ANALYSIS OF TRANSPARENCY COMMISSION EVALUATIONS OF ADOLESCENT INDICATION EXTENSIONS IN RELATION TO CORRESPONDING ADULT EVALUATIONS IN FRANCE

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1. BACKGROUND AND OBJECTIVES

Extending therapeutic indications to adolescent populations presents specific methodological and practical challenges in generating robust clinical evidence. These include difficulties in recruiting enough patients, ethical considerations, and constraints related to the feasibility of conducting dedicated clinical trials in this population[1].

To address these limitations, the ICH E11A guideline provides a methodological framework for extrapolating existing adult clinical data to paediatric populations[2].

➔ **To analyze how the Transparency Commission (TC) evaluated adolescent indication extensions in relation to the corresponding adult indications.**

2. METHODS

Data source

We systematically reviewed TC reimbursement evaluations of indication extensions to adolescents published between 2024 and May 26, 2026.

Comparison with adult evaluations

Conclusions for adolescent indications were compared to those reached for the corresponding adult indications.

Data extraction and analysis

- Identification of drugs, adolescent indications and target populations.
- Classification of clinical evidence by study design (phase III, phase II/IIb or PK/safety data).
- Comparison of SMR and ASMR ratings between adolescent and adult indications.
- Qualitative analysis of TC decision drivers, including endpoints, comparators, methodological limitations and generalisability.

3. OVERVIEW OF TC EVALUATIONS

13 adolescent indication extensions evaluated between 2024 and June 2026

9 Appraisals aligned with adult evaluations

3 Lower ASMR rating

1 Lower SMR rating

4. RESULTS

Clinical data submitted

- Most submissions were supported by phase III, randomized, comparative trials with a primary efficacy endpoint (n=7; 54%), while two were based on phase II/IIb efficacy data.
- Four assessments relied solely on PK and safety data, with efficacy extrapolated from adults.
- When efficacy was extrapolated from adult data, the TC considered the scientific justification for extrapolation and the relevance of the evidence to adolescents.

TC appraisal compared with adults

- TC conclusions on clinical benefit (SMR) and clinical added value (ASMR) were consistent with adult evaluations in 9 of 13 cases.
- Four adolescent evaluations received less favourable ratings: three lower ASMR ratings and one lower SMR rating.
- Less favourable assessments were associated with limitations in the submitted evidence, including reliance on biological endpoints, lack of relevant comparators, absence of statistically significant differences, and limited generalisability to the target population.

Drug	Indication	Clinical data	SMR/ASMR in adults	SMR/ASMR ado vs adults	TC comments
OLUMIANT (baricitinib)	Moderate-to-severe atopic dermatitis; systemic treatment; **≥2 years**	A	Low / V	**Aligned**	
CIBINQO (abrocitinib)	Moderate-to-severe atopic dermatitis; systemic treatment; **≥12 years**	A	Substantial / IV	**Downgraded ASMR** (V vs IV)	• Lack of comparative data versus available treatments in the pediatric population
OTEZLA (aprémilast)	Moderate-to-severe plaque psoriasis; systemic treatment; **≥6 years, ≥20 kg**	A	Moderate / V	**Aligned**	
SPEVIGO (spésolimab)	Generalized pustular psoriasis flares; monotherapy; intravenous infusion; **≥12 years**	B	Substantial / IV	**Aligned**	
SYNJARDY (empaglifozine, metformine)	Type 2 diabetes mellitus; **≥10 years**	A	Substantial / IV	**Downgraded ASMR** (V vs IV)	• Efficacy demonstrated based on a biological endpoint in adolescents (without demonstrated benefits on morbi-mortality), compared with clinical endpoints (cardiovascular and renal outcomes) in adults
JARDIANCE (empagliflozine)	Type 2 diabetes mellitus; **≥10 years**	A	Substantial / IV	**Downgraded ASMR** (V vs IV)	
PRALUENT (alirocumab)	Heterozygous familial hypercholesterolemia; **≥8 years**	A	Substantial / V	**Aligned**	
FERINJECT (carboxymaltose ferrique)	Iron deficiency; **1–13 years**	A	Substantial / V	**Downgraded SMR** (moderate vs substantial)	• No statistically significant difference demonstrated versus the study comparator • Study population only partially representative of the target population, limiting the generalizability of the results
MIRCERA (méthoxy polyéthylène glycol-époétine bêta)	Symptomatic anemia associated with chronic kidney disease; **≥ 3 months < 18 years**	B	Substantial / V	**Aligned**	
REKAMBYS (rilpivirine) / **VOCABRIA** (cabotégravir)	HIV-1 ; **≥12 years ≥35 kg**	C	Substantial / V	**Aligned**	• In accordance with the European guidelines on the clinical development of medicinal products for the treatment of HIV (EMEA/CPMP/EWP/633/02 Rev. 3)
XYDALBA (dalbavancine)	Acute bacterial skin and soft tissue infections; **≥3 months**	C	Substantial / V	**Aligned**	• In accordance with the European guidelines on the clinical development of medicinal products for the treatment of bacterial infections (EMA/CHMP/187859/2017)
ADEMPAS (riociguat)	Pulmonary arterial hypertension; **<18 years ≥50 kg**	C	Moderate / V	**Aligned**	• In accordance with the Paediatric Investigation Plan (PIP)
OFEV (nintédanib)	Progressive, clinically significant fibrosing interstitial lung diseases and systemic sclerosis-associated interstitial lung disease; **≥ 6 years**	C	Moderate / IV	**Aligned**	• Lack of robust data on clinically relevant endpoints and quality of life in a pediatric population. • Limited extrapolation of clinical data from adults to children due to differences in the clinical heterogeneity of interstitial lung disease between the two populations.

A pIII, multicenter, randomized, comparative (mostly double-blind) trials, with efficacy as the primary objective

B pII/IIb, with efficacy as the primary objective

C PK/safety data combined with extrapolation of efficacy data from adults

5. CONCLUSION

- Despite the challenges of paediatric drug development, most adolescent indication extensions were supported by robust evidence and received TC evaluations consistent with those of the corresponding adult indications.
- The limited number of cases relying on extrapolation from adult data did not result in less favourable evaluations, highlighting the TC's acceptance of extrapolation approaches when supported by an appropriate scientific rationale and regulatory framework.

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References

1. *Lagler FB, et al. Challenges in clinical trials for children and young people. Arch Dis Child. 2021 Apr;106(4):321-325.*
2. *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ICH Harmonised Guideline E11A: Pediatric Extrapolation. Final version. 21 August 2024.*

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