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Introduction & Background

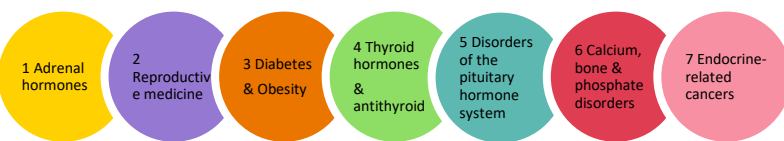
Medicine shortages are a critical issue for physicians and patients in the Global rare disease community. Medicines and orphan drug shortages or supply issues may have various causes, such as lack of active product ingredients (API), pricing and reimbursement hurdles, withdrawal from market because of commercial or clinical reasons or concerns¹. The impact of drug shortages can vary across these stakeholders. In some cases similar alternative products are available for medical staff to prescribe though impact on patients remains high due to reimbursement criteria of insurance policies². In other situations where alternatives do not exist or have a different safety and efficacy profile, there may be an impact on disease control and patient quality of life. For patients reliant on orphan drugs (ODs) as the only available therapy a shortage becomes critical to their wellbeing.

To understand and map the impact of the OD shortage on these different stakeholders in the care process for rare endocrine conditions, the European Society of Endocrinology has issued this survey study in a joint effort between European Society of Endocrinology (ESE), European Society for Paediatric Endocrinology (ESPE), Endo-ERN and their respective Patient Advocacy Groups (PAG). The results of this survey study will inform a report addressing the availability of the most needed endocrine drugs in Europe and the level of awareness raised across different stakeholders on the impact to the patient.

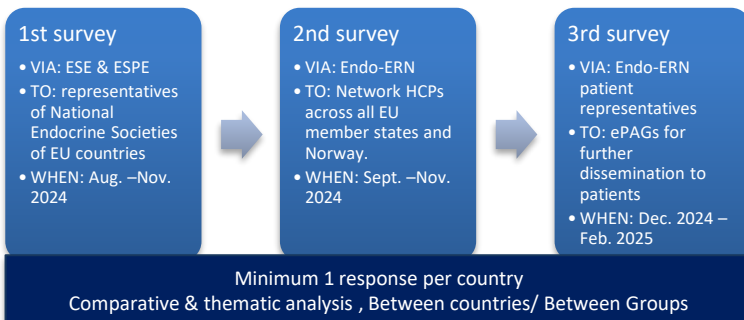
Key research questions:

- What are the medicines most affected by drug and medicine shortages in the EU over the course of 2023/24 per country, and are there geographical differences?
- Are the lists of essential and/or critical medicines meeting rare endocrine care and treatment requirements?
- How impactful are shortages in specific OD drugs treating rare endocrine conditions?

Method



Data was gathered via a multi-stakeholder survey to 3 target groups created with 8 specific drug categories (see above) and disseminated separately to each group from a dedicated coordinator (ESE, Endo-ERN, ePAGs respectively). Analysis will result in a report profile per country.



Preliminary Results & Findings

We received 32 responses in total from 25 Endo-ERN HCPs from 14 different countries. All 7 drug categories had at least 1 response.

Most mentioned Drug shortage	Hydrocortisone	transdermal estradiol	liraglutide, semaglutide	Liquid Levothyroxine /L-thyroxine	Somatropin, CRH	Phosphorus	Sandostatina
Most common reason cited for shortage	Withdrawal from market because of commercial reasons/ I don't know	Production and or quality issues/ I don't know	Production and or quality issues	Production and or quality issues	Production and or quality issues	I don't know/ None	I don't know/ None
Countries reporting Severe Clinical Impact to a patient due Shortage	Greece, Italy	Italy	France, the Netherlands	Italy	Greece, Denmark	Italy	None

A further look at Adrenal Hormones, the most represented drug category, reveals that all drugs listed experienced a shortage and 4 drugs were in prolonged shortage in Italy, with 1 also in Austria.

Drug Shortage last 2023/24	N countries with some reported shortage in last 12 months	Counties reporting shortage for prolonged period(s) of time (> 1 month)
Fludrocortisone tab	4	
Hydrocortisone tab 1 mg and/or 2 mg	2	
Hydrocortisone tab 5 mg and/or 10 mg	2	Italy
Hydrocortisone tab 20 mg	4	Austria, Italy
Pharmacy-prepared hydrocortisone	1	Italy
Hydrocortisone Modified Release tab	2	Italy
Hydrocortisone IM Injection 100 mg	3	
Cortisone acetate tab	1	
Prednisolone tab 1 mg and/or 2 mg	1	
Prednisolone tab 5 mg	2	
Prednisolone tab 20 mg and/or higher dose	2	
Prednisolone liquid 1 mg/ml	1	
Prednisolone liquid 5 mg/ml	1	
Dexamethasone tab 0,5 mg	1	
Dexamethasone tab 1,5 mg	1	

Next Steps

As our data only represents 14 of the 27 member states and Norway our next step is to issue a second targeted survey round to Endo-ERN HCPs in countries not yet represented. Once all data from 3 target groups is available, comparative analysis will be performed between the 3 groups to identify differences in experience of drug shortages, awareness of issue and the effects/ impact felt by each of the target groups. As of 2021, the WHO essential medicines list officially includes 70 (out of 478) orphan drugs³, with the most recent update

References

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2. Jakubowski S, Holko P, Nowak R, Warmuth M, et al. Clinical and non-clinical aspects of reimbursement policy for orphan drugs in selected European countries. *Front Pharmacol.* 2024;1498386. Available from: <https://doi.org/10.3389/fphar.2024.1498386>
3. Costa E, Moja L, Wirtz VJ, et al. Uptake of orphan drugs in the WHO essential medicines lists. *Bull World Health Organ.* 2024;102(1):22-31. doi:10.2471/BLT.23.289731

1. Dutch Pituitary Foundation, Nijkerk, The Netherlands

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4. Department of Endocrinology and Metabolism, Amsterdam University Medical Center, Amsterdam, the Netherlands

5. Endo-ERN European Reference Network on Rare endocrine condition

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