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

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

Spain	**Standard appraisal/reimbursement process for innovative treatments**
Overview of health system and P&R/HTA process	Tax based health system [1] The Spanish MoH coordinates the health system with the Consejo Interterritorial del Sistema Nacional de Salud (CISNS - a collegiate governance body composed of the National Ministry of Health and 17 regional ministries of health (Autonomous Communities: ACs)). The MSSSI receives support from 4 specialized agencies, including the Spanish Agency for Medicines and Medical Devices (AEMPs). Within the ACs, main actors include departments of health, specialized agencies, and sometimes a HTA body. [2] The Spanish MoH, in particular, the Comisión Interministerial de Precios de los Medicamentos (Interministerial Committee for Pricing and Reimbursement, comprised of representatives from the MoH, Minstry of Economy, Ministry of Finance and regional health care services, among others) is **the body responsible for setting the price of drugs**. For the final P&R decision they use, among other relevant information, the **drug appraisal report** coordinated by AEMPS. The main actors in the appraisal process are the AEMPs (as a coordinator), Dirección General de Cartera Básica de Servicios del Sistema Nacional de Salud y Farmacia (General Directorate of Basic Portfolio of Services of the National Health and Pharmacy System) and the medicines department from the healthcare bodies of the ACs. Although the P&R decision is made by the MoH and valid for all regions, the healthcare bodies from the different ACs are the ones who will take care of the costs of the drugs once the healthcare providers prescribe it. The MoH systematically applies rebates in the medicines invoice; for OMPs the rebate is lower. No special procedure for innovative medicines (which includes RDTs), but one article can be applied for RDTs - Art. 92 – Pricing and reimbursement legislation (specific necessities of certain patients) - which outlines specific criteria to be used for P&R (see below 'appraisal framework).
Differentiation of rare disease treatments in the P&R system	There is no differentiated process specifically for the evaluation of OMPs in Spain. Ultra-rare disease treatments that affect very few patients, e.g.: cystic fibrosis, muscular dystrophies, metabolic diseases, etc. are not formally differentiated by different criteria, but may be can be accounted for within the deliberation.

Eligible medicines	Medicines with marketing authorization – manufacturer needs to submit a dossier to apply for pricing and reimbursement (single procedure).
Process	1. Marketing authorization by EMA 2. Manufacturer submits dossier to the Interministerial Committee for pricing and reimbursement 3. **Drug appraisal report** by AEMPS in coordination with Dirección General de Cartera Básica de Servicios del Sistema Nacional de Salud y Farmacia and the medicines department from the ACs healthcare body 4. Decision by the Interministerial Committee for Pricing and Reimbursement The appraisal can be appealed by scientific societies, the marketing authorization holder and patients' associations. The P&R decision can be also appealed by the marketing authorization holder. Regional healthcare services can comment and give opinion during the processes. The final appraisal and listed price are publicly available.
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	In the appraisal coordinated by AEMPs, scientific societies and patient associations can take part. In order to do so, these societies must receive an invitation from the AEMPs.
Key domains in assessment	- Clinical effectiveness - Safety - Cost effectiveness (minor role) - Budget impact
Evidentiary requirements	No special leniency given to orphan drugs
PROMs	Since a specific threshold in cost-utility is not used for P&R decisions, quality of life questionnaires are not mandatory. PROMs are therefore considered when meaningful and available, but play a minor role. Applicable instrument for measuring QoL depends on the pathology. Generic and specific are accepted.

Appraisal framework	In addition to the key domains, the following aspects are considered: - Innovation (e.g. meets unmet need, shows significant benefit) - Unmet need - Severity of the disease - Applicability - Relative effectiveness and safety When Art. 92 for rare diseases is applied, the following criteria are considered for OMPs: a) Severity, duration and sequelae of the different pathologies for which they are indicated b) Specific needs of certain subpopulations c) Therapeutic and social value of the drug and its incremental clinical benefit, taking into account its cost-effectiveness d) Rationalization of public spending for pharmaceutical benefit and budgetary impact on the National Health System e) Existence of medications or other therapeutic alternatives for the same conditions at a lower price or lower cost of treatment f) Degree of innovation of the medicine
Reimbursement decision	Decision is made by the Interministerial Committee for Pricing and Reimbursement within the MoH, and is valid for all regions in Spain. The decision is informed by, the **drug appraisal report** coordinated by AEMPS, and other relevant information. The following decision can be made: - Complete reimbursement (no restrictions included in the indication of the product) - Reimbursed with restrictions (depending on the uncertainties and the price of the product) - Reimbursed within a mandatory managed entry agreement - Negative P&R decision
Pricing process	International Reference Pricing
Managed entry agreements	- Confidential discount - Budget cap - Outcome based scheme to collect additional evidence for later reassessment - Outcome based scheme for individual patients, only paying for certain performance - Restriction of ex-ante use - Based on previous treatments received or subpopulations of patients as evidence *Very few MEAs at national level, more often at regional level

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 ☐ Introducing value for money ☐ Monitoring treatment efficacy X Managing budget impact ☐ Lack of criteria/transparency of OMP P&R processes ☐ Making arrangements to work for all stakeholders X Lack of long-term meaningful outcomes X Other (High cost- medicines, use throughout compassionate use , social demand)
Impact of special processes	No special processes
Proposed policy change	1. More transparency in the process (according with the CNMC – Competition Authorities report) 2. Introduction of a more extensive economic evaluation section in the assessment report 3. Efforts towards generating national manage entry agreements and registries 4. Special committee for special medicines (compassionate use, off label, etc.)
Joint initiatives	National Level: Central procurement (vaccines, biosimilars) International Level: Valleta Agreement
SOURCES	
1	http://www.euro.who.int/__data/assets/pdf_file/0004/128830/e94549.pdf
2	Health systems in transition pdf
3	

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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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