Patient Experience Data in regulatory decision-making:

An analysis of non-interventional studies in marketing authorisation applications submitted to the EMA in 2018-2023

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Background and context

BDSG workplan on PED

(included in a broader EMA's PED community action plan)

- **Understand and increase transparency on the current use of PED** in regulatory context to support evaluations and decision making
- **Identify challenges and opportunities** for enhancing optimal and impactful use of PED
- **Establish the value of PED** in regulatory decision making and beyond, in collaboration with patients and other stakeholders

Review of PED use cases in regulatory decision-making

Complement recent reviews:

- Review of SmPC – PRO - Oncology A review of patient-reported outcomes used for regulatory approval of oncology medicinal products in the European Union between 2017 and 2020 - PubMed (nih.gov)
- Review of SA – PRO, ObsRO, PerfO - all TAs *Brit J Clinical Pharma - 2023 - Silva - Patient-reported observer-reported and performance outcomes in qualification.pdf
- Review by the labelling team (2016 - https://docs.eudra.org/webtop/drl/objectId/090142b2832a6bde)

Perform a review of **use of PED from NIS** in MAAs and EoI

- All TAs – Time period: TBC
- All PED (PRO, ObsRO, PerfO, PPS, PE data)
- Type of instrument: generic vs disease specific - new vs already validated and used – prior SA sought (Y/N), prior qualification (Y.N)
- Scope of use: pre-approval vs. post- approval

- Purpose: evidence category (main vs supportive)
- Endpoint type (primary, secondary, exploratory)
- Assessor feedback: supporting, limited support, not supporting
- Highlighted limitations (inform areas for further work (e.g. specific methods)

➔ *Repeat in 3-5 years to assess impact of ongoing effort (PED RP, PED action plan…)*

PATIENT EXPERIENCE DATA

1. Patients are the experts in their own experience.
2. Patients are the ultimate users of medical products.
3. Patients should participate in decisions that affect their care.

PATIENT EXPERIENCE DATA

> Data that directly reflect the experience of a patient or carer, without input or interpretation by a healthcare professional, third party or device. These data can be collected from a variety of data sources, including patient engagement activities.
>
> *European Medicines Agency*

Patient-reported outcomes, **patient preference studies** and **data from patient engagement** correspond to types of PED. PED ensures that <u>medicine development and approval</u> consider <u>patients' perspectives and experiences</u>**,** leading to more patient-relevant decisions.

PATIENT EXPERIENCE DATA IN MAAs

Applied Health Economics and Health Policy (2023) 21:925–935
https://doi.org/10.1007/s40258-023-00827-3

ORIGINAL RESEARCH ARTICLE

The Assessment of Patient-Reported Outcomes for the Authorisation of Medicines in Europe: A Review of European Public Assessment Reports from 2017 to 2022

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Neurological Sciences (2023) 44:2933–2937
https://doi.org/10.1007/s10072-023-06825-6

BRIEF COMMUNICATION

Patient-reported outcome measures in drugs for neurological conditions approved by European Medicines Agency 2017–2022

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A review of patient-reported outcomes used for regulatory approval of oncology medicinal products in the European Union between 2017 and 2020

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Patient-Reported Outcomes (PROs)

Interventional studies (pre-authorisation)

Particular disease areas

RESEARCH QUESTION

Are Patient Experience Data being used in **non-interventional studies (NIS)**, both in **pre- and post-authorisation** settings, of new marketing authorisation (MAA) and extension of indication (EoI) applications containing Real-World Data submitted to the EMA between 2018 and 2023?

DEFINITIONS

Patient Experience Data (PED)

Patient-Reported Outcomes (PRO)	Health outcomes that directly report the patient’s experience of their health status without amendment or interpretation by a clinician or other party.
Patient Preference Studies (PPS)	Qualitative or quantitative assessment of the relative desirability or acceptability to patients of aspects that differ among alternative health interventions.
Data from Patient Engagement (PE) activities	Data from interactions with patients to gather their experience with a disease and their preferences regarding treatments and outcomes.

European Medicines Agency (2025). Reflection paper on patient experience data (Draft).

