Is The New EU HTA Process Fit For Rare Patient Engagement?

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INTRODUCTION

Patient engagement in European Health Technology Assessments (HTA) has grown. During European Network for Health Technology Assessment (EunetHTA) Joint Action 3 (2016-2021), engagement with patient associations strengthened, leading to the inclusion of patient experience in the European Union (EU) HTA regulation (2021/2282)[1] and a statement on "the importance of engaging stakeholders, including patients, throughout the Joint Clinical Assessment (JCA) process".

Rare diseases are often life threatening and affect mainly children, so the experiences of individual rare disease patients and their representation can be less visible.

OBJECTIVES

To assess how the JCA Implementing Act (IA)[2] accounted for the concerns raised by rare disease and rare cancer patient representatives during public consultation.

MATERIALS & METHODS

Feedback from individual patients/patient organisations representing rare diseases/rare oncology was compiled from the public consultation (March 05 – April 2, 2024) of the draft[3] for JCA of medicinal products. Key themes were derived from these public responses. Only English language feedback was considered.

In the EU, a rare disease is defined as prevalence of not more than 5 per 10,000.[4] In the case of rare cancers, incidence is more appropriate, as prevalence is affected by mortality. The incidence of rare cancers is less than 6 per 100,000 persons per year[v]. We used these thresholds in the selection of responders (Table 1).

RESULTS

Feedback was received from a wide number of European organisations (47) including patient relevant input from academics, medical societies, and public health bodies. Of the 47 organisations, 12 were considered in scope as rare disease and rare cancer patient/patient organisations (Table 1).

Table 1: Selection of Participating Rare Disease and Rare Cancer Patients/Patient Organisations

Organisations	Remit	Country	Disease/Therapeutic Area(s)	Prevalence/Incidence
Neurofibromatosis Patients United	European	Netherlands	Rare/Neuroscience/Oncology	The estimated prevalence of 1. Neurofibromatosis is approximately 1 in 60,000
Cancer Patients Voice	National	Czech Republic	Oncology (Rare)	Inclusion of Rare Cancers and incidence of 6 per 100,000
Rare Diseases Czech Republic	National	Czech Republic	Rare Diseases	Inclusion of rare diseases with prevalence of 50 per 100,000/5 per 10,000
Gynecological Cancer patients in Finland	National	Finland	Oncology (Rare)	Inclusion of rare gynaecological cancers, incidence <6 per 100,000
Cancer Patients Europe	European	Belgium	Oncology (Rare)	Inclusion of rare cancers, incidence <6 per 100,000
Lymphoma Coalition (Europe)	European	France	Hemato/Oncology (Rare)	Inclusion of rare haematological cancers, incidence <6 per 100,000
Kidney Cancer Network Germany	National	Germany	Oncology (Rare)	Mostly a common cancer except for some rare sub-types with incidence <6 per 100,000
Confederation of European Otorhinolaryngology and Head and Neck Surgery	European	Austria	Otorhinolaryngology-Head and Neck Surgery (Rare)	Inclusion of rare head and neck cancers, incidence <6 per 100,000
Digestive Cancers Europe	European	Belgium	Oncology (Rare)	Mostly a common cancer except for some rare sub-types with incidence <6 per 100,000
SJOGREN EUROPE	European	Switzerland	Rare Diseases	Primary Sjogren disease 38.95/100 000, or one person per 2,567
Eurordis	European	France	Rare Diseases	Inclusion of rare diseases with prevalence of 5 per 10,000
SIOPE (European Society for Paediatric Oncology)	European	Belgium	Paediatric Rare Oncology	Inclusion of rare cancers, incidence <6 per 100,000

Participating Nations, Organisations, and Individual Representation

The draft IA public consultation received feedback from 129 organisations in total, including 47 patient organisations, of which 12 had a rare disease/rare cancer remit (Table 1). Of the 27 EU member states, 7 were represented in this cohort: Austria, Belgium, Czechia, Finland, France, Germany and Netherlands; plus non-EU Switzerland.

