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

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

Belgium	**Standard HTA process (non-orphan drugs)**	**Special process (orphan drugs) – Expedited**
Overview of health system and P&R/HTA process	Tax based health system.[1] Healthcare policy responsibility is shared between federal and regional governments.[3] All drug reimbursement processes/assessments/decisions conducted at national level. The Commission for the Reimbursement of Pharmaceuticals (CTG – CRM) board assess proposals based on preliminary reports written by a group of experts of the Rijksinstituut voor Ziekte en Invaliditeitsverzekering - Institut National d'Assurance Maladie-Invalidité (RIZIV – INAMI). CTG – CRM is responsible for all reports supporting a recommendation and/or proposal. Pricing decisions are made by the Minister of Economic Affairs (advised by the Committee of Pricing for Pharmaceutical Specialties (Commission des Prix des Spécialités Pharmaceutiques (CPSP) – Prijzencommissie voor de Farmaceutische Specialiteiten (PFS)). Minister of Social Affairs makes final reimbursement decision after the Minister of Budget has given his/her binding advice: positive (positive list) or negative.[2]	
Differentiation of rare disease treatments in the P&R system	EMA orphan designation	
Eligible medicines	Drugs with marketing authorization in one of the three classes: Class 1 - added therapeutic value Class 2 - analogous or similar therapeutic value Class 3 - generics/copies [3]	Orphan designated drugs with marketing authorization follow the regulation of one of the three classes.
Process	1. Reimbursement request assessed by the CTG-CRM board and a group of experts of the RIZIV – INAMI (who prepare assessment report). 2. Assessment report is presented at a CTG-CRM meeting, followed by a discussion on assessment elements and their relative importance.	Same as standard process, but: - Applicant does not have to submit a pharmaco-economic model in case of Class 1 application - Companies can initiate the price-setting procedure as soon as a

Belgium	Standard HTA process (non-orphan drugs)	Special process (orphan drugs) – Expedited
	3. The assessment report and discussion are used to prepare a preliminary reimbursement (provisional proposal) to which companies have a set amount of time to react. 4. Any reactions are taken into account, and the proposal is voted on by the CTG-CRM to reimburse or not (2/3 majority is needed for a positive response). 5. Depending on voting response, a final motivated proposal is created and voted on again. 6. If a 2/3rd voting majority is reached, a preliminary proposal becomes a 'final' proposal (not yet a decision). 7. The final proposal is sent to the Minister of Social Affairs to make the reimbursement decision. The process timeline is as follows: - Reimbursement request, evaluation report (after 60 days), - Provisional proposal (after 120 days) - Final proposal (after 150 days) - Decision - a 2/3 majority is required to approve or reject a proposal (after 180 days) [2]	positive opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA is available, so before the definitive market authorization is issued --> This allows pharmaceutical companies to gain up to 67 days in the price setting process. [2]
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	CTG-CRM can appeal to external and/or internal (employees at the INAMI/RIZIV) experts (contracted medical doctors selected by the INAMI/RIZIV, and state-employed pharmacists) with scientific clinical and/or economic evaluation skills. Experts critically assess the request for added therapeutic value and draft reimbursement proposals for the CTG-CRM. [3]	OMP reimbursement is conditional upon approval of an advisory physician of sickness funds. A college of physicians (medical experts) may be established to support and advise the advisory physician, but this is not always and not systematically done. The decision to establish a college is made by the CTG-CRM. [2]
Key domains in assessment	- Clinical effectiveness - Cost effectiveness - Budget impact - Other [2, 3]	Same, but pharmaco-economic model not required.

