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

Russia	**Standard appraisal/reimbursement process for innovative treatments**
Overview of health system and P&R/HTA process	The Russian reimbursement system includes[1]: 1. **Essential Drugs list (EDL):** the EDL is the basis for further inclusion of medicines into federal outpatient reimbursement list "14 high cost nosologies" (HCN), as well as for further drug provision in inpatient care settings. 2. **Drug provision program for beneficiaries in accordance with the Federal Law No 178:** applies to specific categories of citizens in outpatient care settings. Beneficiaries are disabled patients within any category of disability, disabled children, participants of the Great Patriotic War, war veterans, and other categories of citizens. The program covers drug provision of any diseases, including rare diseases, with the drugs included in the "EDL" list. **Drug therapy is covered by the federal budget.** 3. **14 HCN list includes specific medicines** used for the treatment of individuals with haemophilia, cystic fibrosis, pituitary dwarfism, Gaucher disease, malignant neoplasms of lymphoid, hematopoietic, and related tissue, multiple sclerosis, hemolytic-uremic syndrome, juvenile arthritis with systemic onset, mucopolysaccharidosis types I, II, and VI, unspecified aplastic anemia, hereditary deficiency of factor II (fibrinogen), VII (labile), X (Stuart-Prower) and after organ/tissue transplantation. **The majority of these diseases are rare. Drug therapy is covered by the federal budget.** 4. **List of 17 orphan diseases (OD): defined as life-threatening and chronic progressive rare (orphan) diseases leading to a reduction in life expectancy of citizens or to lifelong disability). It includes:** paroxysmal nocturnal hemoglobinuria, idiopathic thrombocytopenic purpura, complement deficiencies, central precocious puberty, aromatic l-amino acid decarboxylase, tyrosinemia, maple syrup urine disease, and other disorders of branched chain amino acid metabolism, fatty acid oxidation disorders, homocystinuria, glutaric aciduria, galactosemia, other sphingolipidoses, acute intermittent porphyria, Wilson's disease, osteogenesis imperfecta, pulmonary arterial hypertension. **Drug therapy is covered by regional budgets.** 5. **Regional reimbursement lists are formed** in accordance with the Federal Law No. 890. Beneficiaries with the provision of drugs for free are: disabled persons of group I (the most severe disability group; inability to self-service or complete dependence on others), unemployed disabled persons of group II, disabled children under age of 16, children 0–3

[1] As of January 1st 2021, the **"ONLS" drug provision program** will no longer exist due to changes in the legislation. This programme applied to specific categories of citizens in outpatient care settings, e.g. disabled patients within any category of disability, disabled children, participants of the Great Patriotic War, war veterans, and other categories of citizens

Russia	Standard appraisal/reimbursement process for innovative treatments
	years, children under 6 years from multiple children families, other categories of citizens, and patients with particular diseases (e.g., diabetes, oncology, bronchial asthma, phenylketonuria and other diseases). Beneficiaries with the provision of drugs with 50% discount are: working people with group II disability, people with disabilities of group III, retirees and other categories of citizens. **Drug therapy is covered entirely or by 50% by regional budgets**. Patients with orphan diseases not included in any of these lists (14 HCN, 17 OD lists and several rare diseases covered by Federal Law No. 890) pay out-of-pocket for these drugs. In case of disability or for vital reasons (clear definition of "vital reasons" doesn't exist) patients may have these drugs covered by federal or regional budgets.
Differentiation of rare disease treatments in the P&R system	Federal law #323: "Rare (orphan) diseases are diseases that have a prevalence of no more than 10 cases of the disease per 100'000 population".
Eligible medicines	**14 HCN and 17 OD lists include specific medicines. Nomenclature of medicines for the 14 HCN list is defined by the committee at the federal level. For inclusion in the list of 14 HCN medicines should be preapproved in the EDL. Nomenclature of medicines for the 17 OD list is defined on the regional level.**