Oncology was the most prominent focus of the European rare patient organisations: oncology (5), haemato-oncology (1), rare paediatric oncology (1), rare disease patients (3), otorhinolaryngology (head and neck) (1) and neuroscience (1).

Main Themes

7 main themes were extracted as part of this study. Topics which were raised more than 4 times were included in this review, as well as paediatric rare concerns represented by at least 1 organisation.

Table 2: Key Themes Raised by Rare Disease and Rare Cancer Patients/Patient Organisations

Theme	Count of Themes	Addressed in IA
Timeliness/Early-Stage Patient Involvement	10	Yes
Representativeness/Diversity/Conflict of Interest/Inequalities and Socio-Economic and Financial Barriers	9	Representativeness (Vague)/Conflict of Interest (Yes)
QoL/Patient and Paediatric Experience Studies/RWE	7	Yes but not explicitly in terms of paediatric-centric tools or single-arm trials
Individual vs Collective Perspective	6	Yes
Transparent Patient Expert Selection Criteria	5	Not in IA Regulation
Trainings and Equipping Patients for Engagement Process	5	Not in IA Regulation
Plain Language Summary	4	Not in IA Regulation

Timeliness:
Timeliness was a top concern, with requests for "ongoing, timely and relevant communication" beyond established intervals. Rare patient groups questioned whether the new processes would result in "poorly communicated timelines" that could hinder diverse patient perspectives. The Implementing Act (IA) aims for "clear deadlines" to improve "timely patient access to health technologies."

Early-Stage Patient Involvement:
Calls for early[6] patient involvement have been addressed, with the JCA coordination group possibly reaching out to patients when marketing authorisation applications are shared, potentially a year before JCA submission.

Representativeness:
The draft IA proposed a shortlist from the HTA stakeholder network. Rare patient feedback felt this limits representativeness, noting the dominance of Western European groups. Eastern European organisations expressed concern that Western-based groups or employees dominate, rather than actual patients or caregivers. The IA includes no provision for representativeness.

Conflict of Interest (COI):
Stringent COI policies were requested to ensure impartiality and transparency. The current lack of financial reimbursement for participation may limit involvement from lower socio-economic backgrounds. The IA does not reference co-creation of patient/carer lists or regular rotation.

Individual vs Collective Perspectives:
Despite limited individual patient representatives, organisations felt engaging rare patients would better represent their voice. The final IA[2] mentions "general procedural rules" and "the right to good administration," addressing the need for clarity between individual and collective perspectives.

Transparent Patient Expert Selection:
There were calls for a transparent, inclusive process for selecting patient representatives, which was only partially addressed through COI statements.

Unaddressed Issues:
- Quality of Life/Real World Evidence (RWE)
- Training Patients for Engagement
- Plain Language Summaries

CONCLUSIONS

This study has assessed the feedback from European rare patients and patient organisations, and concludes that the final IA addressed calls for earlier communications around "timeframes" and provided assurance via "general procedural rules" for consistent patient involvement in JCA. COI/confidentiality clauses have been addressed in the final IA.

However, open and transparent processes around: the selection of rare patient representatives, training, plain language summaries for diverse European patient populations with varying levels of health literacy and linguistic backgrounds, and acceptance of study designs such as paediatric-centric tools or single-arm trials, remain topics that require clarification.

REFERENCES

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2. Commission Implementing Regulation (EU) 2024/1381 of 23 May 2024 laying down, pursuant to Regulation (EU) 2021/2282 on health technology assessment, procedural rules for the interaction during, exchange of information on, and participation in, the preparation and update of joint clinical assessments of medicinal products for human use at Union level, as well as templates for those joint clinical assessments https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ%3AL_202401381
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5. European Society of Medical Oncology (ESMO). Definition of rare cancers. Accessed October 29, 2024. https://www.esmo.org/policy/rare-cancers-working-group/what-are-rare-cancers/definition-of-rare-cancers
6. Summary 12: The selection should start as early as possible, whenever the Coordination Group, via the HTA secretariat, receives information about upcoming submissions of applications for marketing authorisations for the medicinal products referred to in Article 7(1) of Regulation (EU) 2021/2282