



Regulatory Updates regarding Pediatric Drug Development in Japan

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Disclaimer



The views expressed in this presentation are those of the presenter and do not necessarily reflect the official views of the Pharmaceuticals and Medical Devices Agency.





Regulatory Updates in Japan



- Pediatric drug development is **duty to endeavor**
(2025 Amendment of Pharmaceutical and Medical Device Act)
- PMDA has started requesting companies to consider development of pediatric medicines in Japan through scientific consultation for adult drug development.

<Related PMDA Notification>

Initiatives to Promote Pediatric Drug Development

March 21, 2025 PMDA/CPE Notification No. 1618 • PMDA/CRS Notification No. 15

<https://www.pmda.go.jp/files/000274940.pdf>

- Pediatric drug development symposium was held by PMDA
(August 27, 2025)





Two approaches to addressing drug loss



Resolving existing drug lag/loss

- Council for unapproved and off-label drugs with high medical needs
etc.

Preventing new drug lag/loss

- Participation in pediatric MRCT planned in PIP/PSP from Japan
- Monitoring global pharmaceutical development trends and PIP/PSP trends

Drug lag: The time lag between approval in global and approval in Japan.

Drug loss: A situation where a drug approved overseas has no planned development in Japan.





PMDA Pediatric Drug Development Symposium



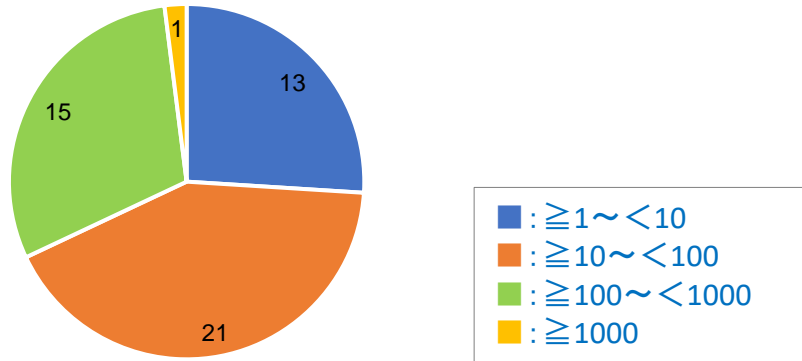
- Held on Aug 27th, 2025
- PMDA has stated commitment to better access to pediatric medicines
 - ✓ PMDA is also one of the stakeholders contributing to the acceleration of global pediatric drug development.
 - ✓ No more new “drug lag/loss”
 - ✓ Participation in pediatric MRCT from Japan



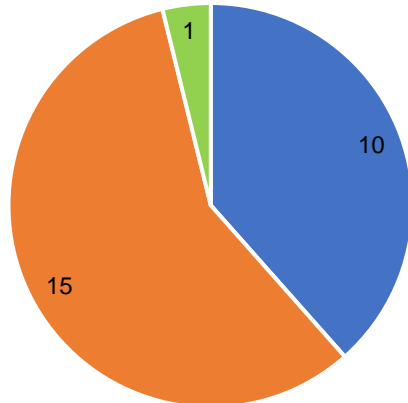
Participation in pediatric MRCT from Japan



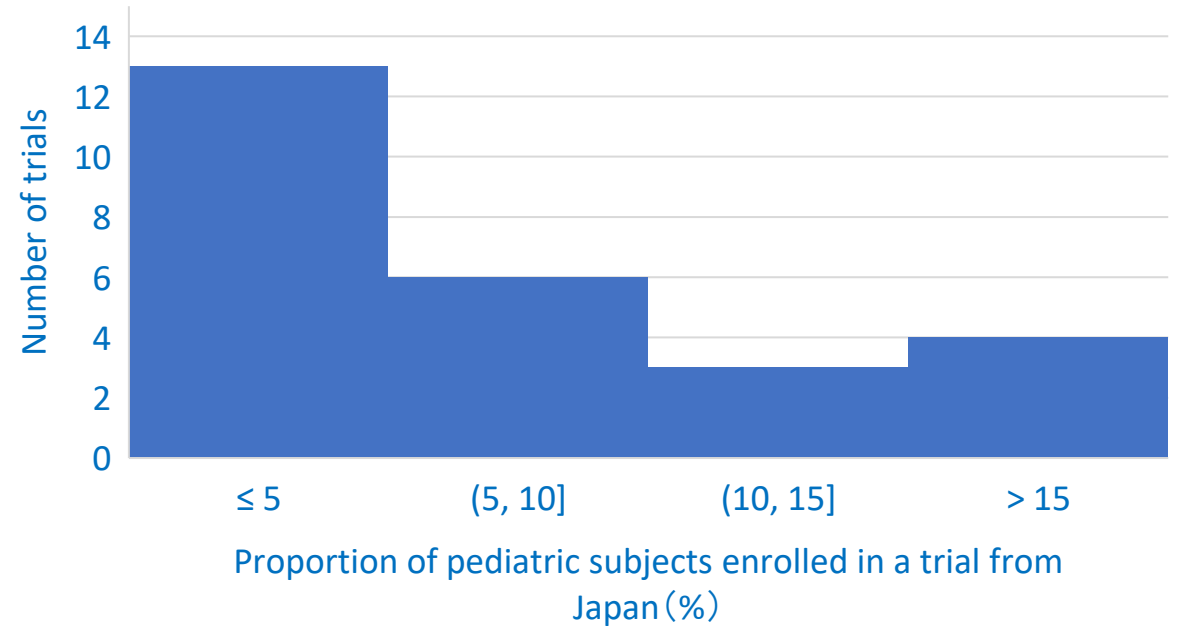
Number of pediatric subjects enrolled in global phase III trial