DATA SOURCES & ELIGIBILITY

Pre-authorisation NIS:

Assessment Reports

Post-authorisation NIS:

Assessment Reports/Risk Management Plans

Post-Authorisation Studies' Protocols

Assessment Reports of Post-Authorisation Studies' Protocols

Finalised applications for **MAAs and EoIs containing RWD** submitted to the EMA between **2018 and 2023**.

Exclusion of generic medicines, biosimilars, informed consent applications and well-established use.

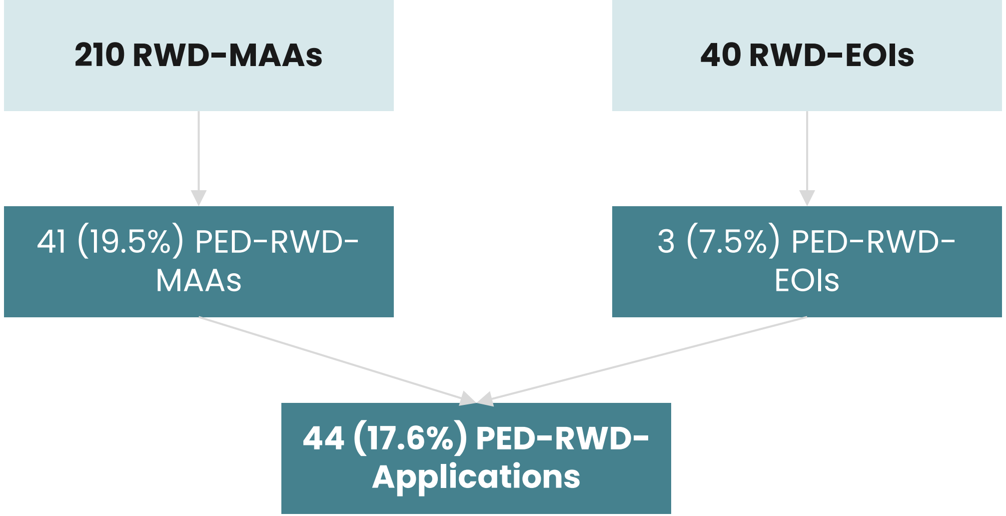
DATA COLLECTION & ANALYSIS

1. **PED identification** was conducted using a **keyword search strategy** applied to the screened documents.
2. **Relevant information on PED** use was **systematically extracted** according to pre-defined variables.
3. **A 20% subset** of the sample was **double-checked by an independent reviewer**, and any disagreements were resolved through a consultation with a third researcher to reach **consensus**.
4. **Descriptive analyses** were performed for both numerical and categorical variables. Comments from assessors were **inductively categorised** into broader thematic groups.

MAAs AND EOIs CHARACTERISATION

During 2018-2023…

250 applications presenting RWD were submitted to the EMA.



