

# Approaching Current and New Drug Therapies for Pediatric Asthma



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## KEYWORDS

- Drug development • Drug delivery • Adherence • Inhaled corticosteroids
- Long-acting  $\beta$ -agonists • Tiotropium • Biologics • Omalizumab

## KEY POINTS

- Extrapolation for the management of childhood asthma from adult pharmaceutical studies is limited, emphasizing the imperative for pediatric specific drug trials and indications.
- Families should be educated on the appropriate delivery technique for inhaled therapies, and new delivery devices that overcome technique obstacles should be considered.
- Age-specific challenges must be considered before choosing or escalating therapy, including appropriate diagnosis, family and school engagement, adherence, and psychosocial comorbidities.
- Inhaled corticosteroids (ICSs) and long-acting  $\beta$ -agonists (LABAs) are the principal controller therapies for persistent asthma, with new ICS formulations improving delivery and recent studies supporting the safety of LABAs.
- Controller therapies previously approved for adult asthma, including tiotropium and biologics, are now being investigated in younger children with associated clinical benefits.

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Disclosure Statement: SJ Szefer is supported by the Colorado Department of Public Health and Environment 15 FLA 65765, 16 FHLA 76546 and 17FHLA87312, Caring for Colorado Foundation, the McCormick Foundation and Glaxo Smith Kline FLV116794. Also supported by NHLBI AsthmaNet U10 HL098075 and supported in part by Colorado CTSA Grant UL1 RR025780 from NCCR/NIH and UL1 TR000154 from NIH/NCATS.

MC Gleason is supported by Colorado Department of Public Health and Environment 15 FLA 65765, 16 FHLA 76546 and 17FHLA87312, Caring for Colorado Foundation, the McCormick Foundation and GlaxoSmithKline FLV116794.

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Pediatr Clin N Am 64 (2017) 1197–1207  
<http://dx.doi.org/10.1016/j.pcl.2017.08.001>

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## INTRODUCTION: PEDIATRIC ASTHMA DRUG DEVELOPMENT

A gap exists between the imperative need for novel pharmaceutical therapies for children and their development. A recent review demonstrated that despite children being responsible for almost half of the disease burden from asthma in high-income countries, less than 20% of asthma trials during that time had a pediatric focus.<sup>1</sup> Interventions have been made to spur pediatric drug development. The Best Pharmaceuticals for Children Act allows an additional 6 months of market exclusivity if the sponsor voluntarily includes pediatric studies.<sup>2,3</sup> The Pediatric Research Equity Act mandates that new drug studies include children if there is the potential for the drug to be used in the pediatric population.<sup>2,3</sup> Collectively, the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act successfully resulted in more than 500 pediatric labeling changes since their inception.<sup>4</sup> Nonetheless, drugs for asthma are still frequently prescribed off-label in children, primarily secondary to age limits, with 24% to 45% of short-acting  $\beta$ -agonists (SABAs) and 26% to 80% of ICSs used off-label.<sup>5</sup>

The extrapolation of efficacy findings from adults to the pediatric population has streamlined the developmental process in adolescents and older children.<sup>6</sup> This strategy cannot be used in neonates, infants, and children given differences in respiratory function, immunology, and disease pathogenesis,<sup>7</sup> creating a substantial unmet need. Without evidence to support this off-label use, patients may be exposed to potential unintended harms.<sup>3</sup> Trying to extrapolate from adult studies to design pediatric studies can lead to study failure and subsequent lack of pediatric labeling, secondary to a lack of efficacy, inability to use the delivery device, limited drug dosing ranges, or safety concerns.<sup>8</sup>

This review highlights the forefront of pharmacologic therapies for the management of asthma in children, with a focus on their implications for clinicians in practice and potential limitations.

## DELIVERY DEVICES

Inhaled medications, especially ICSs and ICSs/long-acting  $\beta$ -agonists (LABAs), are the mainstay of treatment of the management of pediatric asthma.<sup>9</sup> The inhaled route for delivery of asthma medication is preferred to oral administration due to advantages associated with local delivery, including lower dosage, fewer systemic side effects, and quick onset of action.<sup>10</sup> The downside of inhaled therapy is the difficulty some patients, especially children, may have in applying appropriate inhaler technique, emphasizing the attention that must be paid to technique and delivery device when choosing a therapy.<sup>11</sup>

A metered-dose inhaler (MDI) with an add-on valve holding chamber (VHC), with or without a mask, is the principal delivery device in the pediatric population, improving delivery of medication to the lower respiratory tract.<sup>12</sup> When caregivers of children with asthma were surveyed, however, fewer than 4% were able to perform all the essential steps to correctly use an MDI with a VHC.<sup>13</sup> Technique should be checked and reinforced at every health care visit, and trainers, if available, should be used to assess adequate technique before dispensing. Families may feel nebulizers are an alternative to MDIs; however, studies using MDIs with spacers for SABAs found MDIs noninferior and more cost-effective than nebulizers.<sup>14,15</sup> Dry powder, breath-actuated devices are successful at removing some of the coordination barriers with MDI with VHC, but patients, including children, may have difficulty generating the appropriate inspiratory force to utilize these devices.<sup>11</sup>

Recently, new medication delivery devices with pediatric indications have been introduced to enhance optimal deposition into the lower respiratory tract and ease

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