Executive summary

Implementation of controlled access to and distribution of medicinal products in the European Union (CONTROL-EU)

1. Project information

1.1 CONTROL-EU

- EU PE&PV research network
- ROC21 - SC02 - EMA/2020/46/TDA/L4.02
- EUPAS1000000313
- Study Report Version 2.1, February 18, 2026
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1.2 Keywords

Controlled Access Programme (CAP), Controlled Distribution System (CDS), Risk Minimisation Measures (RMMs), Risk Minimisation Control Programmes (RMCPs), Implementation, Barriers, Enablers.

1.3 Disclaimer & Acknowledgments

The research leading to these results was conducted as part of the activities of the EU PE&PV (Pharmacoepidemiology and Pharmacovigilance) Research Network led by Utrecht University. The scientific work for this project was coordinated by Utrecht University (UU) and the National Institute for Public Health and the Environment (RIVM). The project has received support from the European Medicines Agency under the framework contract EMA/2020/46/TDA/L4.02. This document expresses the opinion of the authors of the paper and may not be understood or quoted as being made on behalf of or reflecting the position of the European Medicines Agency or one of its committees or working parties. This study has been registered in the HMA-EMA Catalogues of Real-World Data Sources and Studies: EUPAS1000000313.

2. Study

2.1 Rationale and Background

Risk minimisation control programmes (RMCPs), formerly known as controlled access programmes (CAP) and controlled distribution systems (CDS) are the most stringent additional Risk Minimisation Measures (aRMMs) in the EU, intended for products requiring the highest level of safety control. While conditions are agreed upon at the EU level, further elaboration and adaptation to national health systems occurs at the Member State level. Currently, there is insufficient information on how these requirements are implemented nationally and how they are experienced by stakeholders, representing a significant knowledge gap for these high-risk tools.

2.2 Research Question and Objectives

The study aimed to evaluate national implementation processes for RMCPs and analysed stakeholder perspectives across eight EU Member States. The objectives were:

- Identify and describe national processes for implementation, focusing on roles, responsibilities, pathways, and timelines.
- Analyse stakeholder experience (patients, HCPs, MAHs, and regulators) regarding the feasibility and challenges of implementing control elements for eight purposively selected products.
- Identify key enablers and barriers for adherence and successful implementation at the national level.

2.3 Study Design

The study used a mixed-methods approach composed of three work packages:

- Work Package 1 (WP1): Document analysis and mapping of national regulatory implementation pathways.
- Work Package 2 (WP2): A quantitative cross-sectional survey (WP2a) and qualitative semi-structured interviews (WP2b) with regulators, MAHs, HCPs, and patients (interviews only).
- Work Package 3 (WP3): Triangulation of findings using the Consolidated Framework for Implementation Research (CFIR) to identify determinants of successful implementation.

2.4 Setting

The multi-country study was conducted in eight EU Member States: Austria (AT), Greece (EL), Latvia (LV), Netherlands (NL), Portugal (PT), Slovenia (SI), Spain (ES), and Sweden (SE). The countries are distributed across the four different geographic regions (North, East, West, South) of the European Union and have different health care systems and structures.

2.5 Subjects and Study Size

- WP1 Mapping: Covered 8 national pathways and 8 Centrally Authorised Products: Aspaveli, Fintepla, Revlimid (and generics), Soliris (and biosimilars), Spravato, Strimvelis, Uptravi, and Yescarta.
- WP2a Survey: A total of 5,112 invitations were sent, resulting in 202 participants. These represented 286 stakeholder-product combinations which were finally included.
- WP2b Interviews: 262 individuals were approached, resulting in 85 interviews conducted across all stakeholder groups.

2.6 Variables and Data Sources

Variables: Six implementation steps (Submission, Assessment, Feedback, Approval, Integration, Follow-up); perceived ease of implementation (4-point Likert scale); and

barriers/facilitators mapped to five CFIR domains (Innovation, Outer Setting, Inner Setting, Individuals, Implementation Process).
Data Sources: National regulatory documents, public statements, educational materials, survey responses via Qualtrics, and verbatim interview transcripts.

2.7 Results

Regulatory implementation pathways show considerable alignment across countries, but variation exists in stakeholders' involvement in assessment of RMCPs, and feedback frequency. Product-specific mapping shows that prescribers and marketing authorization holders are key actors, with pharmacists playing a secondary role. Implementation was frequently described as easy rather than difficult; however, regulatory implementation was generally considered more challenging than clinical integration and use of the programmes. MAHs often reported that both phases were difficult. Key barriers included design complexity, administrative burdens (innovation domain), misalignment with national contexts and legal frameworks (outer setting domain), and lack of experience (individuals domain). Enablers included flexible designs (innovation domain), integration into existing workflows (inner setting domain), and effective stakeholder communication (implementation process domain).

2.8 Discussion

National pathways show considerable alignment in core steps, but operational follow-up is often limited to pharmacovigilance triggers rather than routine assessment. Findings suggest that programmes matching end-user needs and context are more successful, while rigid designs increase administrative friction. Flexible designs and effective stakeholder collaboration enable implementation and use, whereas measures perceived as redundant or disproportionate to the risk can hinder adherence, emphasizing the need for balanced and relevant RMCPs. Study strengths include broad multi-country coverage and mixed-methods triangulation, while limitations involve potential recall bias and incomplete publicly available records of programme implementation.

2.9 Conclusion

While RMCPs are critical for minimizing serious associated risks, implementation introduces national variation and complexity. Key recommendations include drafting measures with high-level intentions for flexibility, formalization of national feasibility assessment prior to programme launch, and establishing NCA focal points to coordinate cross-programme learning.

3. Investigators

The Coordinating Team (CT) is composed of:

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The Steering Committee (SC) is composed of:

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