

Innovations in Pediatric Pharmacotherapy: Advances in Safety, Efficacy, and Patient Compliance

¹Dr.dhananjay Dilip Deshmukh, ²Pranit Saraswat, ³Dr.V.Karthikeyan, ⁴Priyam Kar

¹Associate professor & HOD, department of Balrog at Dronacharya educational institute & Hospital, saharanpur, uttar pradesh

²Associate professor, Pharmaceutical chemistry, Saraswati College of Pharmacy, Gharaun Mohali, Punjab

³Department of Prosthodontics, SRM Dental College, Ramapuram, Chennai 600089

⁴Botany, Ramakrishna Mission Vivekananda Centenary college, West Bengal State University.

Abstract

Children have long been treated as "therapeutic orphans," dosed with medicines developed and tested almost exclusively in adults. This review synthesizes recent advances across four connected fronts in pediatric pharmacotherapy: regulatory policy, dosage-form engineering, precision/pharmacogenomic dosing, and digital adherence support. Legislative mechanisms such as the U.S. Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act (PREA), alongside the EU Paediatric Regulation, have measurably increased the volume of pediatric-specific clinical data and label changes since the late 1990s, though gaps remain for neonates and rare diseases. Formulation science has moved toward mini-tablets, multiparticulates, orodispersible films, and 3D-printed dosage forms that improve swallowability, dose flexibility, and taste-masking, directly targeting the palatability and dosing-accuracy barriers that undermine compliance. Pharmacogenomic dosing, exemplified by CYP2D6-guided codeine avoidance and TPMT/NUDT15-guided thiopurine dosing, is shifting pediatric prescribing from population-average dosing toward genotype- and model-informed individualization. Digital adherence tools, including electronic monitors and smart inhalers, show consistent but modest improvements in measured adherence in randomized trials, with effects strongest when paired with caregiver feedback. To illustrate how these innovations might jointly influence outcomes, the review includes an illustrative (hypothetical, non-empirical) comparison table modeling adherence and safety-signal differences across formulation types; this table is explicitly not drawn from a real trial. The review concludes that safety, efficacy, and compliance in pediatric pharmacotherapy are improving in parallel, but that equitable translation to low-resource settings, neonates, and rare pediatric conditions remains the field's central unfinished task.

1. **How to cite this article:** 1Dr.dhananjay Dilip Deshmukh 2Pranit Saraswat 3Dr.V.Karthikeyan 4Priyam Kar. Innovations in Pediatric Pharmacotherapy: Advances in Safety, Efficacy, and Patient Compliance. Int J Drug Deliv Technol. 2026;16(84s):326-330. DOI: 10.25258/ijddt.16.84s.38.

Introduction

For most of the twentieth century, pediatric drug therapy was built on extrapolation rather than evidence. Because children were rarely enrolled in clinical trials, an estimated 50-75% of medicines used in pediatric wards through the 1990s carried no pediatric-specific efficacy, safety, or dosing data, forcing prescribers to scale adult doses by body weight or surface area despite well-documented differences in drug absorption, hepatic metabolism, renal clearance, and receptor sensitivity across neonatal, infant, and adolescent development [1]. This practice produced two recurring failure modes: underdosing that left disease inadequately treated, and overdosing that produced disproportionate adverse events, most infamously the "gray baby syndrome" associated with chloramphenicol in neonates [1].

Three structural problems compounded the evidence gap. First, pediatric populations are physiologically heterogeneous by age band (preterm neonate through adolescent), so a single "pediatric dose" rarely exists. Second, children cannot reliably swallow adult solid dosage forms, and taste aversion to bitter active

ingredients undermines adherence to liquid formulations. Third, the commercial incentive to conduct pediatric trials was historically weak, since pediatric indications represent a smaller market than adult indications for most chronic-disease drugs [1].

The past two decades have seen convergent innovation across regulation, chemistry, genomics, and digital health aimed at closing this gap. This review organizes recent advances into four themes -- regulatory policy, dosage-form engineering, precision/pharmacogenomic dosing, and digital adherence support -- and closes with an illustrative, clearly hypothetical dataset used only to demonstrate how these innovations might be compared empirically, not as a substitute for real trial evidence.

2. Regulatory and Policy Innovations

Legislative innovation, not chemistry, was the first lever pulled to close the pediatric evidence gap. In the United States, the Best Pharmaceuticals for Children Act (BPCA, reauthorized periodically since 1997) offers manufacturers a period of additional marketing exclusivity in exchange for voluntarily conducting FDA-requested pediatric studies, while the Pediatric

Research Equity Act (PREA, 2003) makes pediatric assessment mandatory for most new drugs and biologics unless a waiver is granted [2]. FDA now maintains a public, continuously updated record of pediatric labeling changes made under BPCA, PREA, and the earlier Pediatric Rule since 1998; the agency's own trend data show a sustained increase in the annual number of pediatric label changes over that period, covering dosing, safety warnings, and new pediatric indications across therapeutic areas [3]. BPCA additionally funds NIH-sponsored studies of already-off-patent drugs that hold no exclusivity incentive for manufacturers, a mechanism that has generated pediatric dosing data for older, frequently used drugs that would otherwise never be formally studied in children [2].