210 RWD-MAAs

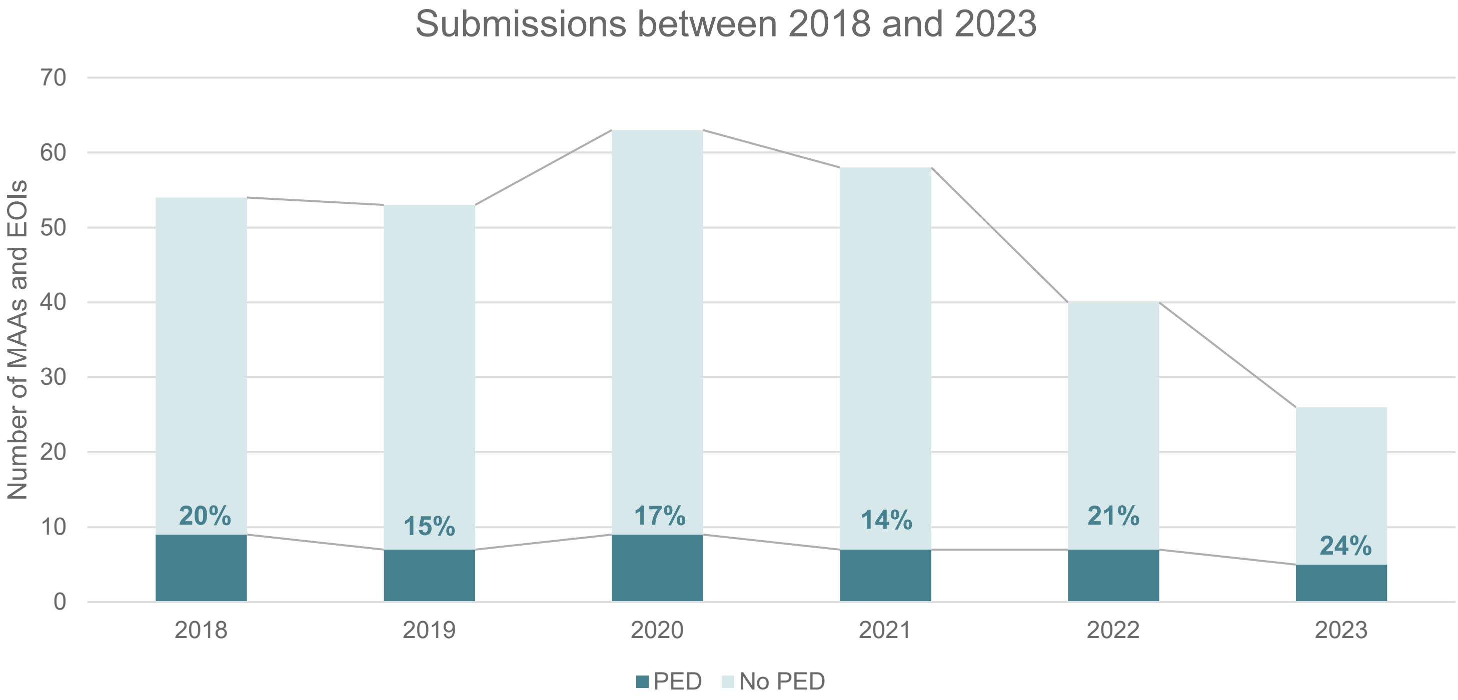
40 RWD-EOIs

41 (19.5%) PED-RWD-MAAs

3 (7.5%) PED-RWD-EOIs

44 (17.6%) PED-RWD-Applications

MAAs AND EOIs SUBMISSION YEAR



MAAs AND EOIs CHARACTERISATION

Variables	***N* (%)** (Total=44)
ATC Code	
A	9 (20.4%)
B	7 (15.9%)
H	4 (9.1%)
J	1 (2.3%)
L	12 (27.3%)
M	5 (11.4%)
N	3 (6.8%)
R	1 (2.3%)
S	2 (4.5%)
Orphan designation	24 (54.5%)
ATMP classification	8 (18.2%)

Variables	***N* (%)** (Total=44)
Marketing Authorisation Type	
Standard	31 (70.4%)
Conditional	9 (20.4%)
Exceptional circumstances	4 (9.2%)
Marketing Authorisation Status	
Authorised	40 (91.0%)
Withdrawn	2 (4.5%)
Refused	2 (4.5%)

