Trends in the Incorporation of Clinical Outcome Assessments in Asthma Drug Development in Japan: A Five-Year Review (2020–2024)

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Authors: *Sakai Y, Crawford B* ***Affiliations:*** *Vista Health Japan K.K., Tokyo, Japan*

1. INTRODUCTION

- Clinical outcome assessments (COAs) are essential for evaluating treatment benefits from a patient-centered perspective[1]. COAs, including patient-reported outcomes (PROs), provide critical evidence on the impact of a treatment from the patient's perspective and play an important role in regulatory decision-making[1].
- Clinical trials incorporating PROs have steadily increased from 2009 to 2023, with Japan showing a growth rate comparable to other regions[2]. In September 2021, the Pharmaceutical and Medical Devices Agency (PMDA) issued the "Guidance on Patient Participation," recognizing PROs as a useful tool to evaluate patient benefit during regulatory review and highlighting their potential to improve approval efficiency[3].
- Despite this, our review of asthma medication label approvals and changes from 2010 to 2019 found that only 2% of products incorporated PROs in the regulatory process in Japan, and only one label reported PRO results[4]. This indicates that the use of PROs in asthma treatment remains limited within the Japanese regulatory framework.
- In Japan, Patient Guidance Forms (PFs), Pharmaceutical Interview Forms (IFs), and package labels are submitted as part of new drug approval applications. While not mandatory for regulatory approval, PFs and IFs provide important supplementary information: PFs offer patients clear guidance to improve understanding of medications and help prevent severe side effects, whereas IFs support healthcare professionals (HCPs) in explaining products and facilitating clinical discussions[5].
- Results from COAs, including PROs, are often included in these documents to provide evidence of treatment benefit from the patient's perspective.

2. PURPOSE

To evaluate the inclusion of COAs, particularly PROs, in asthma drug development in Japan between 2020 and 2024, building on prior analysis of products approved between 2010 and 2019.

3. METHODS

- Asthma treatments approved or with label changes between 2020 and 2024 were identified from the PMDA website.
- Corresponding labels, patient guidance documents, and IFs were reviewed for content related to COAs.
- Clinical trials assessing the following were considered: health-related quality of life (HRQoL), health status, well-being, satisfaction, adherence, illness perception, preferences, disease control, symptoms, and work productivity.
- Symptoms reported only in the adverse events or safety sections were excluded.
- Generic drugs were excluded because patient data are not required for approval.
- For drugs with multiple formulations, a single interview form covering all formulations was used; products sharing the same form were excluded.

4. RESULTS

- A total of 175 newly approved or relabelled asthma products (excluding generics) were reviewed, covering both adult and pediatric formulations.
- After reviewing labels, PFs, and IFs, only one label and 13 IFs included COAs, while none of the PFs did.
  - Labels did not present COA results and only implied that a COA had been used. No products reported actual COA results on the label.
- The number of products including COAs has been increasing, and by 2024, 12% of product labels/IFs included COAs; however, this remains limited (Figure 1).
- Asthma Control Questionnaire (ACQ) was the most commonly used validated COA measure, followed by the Asthma Quality Life Questionnaire (AQLQ) (Figure 2).
- Among the 13 IFs, six presented COAs in both adult and pediatric clinical trials, and one IF included only pediatric COAs.
- In pediatric clinical trials, COAs were mostly the same as those used in adult trials for the same product, with pediatric versions available for ACT, AQLQ, and ACQ (Table 1).
  - For Xolair, the survey content was not described, making it unclear what was measured.
  - For Relvar, although AQLQ and ACT were used in adult trials, ACQ was used in pediatric trials.
  - For Nucala, ACQ and SGRQ were used in adult trials, whereas ACQ and C-ACT were used in pediatric trials.
  - For Onon Dry Syrup, patient and caregiver impressions were not distinguished, making it unclear how much their assessments differed or which was used.