Belgium	**Standard HTA process (non-orphan drugs)**	**Special process (orphan drugs) – Expedited**
Evidentiary requirements	- Preference for RCTs, which can be complemented (but not replaced by) by non-RCT data [2]	- Same, but greater understanding for the challenges related to OMPs [2] - Despite immaturity of data, they always try to end up at least with a MEA. In general, they are somewhat more flexible with OMPs, as pharmaco-economic data have less impact on the decision in the end (as compared to Class 1).
PROMs	PROMs formally appraised by the CTG-CRM. QoL is one of the assessed elements. No formal definition dictates which PROMs are preferred in appraisal processes.	
Appraisal framework	In addition to the key domains: - Comfort/convenience - Applicability - Safety Different criteria are focused on for each class: - Class 1: therapeutic value (primary evaluation for this class), drug price and reimbursement basis, budget impact, cost effectiveness - Class 2: therapeutic value, drug price and reimbursement, budget impact - Class 3: drug price and reimbursement, budget impact [3]	
Reimbursement decision	If the CTG-CRM board votes 2/3 positive for a proposal, it is sent to the Minister of Social Affairs to make the final reimbursement decision. Reimbursement is defined according to the following four elements: 1. The public price and reimbursement basis, i.e. the key variable for calculating cost-sharing. The reimbursement basis usually equals the public price 2. The reimbursement conditions, i.e. the conditions restricting access to reimbursement, e.g. age range, preliminary diagnostic examinations, maximum dosage, etc. 3. The category of reimbursement, which determines the cost-sharing mechanism. There are five categories based on disease severity, which determine the percentage of reimbursement by the national health insurance. 4. The group of reimbursement, i.e. the group of specialties for which similar conditions of reimbursement are applied, based on the therapeutic chemical classification. There are 23 groups in total. Final decision by the Minister of Social Affairs is either positive (positive list) or negative.[2, 3]	

Belgium	**Standard HTA process (non-orphan drugs)**	**Special process (orphan drugs) – Expedited**
Pricing process	Pricing decision depends on the added therapeutic value adequate return on investment (from societal point of view). Class 1 drugs may negotiate a price above a comparator's price. Maximum price is usually based on internal reference pricing (prices of other similar products) and external reference pricing (prices in other countries). The Minister of Social Affairs fixes the maximum distribution margins for the wholesaler and the pharmacist, as well as the maximum (public) price. [2]	Same, but for Class 1 and OMPs, pharmaceutical companies are authorized to initiate the price-setting procedure as soon as a positive opinion of the Committee for Medicinal Products for Human Use (CHMP) of the EMA is available, so before the definitive market authorization is issued. --> This allows pharmaceutical companies to gain up to 67 days in the price setting process. [2]
Managed entry agreements	- Confidential rebate based on clinical outcome in clinical studies (population level) - Budget cap - OB scheme to collect additional evidence for later reassessment - OB for individual patients - Other *All national - no regional differences. [2]	
Main challenges in appraising medicines for rare diseases (tick all that apply)	X Lack of good quality clinical data X Lack of real world data X Introducing value for money ☐ Monitoring treatment efficacy X Managing budget impact ☐ Lack of criteria/transparency of OMP P&R processes X Making arrangements to work for all stakeholders X Lack of long-term meaningful outcomes ☐ Other? Please specify	
Impact of special processes	Sometimes the process leads to non reimbursement due to clinical and/or budgetary reasons, which cannot be solved within a MEA.	
Proposed policy change	No changes are planned for orphan drugs	
Joint initiatives	BeNeLuxA, EUnetHTA, PPRI, MOCA	
SOURCES		
1	https://ec.europa.eu/health/sites/health/files/state/docs/chp_be_english.pdf	

Belgium	Standard HTA process (non-orphan drugs)	Special process (orphan drugs) – Expedited
2	p 35-38 https://kce.fgov.be/sites/default/files/atoms/files/KCE_288_Improve_Belgian_process_managed_entry_agreements_Report.pdf	
3	https://kce.fgov.be/sites/default/files/atoms/files/KCE_147C_Drug_reimbursement_systems_4.pdf	

Created in March 2019 by the IMPACT-HTA team with the support of the country experts. Last updated in September 2019.

Acknowledgments: We would like to thank thank Inneke Van de Vijver, Acting President of Taskforce Managed Entry Agreements at the National Institute for Health and Disability Insurance (INAMI-RIZIV-NIHDI), for her time and valuable contribution in providing the information used to create and validate this vignette. This research is funded under the EC's Horizon 2020 Programme within IMPACT-HTA. Results reflect the authors' views. The EC is not liable for any use of the information communicated.

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:

- Elena Nicod at elena.nicod@unibocconi.it
- Amanda Whittal at amanda.whittal@unibocconi.it