The European Union's Paediatric Regulation (2007) took a parallel but distinct approach, requiring a Paediatric Investigation Plan (PIP) for most new medicines and biologics as a condition of marketing authorization, agreed with the European Medicines Agency's Paediatric Committee before adult marketing authorization in many cases [1]. Japan, and more recently the WHO's Better Medicines for Children initiative, have pursued similar model lists and study-incentive frameworks aimed at low- and middle-income settings where the pediatric evidence gap is compounded by weaker manufacturer incentives and limited local trial infrastructure [1].

These frameworks have not closed the gap evenly. Neonates, children with rare diseases, and pregnant/lactating adolescents remain the most poorly studied subgroups, since study feasibility (small population size, ethical constraints on placebo-controlled pediatric trials, and difficulty obtaining consent/assent) scales inversely with clinical need [2]. Waivers and deferrals under PREA, while sometimes clinically justified, have also been used to delay pediatric study completion well beyond adult approval in some cases, a persistent policy tension between speed of adult access and completeness of pediatric evidence [2].

3. Formulation Innovations for Safety and Compliance

Even a well-dosed drug fails if a child cannot or will not take it, which has made dosage-form engineering one of the most active areas of pediatric pharmaceutical innovation.

Mini-tablets and multiparticulates. Mini-tablets (typically 2-4 mm in diameter) and coated micropellets allow a single manufactured unit to be dosed flexibly by counting or weight-based sachets, avoiding the compounding errors common with extemporaneous liquid preparation. A 2025 expert review highlights their particular value for APIs that are chemically unstable in liquid suspension or have

narrow therapeutic windows, since solid multiparticulates offer better shelf stability and more accurate unit dosing than compounded syrups [4]. Swallowability studies cited in that review report that children as young as six months can safely swallow mini-tablets when co-administered with soft food, comparable to or better than liquid formulations in observed acceptance.

Orodispersible films and tablets (ODFs/ODTs).

These dissolve on the tongue without water, which is particularly useful for children who resist swallowing tablets or who need dosing outside mealtimes. Recent reviews describe ODFs as a maturing platform with several marketed pediatric products, citing improved dosing accuracy over liquids and higher reported acceptability in comparative caregiver surveys, though manufacturing at low unit doses for very young children remains technically difficult [5][6].

Taste-masking. Bitterness is consistently identified as the single largest driver of pediatric non-adherence to oral liquids. Current strategies include ion-exchange resin complexation, cyclodextrin inclusion complexes, lipid/polymer microencapsulation, and functional film coatings; a 2025 review of taste-masking specifically for centrally-acting pediatric drugs (where bitterness is often most pronounced) found film-coated mini-tablets achieved both rapid disintegration and effective bitterness suppression in in vitro and panel taste tests [7].

3D-printed and patient-specific dosage forms. A 2026 review describes 3D printing (fused-deposition modeling and semi-solid extrusion) as a transformative but still largely investigational platform for producing dose-flexible, multi-drug ("polypill"), and patient-specific pediatric tablets on demand, especially relevant for rare-disease and neonatal dosing where no commercial strength exists; the same review flags regulatory pathway uncertainty and manufacturing scale-up as the main barriers to routine clinical use [8].

Across these platforms, the common thread is that formulation science is converging on the same goal by different routes: a dosage form that is accurately and flexibly dosable, does not require compounding, and is palatable enough that a child will reliably take it -- addressing efficacy (accurate dosing), safety (fewer compounding/measurement errors), and compliance (palatability, ease of administration) simultaneously.

4. Advances in Efficacy: Pharmacogenomics and Precision Dosing

Alongside how a drug is formulated, pediatric pharmacotherapy is increasingly asking how much of it a given child should receive, informed by genotype rather than age or weight alone.

The clearest cautionary example remains **CYP2D6 and codeine**: children who are CYP2D6 ultra-rapid

metabolizers convert codeine to morphine unusually fast, which led to reports of fatal and near-fatal respiratory depression in children (notably post-tonsillectomy) and prompted FDA boxed-warning restrictions on codeine use in children [9]. This case is now a standard teaching example for why population-average pediatric dosing can fail catastrophically for a genetically defined subgroup, and it helped establish CPIC (Clinical Pharmacogenetics Implementation Consortium) guidelines as a reference standard for gene-drug pairs in pediatrics [9].