Process	• Inclusion of drugs in the EDL and 14 HCN is based on dossier submission.
	• The following components of the dossier are assessed:
	  ○ Clinical evidence by one of the expert organizations of the Ministry of Health (50 expert organizations, 45 of them are medical universities);
	  ○ Compliance to the methodology of the economic assessment by the Center for Healthcare Quality Assessment and Control of the Ministry of Health of the Russian Federation;
	  ○ Followed by the Chief specialist for the final assessment of the dossier.
	• A dossier is reviewed for reliability and validity of clinical evidence, drug safety, positive clinical and economic outcomes data, adequacy of economic calculations for approved methodology. Some other characteristics are also assessed: such as production sites in Russia, dosage frequency, novelty of mechanism performance. Assessment is characterized by marks in accordance with integrated scales.
	• The whole assessment process is described in the Decree of the Government of the Russian Federation dated August 28, 2014 No. 871 (latest amendments - on December 3, 2020).
	• The assessment results are then discussed by committee[2] members comprised of representatives of different organizations (Federal Antimonopoly Service, Federal Service for Surveillance in Healthcare, etc.) and clinical pharmacologists.
	• Chief specialist, representatives of a manufacturing company, Center for Healthcare Quality Assessment and Control, and the expert organization that reviewed and analyzed dossier, also participate in the committee meeting. In some cases, patient representatives may participate. Any participant may express their opinion.

[2]Committee under Ministry of Health on the formation of lists of drugs and the minimum range of drugs in pharmacies

Russia	Standard appraisal/reimbursement process for innovative treatments
	• The decision on inclusion of a particular medicine on one of the lists is based on open voting. The medicine is included in the list with more than a half of the votes in favor of inclusion. • Information including the assessment of the dossier, voting results and maximum sales price are published on the website of the Ministry of Health. • Appeal (after the decision is made by the committee) is not possible. • A dossier can be resubmitted next calendar year. • Dossier for inclusion in federal reimbursement lists may be submitted every quarter throughout the year. Committee meetings are held 4 times a year (once a quarter). • Reimbursement lists are updated once a year, thus all dossiers submitted before April 10 of the current year will be reviewed for medicines inclusion in the lists of the next year. • Dossiers submitted after April 10 may expect to be included in a year (not next year).
Disease specific expert input (e.g. clinicians or patients in any stage of the process)	The Chief specialist carries out a final evaluation of the submitted dossier (all the information except for the methodology of the clinical and economic studies, and partly the section on additional evidence about the medicine), gives final marks and participates in discussions at the committee meeting of the Ministry of Health.
Key domains in assessment	• Clinical effectiveness and safety of the medicine; • Level of evidence and strength of clinical studies results; • Economic evaluation (results of cost-effectiveness analysis and budget impact analysis); • Methodological quality of studies on economic evaluation; • Additional therapeutic value (dosage frequency, new performance mechanism); • Additional data on the medicine (disease relevance for the society, production sites in Russia, etc.)
Evidentiary requirements	Randomized controlled trials, conducted outside Russia, may be used for marketing authorization of orphan medicines. For inclusion of an orphan drug in the EDL and 14 HCN, the entry mark threshold (assessment are characterized by marks in accordance with integrated scales) is lower for quality evaluation of clinical data, pharmaco-economic data (including budget impact analysis) and evaluation of supplementary (other) dossier data (including information on production sites).
PROMs	Data on patients' quality of life may be included in the section on clinical data and used for cost-effectiveness analysis (cost-utility analysis). This data is not compulsory.
Appraisal framework	*Relates to any medicine, not only orphan drugs* Besides criteria that are assessed with marks, the following aspects influence decision-making while reviewing a dossier: • Price • availability of analogue therapy

