Scope of vignette:
- authorised products (with marketing authorisation)
- decision process about routine use (and not individual requests for reimbursement)
- submissions for P&R made by manufacturers (outpatient) or medical societies (inpatient)

Green = related to/any special considerations for rare disease and ultra-rare disease treatments

Estonia	**Standard HTA process (non-orphan drugs) - outpatient**	**Standard HTA process (non-orphan drugs) - inpatient**
Overview of health system and P&R/HTA process	Health system: tax based solidarity insurance system [1, 2] National level: Ministry of Social Affairs is responsible for organising the policies of medicinal products and medical devices and planning their implementation. Marketing authorisations are issued and renewed by the State Agency of Medicines [3] or European Medicines Agency The Estonian Health Insurance Fund (EHIF) is responsible for handling price agreements and amendments of prices of discount medicines, calculating the discounted prices for medicines, processing the applications for a list of discount medicine products (outpatient) and inpatient services list (includes inpatient medicines), and coordinating the work of the Committee for Medicinal Products. [4],[9] The HTA Council (representatives from the Estonian Health Insurance Fund, Ministry of Social Affairs, Association of Estonian Physicians, Union of General Practitioners, National Institute of Health Development, State Agency of Medicines and University of Tartu) determines HTA report topics, and coordinates activities of the HTA Centre. [5] Rapid assessment of individual applications made by industry, or a Professional Association (medical societies) is organized by the EHIF. [9] The Medicinal Products Committee advises on the management of the health insurance fund. The committee has up to eight members who are appointed by the management of the health insurance fund [6].	
Differentiation of rare disease treatments in the P&R system	EMA orphan designation	
Eligible medicines	Any (outpatient) medicinal products with marketing authorization. [8]	Any (inpatient) medicinal products
Process	- Market authorisation holder makes an application to the EHIF - State agency of medicines gives expert	- Professional Association of Healthcare Providers, or the EHIF submits an application for an amendment of the list of health care

	opinion on medical matters - EHIF gives expert opinion on economic matters - Medicinal products committee gives its advice to the board of EHIF about the inclusion of the product into the list of reimbursed medicines - The EHIF makes the final decision within 180 days, taking into account the recommendations of the Medicinal Products Committee, and forwards the decision to the manufacturer and Ministry of Social Affairs - EHIF signs a price and volume agreement with the market authorisation holder	services - EHIF checks the applications. If necessary, the applicants submit additional information - Experts evaluate medical evidence, Health Insurance Fund evaluates cost effectiveness and compliance with financial possibilities, Ministry of Social Affairs evaluates need for service and compliance with national policies - Management board of EHIF submits proposals to a supervisory board - Health Insurance Fund give opinion on list - Minister of Health and Labor submits list for approval to Government of the Republic - Government of the Republic confirms list of healthcare services [9]
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	As a routine practice, a clinical expert is often invited to the reimbursement committee meetings. Sometimes patient societies give their input (usually in written format). [9]	
Key domains in assessment	- Clinical effectiveness - Cost effectiveness - Budget impact - Other [9, 10]	
Evidentiary requirements	RCTs preferred. Lower level evidence accepted if there are no RCTs and there is high unmet medical need. [11]	
PROMs	EQ-5D for QALYs or any other if generally accepted in specific conditions.	
Appraisal framework	In addition to key domains the following are considered: - Existence of alternatives [10] - Need - Efficacy - Safety - Existing alternatives - Possibilities of misuse/rational use	In addition to key domains the following are considered: - Impact on society and healthcare policy [9] **There is currently no explicit different regulation for drugs for orphan diseases. Implicitly, a different approach is applied . E.g, non-Estonian language reimbursement applications/dossiers are permitted, unlike regular pharmaceuticals, to make application easier. Very different willingness to pay threshold is applied. If the usual cost per QALY cannot be calculated often pricing is accepted that is similar to products that have been

		accepted to reimburse for other very rare diseases.
Reimbursement decision	Positive or negative decision, often for restricted patient groups, reimbursement level (%)	Positive or negative decision, often for restricted patient groups
Pricing process	Price negotiation (for products with no alternatives with the same active substance) or internal reference price (across same active substances and modes of administration). [6]	
Managed entry agreements	- Confidential discount, payback - Budget cap - Outcome based scheme for individual patients, only paying for certain performance - Other, not specified *All national - no regional differences	
Main challenges in appraising medicines for rare diseases	- Lack of good quality clinical data - Introducing value for money - Monitoring treatment efficacy - Managing budget impact - Lack of long-term meaningful outcomes	
Impact of special processes	No separate process for medicines for rare diseases. Named patient use is possible for products which don't have a valid market authorisation (includes medicines for rare diseases). [10]	
Proposed policy change	None	
Joint initiatives	University of Tartu Department of Public Health was in 2010 nominated by the Ministry of Social Affairs to represent Estonia in EUnetHTA. Participation in the working groups of the EunetHTA strengthens the practical application of tools and approaches to cross-border HTA collaboration, and aims to establish a sustainable structure for HTA in the EU. [7]	
SOURCES		
1	https://www.haigekassa.ee/sites/default/files/2017-11/hk_teataja_voldik_a5_eng_web.pdf	
2	https://www.haigekassa.ee/en/general-outline-health-care-system	
3	https://www.riigiteataja.ee/en/eli/530062017002/consolide?leiaKehtiv	
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This vignette was compiled based on information provided by country experts and desk research. The information provided may be incomplete or contain inaccuracies. If you have any comments or updates, please email us at the following email addresses:

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