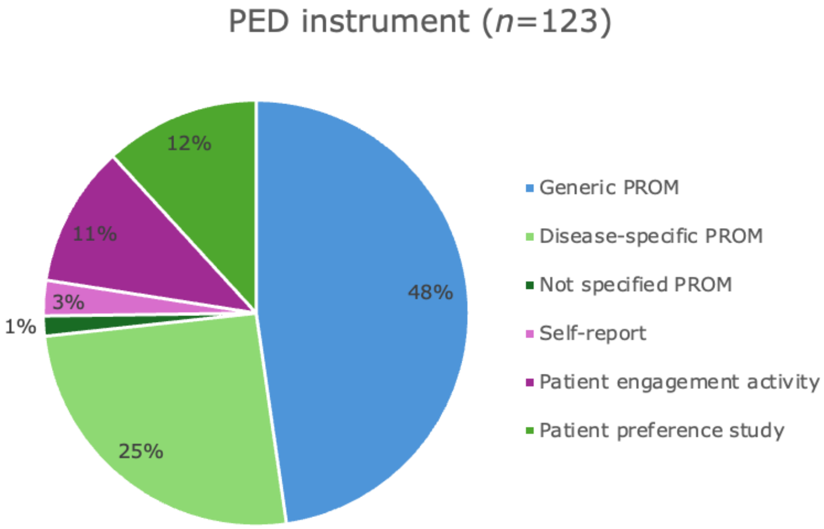
STUDIES PRESENTING PED

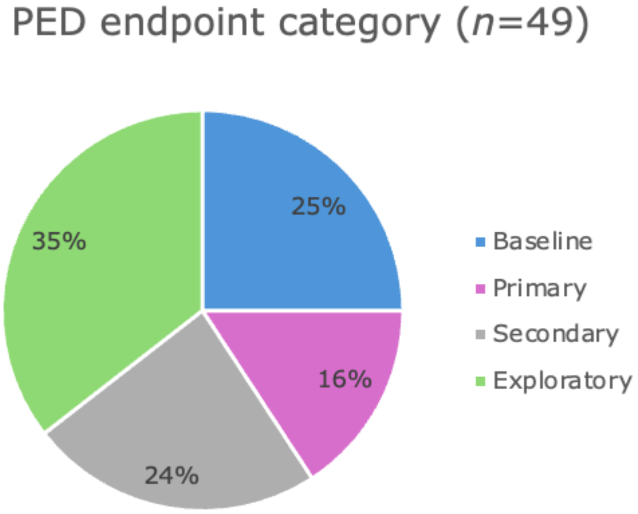
Variables	***N* (%)** (Total=56)
Setting	
Pre-authorisation	13 (23.2%)
Main	1 (7.6%)
Supportive	6 (46.2%)
Not applicable	6 (46.2%)
Post-authorisation	43 (76.8%)
ANX	3 (7.0%)
SOB	3 (7.0%)
MEA	37 (86.0%)

Variables	***N* (%)** (Total=56)
Objective	
Safety	21 (37.5%)
Safety and effectiveness	20 (35.7%)
Effectiveness	6 (10.7%)
Patient experience	9 (16.1%)
Study design	
Cohort	41 (73.2%)
Cross-sectional	9 (16.1%)
Qualitative interviews	2 (3.6%)
Other: *engagement*	4 (7.1%)
Sample size*	300 (150-500)
PED number**	2.2±2.2 [1-12]

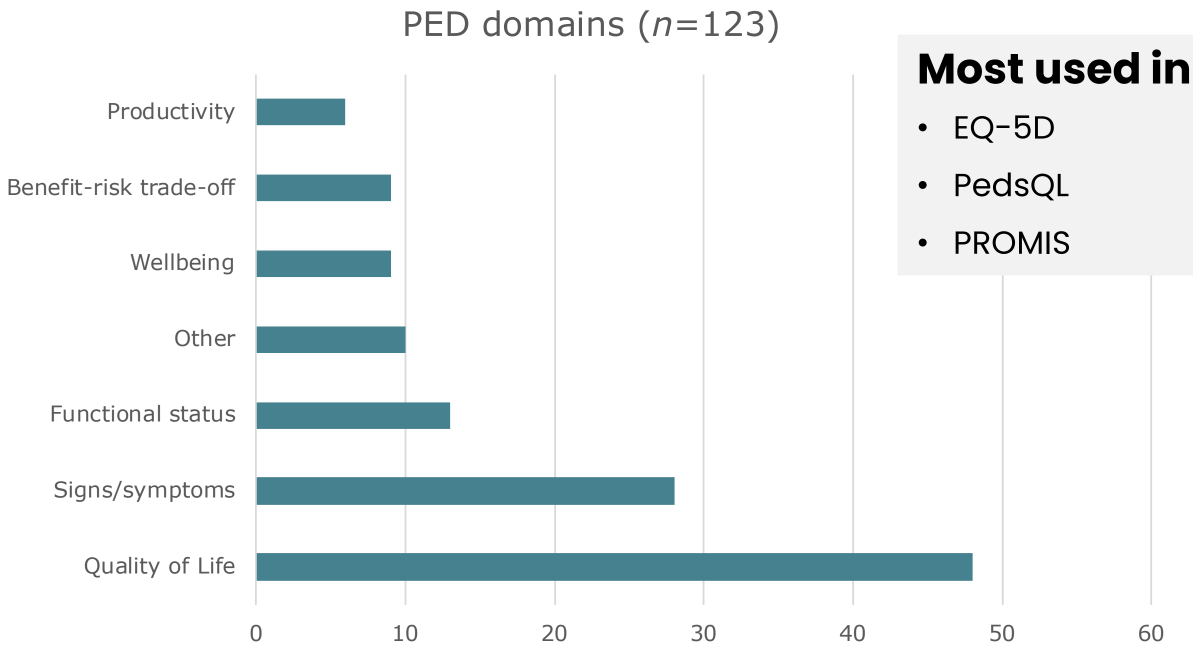
*presented as median (IQR); **presented as mean±SD [range]