TPMT and NUDT15 genotyping before thiopurine therapy (azathioprine, mercaptopurine) is now a comparatively mature example of pre-emptive pharmacogenomic testing in pediatric oncology and inflammatory bowel disease, allowing pre-treatment dose reduction in poor metabolizers to avoid severe, potentially fatal myelosuppression [10]. Pediatric hospitals with embedded pharmacogenomic testing programs report that TPMT/NUDT15 and CYP2D6 are among the most frequently ordered pre-emptive panels, alongside CYP2C19 (for drugs including some SSRIs and proton pump inhibitors) [11].

Beyond single gene-drug pairs, **model-informed precision dosing (MIPD)** -- combining population pharmacokinetic models, real-time therapeutic drug monitoring, and (increasingly) genomic covariates in Bayesian dose-adjustment software -- is being adopted for narrow-therapeutic-index drugs such as vancomycin, aminoglycosides, and some immunosuppressants in pediatric and neonatal intensive care, where traditional weight-based dosing has historically produced wide, clinically significant variability in achieved drug exposure [11][12]. A recurring theme in recent pediatric pharmacogenomics literature is that clinical uptake still lags the evidence base: surveys of children's hospitals report substantial site-to-site variation in which gene-drug pairs are tested pre-emptively versus reactively, and clinician-facing decision support remains inconsistent across institutions [11].

5. Digital Health and Adherence Technologies

Pediatric adherence is uniquely dependent on a third party: the caregiver administering or supervising the dose, which has made digital adherence tools a distinct innovation track from formulation science.

Smart inhalers and electronic monitors are the most studied category, largely in pediatric and adolescent asthma. These devices log the time and, in some cases, the inhalation technique of each actuation, feeding data back to caregivers, clinicians, or an app-based reminder system. A scoping review of randomized controlled trials of digital adherence interventions in pediatric/adolescent asthma found that most trials reported statistically significant improvements in objectively measured adherence relative to usual care,

though effect sizes varied considerably by intervention design, and improvements in clinical outcomes (exacerbation rate, symptom control) were less consistently significant than the adherence improvements themselves [13]. A related systematic review and meta-analysis of electronic adherence monitoring in pediatric asthma similarly concluded that monitoring plus feedback improves measured adherence more than monitoring alone, suggesting the behavioral feedback loop -- not just the sensor -- is what drives the effect [14].

Stepped-care and behavioral-technology hybrids are emerging as a refinement: rather than applying the same digital intervention to every family, pilot programs escalate support (from automated reminders to caregiver coaching) only for adolescents whose objectively monitored adherence remains low, an approach early pilot data describe as feasible and acceptable to families, with promising but still preliminary effects on adherence trajectories [15]. More recent (2025) clinical reviews of smart inhalers describe a persistent "innovation-to-practice" gap: the sensor and app technology has matured faster than the health-system workflows, reimbursement pathways, and clinician time needed to act on the data these devices generate, meaning technological capability currently outpaces routine clinical integration [16]. Taken together, the digital-health evidence base supports a specific, more modest claim than "apps fix adherence": objective monitoring reliably improves measured adherence behavior, particularly when paired with a feedback loop to the caregiver or clinician, but translating that improved adherence into better clinical outcomes, and into routine practice, remains an active area of study rather than a solved problem.

6. Illustrative Comparative Data

The table below is entirely hypothetical. It was constructed for this review to illustrate, in numeric form, the kind of comparative outcomes the formulation and adherence literature above would predict -- it is not drawn from any real trial, registry, or dataset, and the figures should not be cited as evidence. It is included only because the request for this paper specifically asked for an illustrative data example.

Formulation type (hypothetical cohort, n=120 each)	Illustrative caregiver-reported adherence at 12 weeks	Illustrative dosing-error rate	Illustrative taste-acceptability score (1-10)
Conventional oral liquid (unmasked)	61%	14%	4.2
Taste-masked oral suspension	74%	11%	6.8
Mini-tablets / multiparticulates	81%	6%	7.1
Orodispersible film	83%	5%	7.6
Mini-tablets + digital reminder app	89%	4%	7.3

Read as intended, this illustrative table encodes three real, literature-supported directional claims from the sections above -- that taste-masking improves on unmasked liquids, that solid multiparticulate/ODF forms reduce dosing error relative to liquids, and that pairing a formulation improvement with a digital adherence tool compounds the benefit -- without asserting any of the specific numbers as measured facts. A real head-to-head trial comparing these formulation classes directly, with pre-registered adherence and safety endpoints, does not appear to exist in the current literature and would be a natural next step suggested by this review.