Number of pediatric subjects enrolled in global phase III trial from Japan



Distribution of the proportion of pediatric subjects enrolled at Japanese clinical sites in global Phase III Trials (n=26)



Collected via electronic data





Participation in pediatric MRCT from Japan



Discussion in PMDA symposium

- Japan's barriers to participation in pediatric MRCT
 - Differences in efficacy assessments between Japan and other countries/regions
 - Differences in diagnostic criteria between Japan and other countries/regions
 - Minor protocol amendments (addition of secondary endpoints, etc.) may address the above issues.
- ➔ Participation in pediatric MRCT from Japan as early as possible, ideally from the protocol development stage, is essential.
- Japanese adult data prior to including Japanese children is not always mandatory.
 - Action plan in the case that Japanese pediatric subjects are ultimately not included in the trial.





PMDA Pediatric Drug Development Symposium



- Global panel discussion (including EMA)
 - Participants shared the view that all related stakeholders should collaborate globally to advance pediatric drug development
 - Consultation on pediatric development strategy in Japan on the same timeline as global → Informative discussions within the Pediatric Cluster (monthly teleconference among RA)
 - An opportunity to consider the regional differences in drug regulation





Comparison about pediatric regulation between EU and Japan



	EU (PIP)	JAPAN (Consultation on Confirmation of the Pediatric Drug Development)
Optimal timing	During Phase II of adult development	before filing the approval application of the drug for adults
Modification	Review and formal approval by PDCO is needed	Re-consultation is held as needed
Stepwise	Acceptable only when crucial data are not yet available	Acceptable, full outline of the plan to be presented at the consultation
Incentives		
Benefits	patent protection market exclusivity, etc.	1. Re-examination Period 2. Drug Price Premium
Conditions	if development is compliant with agreed PIP, etc.	1. Consultation and pediatric drug development 2. Consultation and/or pediatric approval
In charge	PDCO	Incentives: MHLW Consultation: PMDA





Planning of Pediatric Drug Development during Adult Drug Development



- If PMDA confirm the pediatric development plan, it is described in
 - records of scientific consultation for adult drug development confidential documents
 - review reports for adult.

Website for review report:

<https://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0001.html>



(Example)

- **POMBILITI** ® for I.V. Infusion (Late-onset Pompe Disease, combination with miglustat)
- **OPFOLDA** ® Capsules (Late-onset Pompe Disease, combination with cipaglucosidase alfa)
- **AIRWIN** ® for Subcutaneous Injection (Pulmonary Arterial Hypertension)
- **TREMFYA**® Intravenous Infusion (moderately to severely active Crohn's Disease (for use only in patients who have not sufficiently responded to conventional treatments))

...etc.





Incentives related to the drug price



- The drug price is defined under the national healthcare insurance scheme by MHLW in Japan.
- The standard of drug price was revised including pediatric incentives in 2024.

<incentives>

1. Child premium (for all pediatric drugs)
2. Price maintenance premium (for all pediatric drugs)
3. Premium rate for pediatric use at the time of drug price listing, drug price revision and repricing for market expansion (for pediatric drugs approved based on the plan confirmed by the PMDA)
4. Premium rate for pediatric use at the time of repricing for market expansion (for adult drugs with pediatric development plan confirmed by the PMDA)



Examples of incentives related to the drug price



Brand Name	Child Premium	Consideration
PREVYMIS Granules 20mg	20%	Development and approval in Japan <u>without lagging behind other countries</u> were considered in most of products.
Uptravi Tablets for Pediatric		
Entresto Granules		
Ceprotin for Intravenous Injection 1000IU	15%	The Japanese inclusion quantity in clinical trials was considered in most of products.
Olumiant® tablets		
FASENRA® Subcutaneous Injection 10 mg Syringe		
ADZYNMA Intravenous 1500		





Take Home Message

- **Pediatric drug development is duty to endeavor (2025 Amendment of Pharmaceutical and Medical Device Act)**
 - Planning of the Pediatric Drug Development Program during Development of Drugs for Adults
 - Incentives related to drug price are given when pharmaceutical companies develop pediatric drugs
- **Participation in in pediatric MRCT from Japan as early as possible, ideally from the protocol development stage, is essential.**

