overall evidence is considered in the light of disease severity and prevalence.
- Re-evaluation via new application if change in indication or significant change in usage or new evidence is provided
- Future developments for Fimea refer to better collection of RWE. RWE can be collected, but Fimea assessments may provide recommendations on specific type of RWE to be collected by manufacturers
- RWE could be better coordinated at an international level – Nordic registries are not looked at

Principle 6: All eligible patients within the authorised label of an OMP should be considered in the reimbursement appraisal although different decisions on access may apply to different sub-populations

Subprinciple	Outpatient	Inpatient
Wherever possible, reimbursement decisions should seek to ensure that all patients specified in the product license should receive access to treatment	✓✓✓	✓✓✓
Reimbursement may be reflective of situations where there is a broad spectrum of disease and clearly defined patient subgroups in which OMP value substantially differs	✓✓✓	✓✓

OUTPATIENT

- Limitation to a certain patient population is relatively frequent
- Restriction occur when there is uncertainty about a drug overall benefit, hence usage is limited initially or there is a subgroup population that would benefit most

INPATIENT

- The overall indication is considered in the assessment but Fimea's looks specifically into subpopulation
- Fimea provides an opinion when different efficacy outcomes are observed in different populations

Principle 7: Funding should be provided at the national level to ensure patient access to OMPs

Subprinciple	Outpatient	Inpatient
Funding for OMPs should be co-ordinated at a national level in order to avoid disparities in access between regions	✓✓✓	✓✓
It is preferable that funding for OMPs should come out of normal healthcare budgets rather than from ear-marked rare disease funds that do not allow for a long-term perspective	✓✓✓	✓✓✓

OUTPATIENT

- No distinction between funding for rare and non-rare disease treatments
- National decision making and national funding is done and works well

INPATIENT

- Since Jan 2017, Fimea undertakes a rapid HTA which aims to reduce disparities
- However funding comes from different sources: hospital products are funded by regions and final decision are done by pharmaceutical boards through a tender process. There different products may be used in different regions

Principle 8: Evidence-based funding mechanisms should be developed to guarantee long-term sustainability

Subprinciples	Outpatient	Inpatient
Manufacturers, payers and HTA agencies should collaborate nationally to improve forecasting of expenditure and ensure adequate funding of OMPs	✓✓	✓✓✓
Early stage dialog between all stakeholders should be put in place to ensure long term sustainability of outcomes	✓	✓

OUTPATIENT

- Horizon scanning where PPB can organise meetings where all stakeholders can be present and manufacturer is invited to present new drugs (medical focus to the meeting)
- No formal early advice provided by HTA agencies, but early dialogue is improving

INPATIENT

- Topic selection procedure by Fimea: monthly monitoring of drugs assessed by EMA, selection of drugs suitable for hospital use
- Fimea also consults hospitals for topic selection
- Horizon scanning where manufacturer is invited to present to Fimea has been recently implemented
- Early dialogue happen informally where companies approach Fimea to introduce some studies but this does not consists of an advice
- Based on tender, quality criteria is not used for all products → some hospitals or therapy areas more or less advanced

Outpatient setting findings were not validated by an external country representative

Principle 9: In the future there should be greater co-ordination of OMP value assessment processes at a European level

Subprinciples	Outpatient	Inpatient
Collaborate with other European payers in regard to value assessment and data generation	✓✓	✓✓

OUTPATIENT / INPATIENT

- FIMEA is an active partner for EunetHTA, but it is unclear to what extent this impacts national evidence-based decision making and processes
- HTA collaboration between Finland, Norway and Sweden (FINOSE), but process not very visible so far, many products that should go under FINOSA still go through outpatient route; even if FINOSE makes a decision, it is still sent to pricing board and outpatient route