Figure 1: Yearly breakdown of products with COAs description in labels or IFs

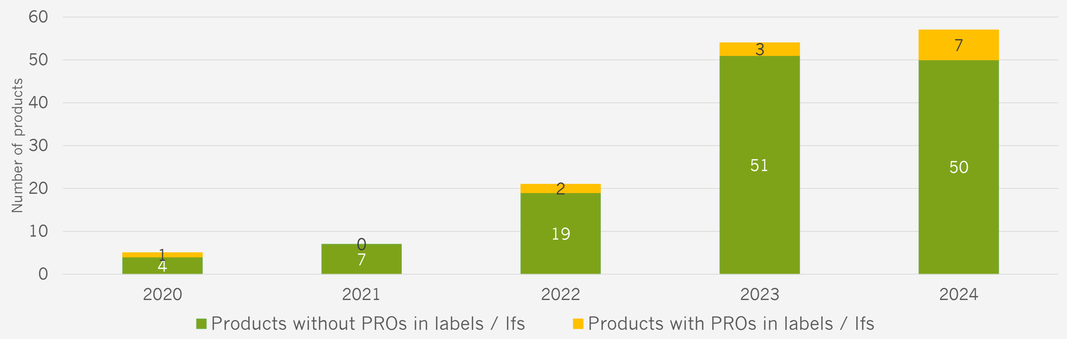
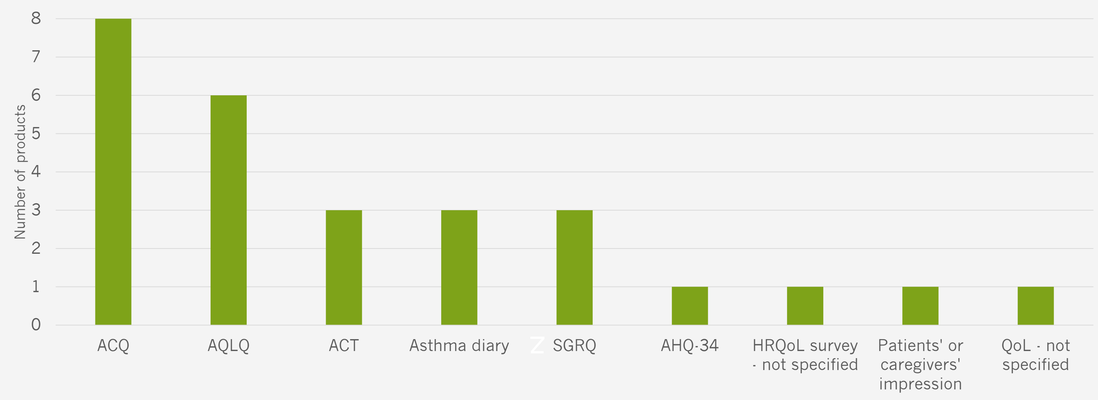


Figure 2: COAs identified in IFs



Asthma Control Questionnaire (ACQ), Asthma Control Test (ACT), Asthma Health Questionnaire (AHQ), Asthma Quality of Life Questionnaire (AQLQ), Health-Related Quality of Life (HRQoL), Quality of Life (QOL), St.George's Respiratory Questionnaire (SGRQ)

Table 1: Measures used and result presentation in pediatric COAs referenced in IFs

Product name	Measurement	Presentation of results
Xolair	HRQoL survey score	The results are also not presented.
Bricanyl	Asthma diary	The physician evaluated efficacy based on the contents of the asthma diary.
Relvar	ACQ-5	The change from baseline in ACQ-5 score at Week 24 showed a between-group difference of 0.00 (95% CI: -0.09, 0.10) between the treatment and the control group.
Flutiform	ACQ-5	From the start of the treatment period, the change from the baseline ACQ-5 score (0.96) decreased over time through to the final evaluation at Week 24. The mean ACQ-5 score at the final assessment was 0.24, and the least squares mean change from baseline (95% confidence interval) was -0.72 (-0.82 to -0.62).
ONON	Pediatric bronchial asthma patients or their caregivers' impression	The proportion reporting their experience as "good" or "very good" was noted.
Nucala	ACQ-7	At Week 12, the proportion of patients whose ACQ-7 score decreased by 0.5 or more from baseline was 48% in the mepolizumab 40 mg group and 50% in the mepolizumab 100 mg group, with an overall proportion of 48%.
	C-ACT	The C-ACT scores generally increased over time. In the overall mepolizumab group, the change from baseline in C-ACT score peaked at Visit 4 (Week 8).

Asthma Control Questionnaire (ACQ), Asthma Control Test (ACT), Childhood Asthma Control Test (C-ACT), Health-Related Quality of Life (HRQoL)

5. CONCLUSIONS

Compared to the 2010–2019 period, the proportion of asthma products including COAs has increased. Their use in paediatric trials reflects growing recognition of patient-centred evaluation within Japan's regulatory and development landscape. However, overall adoption remains limited, highlighting the need for further integration and transparency of COAs in asthma drug development.

References

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