PED INSTRUMENTS AND DOMAINS





PED INSTRUMENTS AND DOMAINS



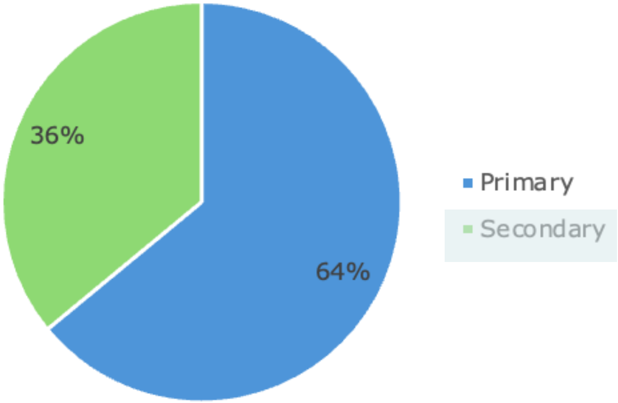
Most used instruments:

- EQ-5D
- PedsQL
- PROMIS

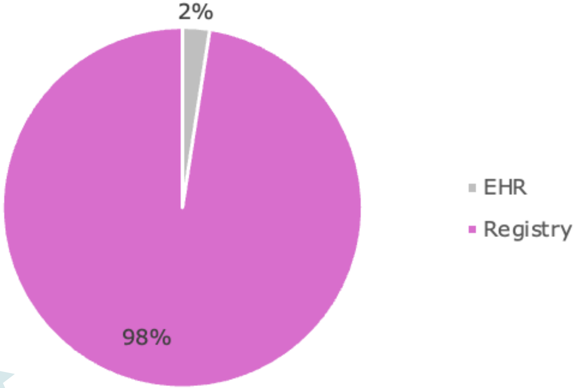
Other includes domains such as Health behaviour, Burden, Knowledge, Patient satisfaction, Medication adherence, Caregiver burden, Socioeconomic status

PED INSTRUMENTS AND DOMAINS

PED collection (n=114)



PED secondary data sources (n=41)