7. Challenges and Future Directions

Several barriers keep these advances from translating evenly across pediatric medicine.

Neonates and rare diseases remain the hardest-to-study groups. Small population sizes, heightened ethical sensitivity around placebo-controlled trials in the sickest and youngest patients, and the difficulty of obtaining meaningful consent/assent all reduce trial feasibility precisely where dosing uncertainty is greatest [1][2].

Manufacturing and regulatory pathways lag the formulation science. 3D-printed and other patient-specific dosage forms remain largely investigational because regulators have not yet established clear approval pathways for point-of-care or small-batch

pediatric manufacturing, and scale-up economics for low-volume pediatric strengths are unfavorable for manufacturers [8].

Equity and access gaps persist globally. Most of the regulatory and technological advances reviewed here originate in high-income regulatory systems (FDA, EMA); WHO's Better Medicines for Children initiative and similar programs are working to extend age-appropriate formulations and dosing guidance to low- and middle-income settings, but availability of taste-masked, dose-flexible pediatric formulations remains uneven globally [1].

Pharmacogenomic testing is not yet standardized in pediatric practice. Which gene-drug pairs are tested pre-emptively versus reactively still varies substantially by institution, and decision-support tools that translate a genotype result into an actionable pediatric dose at the point of prescribing are inconsistently implemented [11].

Digital adherence tools need workflow integration, not just better sensors. The literature increasingly identifies the bottleneck as clinical and health-system capacity to act on adherence data, rather than the sensing technology itself [16].

Looking forward, the most promising direction is convergence rather than any single innovation: pairing a genotype- or model-informed dose with a palatable, accurately dosable formulation, delivered with adherence feedback tailored to the caregiver-child dyad, addresses safety, efficacy, and compliance as one integrated problem rather than three separate ones.

8. Conclusion

Pediatric pharmacotherapy has moved, over roughly three decades, from a field defined by extrapolated adult dosing toward one actively engineering solutions to its three core problems: knowing the right dose (regulatory-driven pediatric trials and pharmacogenomic/model-informed dosing), delivering it accurately and palatably (mini-tablets, orodispersible films, taste-masking, 3D printing), and ensuring it is actually taken (digital adherence monitoring and caregiver feedback). Each front has real, cited evidence of progress, and the four fronts are increasingly designed to reinforce one another rather than operate in isolation. The unfinished work is less about inventing new mechanisms and more about extending what already works -- pediatric trial participation, dose-flexible formulations, pharmacogenomic decision support, and adherence technology -- to neonates, rare diseases, and lower-resource health systems where the original evidence gap remains widest.

References

1. Field, M.J., Boat, T.F. (eds.) [Regulatory Framework - Addressing the Barriers to](#)

- [Pediatric Drug Development](#). NCBI Bookshelf.
2. [Policy Framework for BPCA and PREA - Safe and Effective Medicines for Children](#). NCBI Bookshelf.
3. FDA. [Pediatric Labeling Changes](#).
4. [The Potential of Micropellets and Mini-Tablets in Oral Pediatric Formulations with Challenging APIs](#). Expert Opinion on Pharmacotherapy, 2025;26(16).
5. [Orodispersible Films: Current Innovations and Emerging Trends](#). PMC.
6. [Orodispersible Tablets for Paediatric Use: A Systematic Review and Outlook for Future Research](#).
7. [Film Coating of Small Molded Tablets for Pediatric Formulations with Rapid Disintegration and Bitterness-Masking Properties](#). Molecules, 2025;30(10):2142.
8. [Three-dimensional printing as a transformative platform for patient-centric pediatric drug delivery](#). DARU Journal of Pharmaceutical Sciences.
9. [Perspectives from the Society for Pediatric Research: pharmacogenetics for pediatricians](#). Pediatric Research.
10. [Pharmacogenetic Testing for the Pediatric Gastroenterologist: Actionable Drug-Gene Pairs to Know](#). Pharmaceuticals, 2023;16(6):889.
11. [Characterizing Pharmacogenetic Testing Among Children's Hospitals](#). PMC.
12. [Gene-Based Dose Optimization in Children](#). Annual Review of Pharmacology and Toxicology.
13. [Digital Technologies for Monitoring and Improving Treatment Adherence in Children and Adolescents With Asthma: Scoping Review of Randomized Controlled Trials](#). PMC.
14. [Electronic adherence monitoring devices for children with asthma: A systematic review and meta-analysis of randomised controlled trials](#). ScienceDirect.
15. [Technology-Assisted Stepped-Care to Promote Adherence in Adolescents with Asthma: A Pilot Study](#). Journal of Clinical Psychology in Medical Settings.
16. [Smart inhalers in paediatric asthma: bridging the gap between innovation and clinical practice](#). ScienceDirect.