Review of Rare Disease Policy Developments in Europe and Türkiye (2020–2025) in the Context of Innovative Orphan Drugs

HPR177

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INTRODUCTION

Approximately 900 orphan-designated drugs were authorized in Europe between 2020 and 2024. Among them, 53% were small molecules, 45% were biologics or oligonucleotides, and 8% were advanced therapy medicinal products (ATMPs).

OBJECTIVE

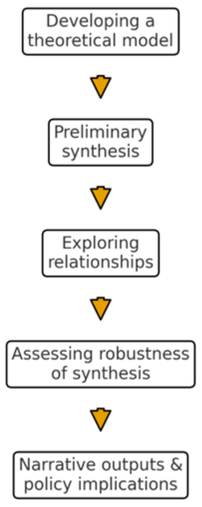
This review aims to assess recent policy developments in Europe and Türkiye in light of this evolving treatment landscape.

METHOD

Following PRISMA$_1$ guidelines, a systematic review was conducted using PubMed to identify peer-reviewed articles published between 2020 and 2025 discussing orphan drug policy in EU countries and Türkiye.

Key words: rare disease, rare disorder, orphan drug, health policy, legislation, HTA, health technology assessment, national plan, access.

Narrative Synthesis (Popay et al.) Flow



Two reviewers independently screened titles, abstracts, and full texts based on predefined inclusion (availability of a policy recommendations, EU or EU country specific or Türkiye specific) and exclusion criteria (not disease-specific or non-drug-focused articles). A narrative synthesis was undertaken based on the **Popay J. framework[2]**.

Policy recommendations from relevant articles were extracted from the full texts by two reviewers.
Details including suitability for review, year of publication, geographic focus, policy type, study type, key themes, main policy recommendations, mention of orphan medicinal product modality, stakeholder involvement, identified barriers and facilitators.

RESULTS

This PRISMA-guided systematic review examined 86 peer-reviewed articles published from 2020 to 2025 that satisfied the inclusion and exclusion criteria. Over the past five years, there has been a consistent rise in the number of policy recommendations observed. All were rated as high quality by the reviewers

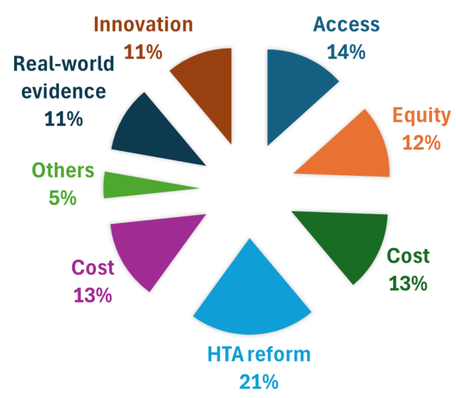
Scope of the Policy Recommendations

A total of 64 papers provide policy recommendations for the entire EU.

Among the country-specific papers, Italy leads with 7, followed by Slovenia, Germany, and Spain, each with 3. Additionally, there was at least one recommendation paper identified for Poland, Turkey, the Czech Republic, Finland, Belgium, and the Netherlands.

Categories of Policy, Associated Themes, Applied Methods, Enablers, and Barriers to Implementation

The focus was on HTA (n=25), followed closely by regulations (n=20) and pricing (n=12). The key themes in the policy recommendations were balanced, with HTA reforms (n=19) receiving the greatest attention.



Most of the policy recommendation papers were policy analyses (n=36), while systematic and narrative reviews, empirical studies, and case studies were also commonly employed methods.
The most reported obstacle in policy implementation was **data gaps** (n=57), followed by **a lack of alignment between HTA and regulatory agencies**, as well as **delays in reimbursement.**

The enablers identified, listed by frequency, are: **HTA reforms, cross-border collaborations, legislative reforms, and patient involvement**.

Compilation of reports:

This review identified evolving orphan-drug policy approaches across Europe and Türkiye, reflecting both shared policy goals and jurisdiction-specific implementation paths. A common aim across countries was to improve **timely and equitable access** to orphan therapies while preserving **health-system sustainability**, with reforms clustering around HTA processes, pricing and reimbursement arrangements, and data infrastructure.
Thematically, three consistent drivers of policy reform emerged:
(1) **HTA alignment and methodological consistency**, including efforts to reduce variation in cost-effectiveness thresholds, incorporate disease-severity modifiers, and strengthen the role of real-world evidence;
(2) **Value-based and managed-entry mechanisms**, used to address uncertainty in clinical evidence and budget impact; and
(3) **Patient-centered policy design**, with increasing formalization of patient input into assessment and decision-making processes.

Despite shared objectives, **substantial cross-jurisdictional differences** persist. Western EU countries reported more established use of performance-based agreements and mature data ecosystems, whereas smaller EU markets and Türkiye emphasized capacity building, adaptive reimbursement tools, and alignment with European data standards. Several jurisdictions referenced the forthcoming EU pharmaceutical legislation as a structural mechanism for greater policy convergence, while others underscored the need for flexibility to reflect national financing constraints and healthcare infrastructure maturity.
Overall, the synthesis highlights a convergence toward structured, evidence-responsive, and patient-inclusive orphan-drug policy, but progress is heterogeneous, and opportunities remain to harmonize HTA approaches, expand real-world evidence platforms, and strengthen cross-country collaboration to ensure that rare-disease patients benefit equitably from innovation.

CONCLUSIONS

While Europe and Türkiye have made progress in rare disease policy and regulatory alignment, major gaps persist in equitable access. Tailored HTA approaches and improved cross-country coordination are essential to close implementation gaps and ensure timely access to orphan therapies.

- ❑ Growing convergence in orphan-drug policy across Europe.
- ❑ Countries increasingly emphasize aligned HTA processes, structured value assessment for ultra-rare therapies, and expanded use of RWE.
- ❑ MEA, performance-based arrangements, and patient-centered decision frameworks are emerging. Still, cross-country variation persists in data maturity, pricing mechanisms, and implementation capacity.

REFERENCES

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2- Popay, J.,et al. (2006). *Guidance on the conduct of narrative synthesis in sytematic reviews*. Institute for Health Research.

CONTACT INFORMATION

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