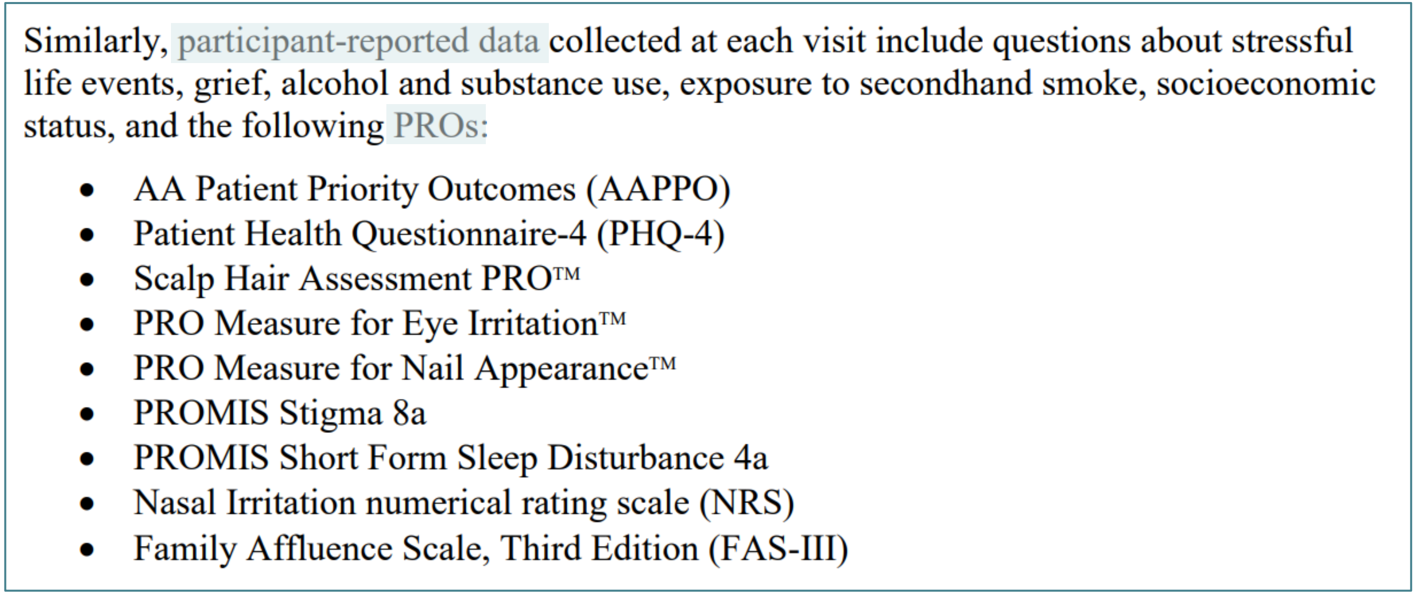
ASSESSORS’ COMMENTS

Assessors’ comments regarding PED use in non-interventional studies were found for 20 submissions.

Patient involvement	“CHMP has received the patient survey performed by the patient organization.” “Patients' perception of benefits and risks of a medicine may be different from the view of medical experts.”
Study design and planning	“Please clarify how changes in [outcome] can be obtained if baseline information on these parameters is not a requirement.” “The MAH has reviewed the PROs in the protocol and decreased the number [to diminish burden, as suggested by assessors]”
Data management and quality	“Information on data management and quality control [...] are presented together in an unclear fashion.” “A detailed SAP is missing.”
Bias and confounding	“Difficulties are anticipated in the interpretation [of the PED-related results]… due to the observational nature [of the study].” “The population […] was very small compared to the total number of subjects from [the clinical trials].”

EXAMPLES

Patient-Reported Outcomes



Similarly, participant-reported data collected at each visit include questions about stressful life events, grief, alcohol and substance use, exposure to secondhand smoke, socioeconomic status, and the following PROs:

- AA Patient Priority Outcomes (AAPPO)
- Patient Health Questionnaire-4 (PHQ-4)
- Scalp Hair Assessment PRO™
- PRO Measure for Eye Irritation™
- PRO Measure for Nail Appearance™
- PROMIS Stigma 8a
- PROMIS Short Form Sleep Disturbance 4a
- Nasal Irritation numerical rating scale (NRS)
- Family Affluence Scale, Third Edition (FAS-III)

HMA-EMA Catalogues of RWD studies - A Prospective Active Surveillance Study to Monitor the RealWorld Safety of Ritlecitinib Among Adolescents with Alopecia areata (EUPAS1000000421)

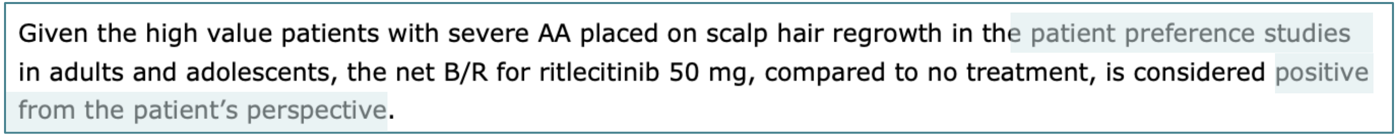
EXAMPLES

Patient Preference Studies

B7981048: Alopecia Areata Benefit-risk trade-off study in adults

The main **objectives** of this study were to: elicit patient preferences for AA treatment attributes and to estimate maximum acceptable risks (MARs) of potential safety concerns associated with JAK inhibitors that AA patients are willing to tolerate for specific treatment benefits, and to assess the net benefit-risk profile of oral ritlecitinib 50 mg QD compared to 30 mg QD and to placebo.

