## Pearls and Evidence for Preferred Therapy with AIR

- GINA Track 1 in which low dose ICS-formoterol is used as a reliever with or without maintenance ICS-formoterol is the preferred treatment approach for children 12+ years of age and adults. This approach reduces severe exacerbations across all treatment steps compared with using SABA as reliever.
- It uses a single inhaler for both maintenance and reliever which is less confusing for patients, and a patient's treatment can be stepped up or down according to clinical need without changing the medication or device. This cannot be done with any other ICS-LABA combination except ICS-formoterol. ICS-formoterol can also be used prior to exercise or allergen exposure.
- Low dose ICS-formoterol is called an anti-inflammatory reliever (AIR) because it relieves symptoms and reduces inflammation. AIR with ICS-formoterol significantly reduces the risk of severe exacerbations compared with using SABA as a reliever with similar symptom control, lung function and adverse effects.

Steps 1-2 (AIR only): low dose ICS-formoterol is used as needed for symptom relief without any maintenance treatment. It reduces the risk of severe exacerbations and ED visits/admissions by 65% compared with SABA alone and by 37% compared to daily ICS with SABA as reliever. Starting ICS-formoterol as reliever avoids training patients to regard SABA as their main asthma treatment.

*Steps 3-5 (S)MART):* maintenance and reliever therapy with ICS-formoterol reduces the risk of severe exacerbations by 32% compared with the same dose of ICS-LABA, by 23% compared with higher dose ICS-LABA, and by 17% compared with the usual care. (S)MART is also an option for children ages 6-11 who require Steps 3-4 therapy.

Sobieraj DM, et al., *JAMA* 2018; 319: 1485-1496. Cates CJ, et al., *Cochrane Database Syst Rev* 2013; 4: CD007313. Crossingham I, et al., Cochrane Database Syst Rev 2021; 5: CD013518.

## Age Based Doses of ICS-formoterol for (S)MART\*

Step	Age (years)	Medication and strength (per 2 puffs of pMDI)	Dosage (number of puffs)
Steps 1-2 (AIR only)	6 - 11 12 - 17 >18	NO EVIDENCE TO DATE Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	1 puff whenever needed
Step 3 ((S)MART)	6 – 11 12 - 17 >18	Budesonide-formoterol 80/4.5 Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	1 puff once or twice daily (once daily for children), PLUS 1 puff whenever needed
Step 4 ((S)MART)	6 – 11 12 - 17 >18	Budesonide-formoterol 80/4.5 Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	2 puffs twice daily (1 puff twice daily for children), PLUS 1 puff whenever needed
Step 5-6 ((S)MART)	6 – 11 12 - 17 >18	NOT RECOMMENDED Budesonide-formoterol 160/4.5 Budesonide-formoterol 160/4.5	2 puffs twice daily, PLUS 1 puff whenever needed

<sup>\*</sup>Table adapted from GINA 2023, Box 3-15, p. 80. Available at ginasthma.org.

- Most evidence for (S)MART and all the evidence for as needed only ICS-formoterol (Antiinflammatory reliever or AIR) only as needed is with budesonide-formoterol 160/4.5 for ages 12+ and budesonide-formoterol 80/4.5 for ages 6-11 years. Other low dose ICS-formoterol products may be suitable but have not been studied.
- For as needed use, the dose is 2 puffs of MDI (see strength below) whenever needed for symptom relief, or before exercise/allergen exposure.
- For maintenance use, the dose is 2-4 puffs of MDI depending on age.
- Patients do not need to wait a certain number of hours between reliever doses (as with SABA)
- Maximum total doses per day for (S)MART is 8 doses for ages 6-11 and 12 puffs for ages 12+