Russia	Standard appraisal/reimbursement process for innovative treatments
	• expected number of patients • availability of appropriate budget (especially when considering inclusion of medicines in the reimbursement lists that imply federal funding)
Reimbursement decision	Decision on inclusion of medicines in the EDL and 14 HCN list are made by the Ministry of Health committee. Since reimbursement lists are approved/endorsed annually by the Government of the Russian Federation, the decision of the Ministry of Health committee may be considered as recommendation-based. However, not once have the Government made adjustments to the nomenclature of drugs lists prior to their approval. Medicines included in the 14 HCN list are provided to patients for free if the patient has one of these conditions. Medicines for treatment of diseases from the 17 OD list are provided to patients for free. Medicines included in the EDL are provided for free as well if the patient has relevant benefits. Medicines included in the regional reimbursement lists may be provided to the patient for free or with 50% discount, if the patient has benefits. Any medicine by vital reasons can be provided to a patient for free based on the decision of the medical board
Pricing process	Inclusion of medicines in the EDL implies compulsory registration of the maximum sales price. After inclusion of a medicine in the EDL, price submitted for registration should not exceed the price indicated in the dossier for inclusion of a medicine in the EDL and used in the economic study. Maximum sales price for an imported medicine proposed for the state registration cannot exceed: minimum price for this medicine in reference countries and volume-weighted average actual price of medicine imports during the reporting period. Maximum sales price for a medicine produced in EEC cannot exceed: volume-weighted average actual sales price for this medicine during the reporting period and minimum price for this medicine in reference countries (if the medicine is distributed in foreign countries) Process and requirements for maximum sales price registration are the same for all medicines, including orphan drugs.
Managed entry agreements	Confidentiality agreement on price, conditions for medicines use as well as innovative models of drugs provision (cost-sharing and risk-sharing) are not used in Russia due to legislation restrictions.
Main challenges in appraising medicines for rare diseases (tick all that apply)	**X Lack of good quality clinical data** ☐ 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** ☐ Lack of long-term meaningful outcomes **X Other**

Russia	Standard appraisal/reimbursement process for innovative treatments
Impact of special processes	Randomized controlled trials, conducted outside Russia, may be used for marketing authorization of orphan medicines. For inclusion of an orphan drug in the EDL and 14 HCN list, entry mark threshold is lower for quality evaluation of clinical data, pharmaco-economic data (including budget impact analysis) and evaluation of supplementary (other) dossier data (including information on the level of localized production). Lower mark threshold allows to consider particular specifics of orphan drugs both in terms of clinical data base (complexity of RCT) and economic indicators (due to high price level for orphan drugs). Drug provision for patients with orphan diseases in outpatient care settings differs from that for other patients with orphan diseases, which are included in 14 HCD and 17 OD lists. Funding of the 14 HCD list is guaranteed by the federal budget. Funding of the 17 OD list is less stable due to difference in regional budgets. Patients with orphan diseases, which are not included in any of these lists, are provided with medicines at their own expense. In case of lifelong disability or for vital reasons, they receive medicines covered by the regional (seldom federal) budget by decision of the medical board.
Proposed policy change	The possibility of changing funding process of medicines included in the 17 OD list from regional to federal level is being discussed.
Joint initiatives	NA
SOURCES	
1	The Decree of the Government of the Russian Federation dated August 28, 2014 No. 871 on Approval of the Regulations for Preparation of the Lists of Drugs for Medical Use and the Minimum Range of Drugs Required for Rendering Medical Care. http://government.ru/docs/14540/
2	The Decree of the Government of the Russian Federation dated October 29, 2010 No. 865 on State regulation of the prices of the medicines included in the vital and essential drugs list" https://fas.gov.ru/documents/576018
3	The Decree of the Government of the Russian Federation dated September 15, 2015 No. 979 on making the amendments to the Decree of the Government of the Russian Federation dated October 29, 2010 No. 865 on Approval of the Methods of Calculation of Selling Prices of Medicines Included into the Vital and Essential Drugs List http://government.ru/docs/19739/
4	Federal Law No. 178-FZ of July 17, 1999 on State Social Assistance http://pravo.gov.ru/proxy/ips/?docbody=&nd=102061042&intelsearch=178-%F4%E7
5	The Decree of the Government of the Russian Federation dated July 30, 1994 No. 890 on State Support for the Development of the Medical Industry and Improving the Provision of the Population and Healthcare Institutions with Medicines and Products for Medical Purpose http://government.ru/docs/all/11699/
6	Federal Law No. 61-FZ of April 12, 2010 on Circulation of Medicines http://government.ru/docs/all/99466/

Created in October 2020 by the IMPACT-HTA team with the support of the country experts. Last updated in December 2020.

Acknowledgments: We would like to thank Dmitry Shchurov and Nuriya Musina from the Center of Healthcare Quality Assessment and Control of the Ministry of Health of the Russian Federation for their 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.

Do not hesitate to contact the Impact-HTA team if you have any comments or updates about the information provided in this vignette at the following email addresses:

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

Legend

OMP = Orphan medicinal product

P&R = Pricing and reimbursement

HTA = Health technology assessment

RDT = Rare disease treatment

EMA = European Medicines Agency

MEA = Managed entry agreement

MA = Marketing authorization

RCT = Randomized controlled trial

EU = European Union