The **design** of the study was a cross-sectional quantitative survey administered online to patients in the United States (US), United Kingdom (UK), France, Germany, Italy and Spain. Patient preferences were elicited using a discrete-choice experiment in which patients were asked to choose between two hypothetical AA treatment profiles and no treatment in a series of questions. Each hypothetical treatment profile was defined by six attributes: the probability of 80% to 100% scalp hair regrowth over 24 weeks of treatment, the probability of moderate or normal eyebrows after 24 weeks of

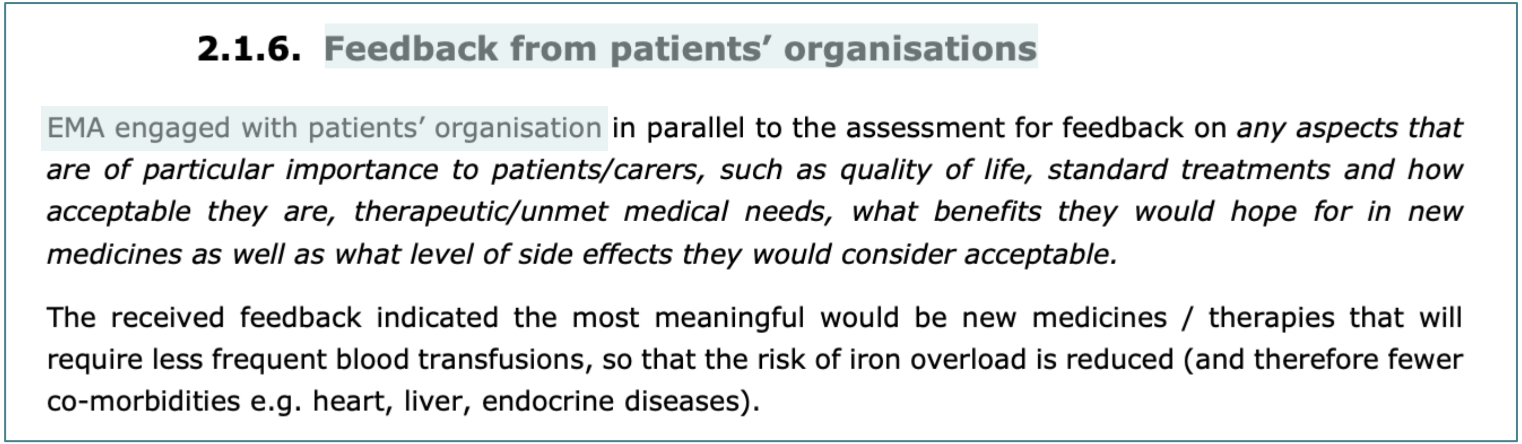


Given the high value patients with severe AA placed on scalp hair regrowth in the patient preference studies in adults and adolescents, the net B/R for ritlecitinib 50 mg, compared to no treatment, is considered positive from the patient's perspective.

European Medicines Agency (2023). European Public Assessment Report - Litfulo.

EXAMPLES

Data from Patient Engagement activities



2.1.6. Feedback from patients' organisations

EMA engaged with patients' organisation in parallel to the assessment for feedback on *any aspects that are of particular importance to patients/carers, such as quality of life, standard treatments and how acceptable they are, therapeutic/unmet medical needs, what benefits they would hope for in new medicines as well as what level of side effects they would consider acceptable.*

The received feedback indicated the most meaningful would be new medicines / therapies that will require less frequent blood transfusions, so that the risk of iron overload is reduced (and therefore fewer co-morbidities e.g. heart, liver, endocrine diseases).

European Medicines Agency (2023). European Public Assessment Report - Casgevy.

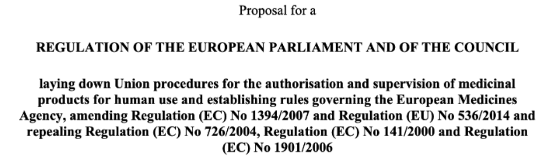
KEY MESSAGES

- Overall **use of PED in NIS** of MAA and EOI applications containing RWD seems to be promising (17.6%).
- **Disease context**: PED-dependent vs. non-PED-dependent therapeutic areas.
- **Early dialogue between stakeholders** to effectively implement PED collection in NIS.
- **Robust study designs** to minimise confounding and bias in the non-interventional context.
- **Clearer PED-specific study objectives** and, therefore, statistical analyses.
- **Patient registries** emerging as a valuable source to implement PED collection in the real-world setting.

FUTURE PED ENABLERS

Legislative advancements

Pharma Legislation



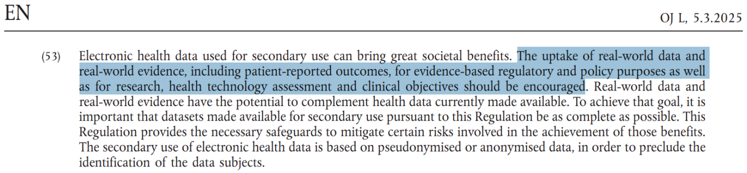
EUROPEAN COMMISSION

Proposal for a

REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing rules governing the European Medicines Agency, amending Regulation (EC) No 1394/2007 and Regulation (EU) No 536/2014 and repealing Regulation (EC) No 726/2004, Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006

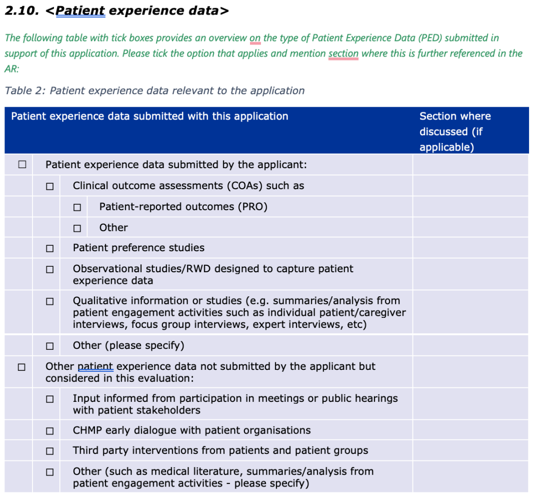
EHDS



EN OJ L, 5.3.2025

(53) Electronic health data used for secondary use can bring great societal benefits. The uptake of real-world data and real-world evidence, including patient-reported outcomes, for evidence-based regulatory and policy purposes as well as for research, health technology assessment and clinical objectives should be encouraged. Real-world data and real-world evidence have the potential to complement health data currently made available. To achieve that goal, it is important that datasets made available for secondary use pursuant to this Regulation be as complete as possible. This Regulation provides the necessary safeguards to mitigate certain risks involved in the achievement of those benefits. The secondary use of electronic health data is based on pseudonymised or anonymised data, in order to preclude the identification of the data subjects.

More transparency



2.10. <Patient experience data>

The following table with tick boxes provides an overview on the type of Patient Experience Data (PED) submitted in support of this application. Please tick the option that applies and mention section where this is further referenced in the AR:

Table 2: Patient experience data relevant to the application

Patient experience data submitted with this application	Section where discussed (if applicable)
☐ Patient experience data submitted by the applicant:	
☐ Clinical outcome assessments (COAs) such as	
☐ Patient-reported outcomes (PRO)	
☐ Other	
☐ Patient preference studies	
☐ Observational studies/RWD designed to capture patient experience data	
☐ Qualitative information or studies (e.g. summaries/analysis from patient engagement activities such as individual patient/caregiver interviews, focus group interviews, expert interviews, etc)	
☐ Other (please specify)	
☐ Other patient experience data not submitted by the applicant but considered in this evaluation:	
☐ Input informed from participation in meetings or public hearings with patient stakeholders	
☐ CHMP early dialogue with patient organisations	
☐ Third party interventions from patients and patient groups	
☐ Other (such as medical literature, summaries/analysis from patient engagement activities - please specify)	

New guidance

New ICH E22
(PPS)

EMA Reflection paper on PED

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