For ages 4–11 years, one blinded RCT[152] used budesonide-formoterol, 80/4.5 mcg, with up to seven rescue puffs of budesonide-formoterol, 80/4.5 mcg (36 mcg total daily dose of formoterol; SMART) or SABA as quick-relief therapy. SMART reduced the RR for exacerbations by 72 percent (moderate certainty of evidence) and showed superiority in one unvalidated outcome measure of asthma control (nighttime awakenings). Growth rates and other safety measures did not differ between treatment groups.

Rationale and Discussion

Because the only SMART studied has included formoterol, the Expert Panel's recommendation favors the use of ICS-LABA combinations containing formoterol rather than those that contain ICS-salmeterol. Daily ICS-salmeterol remains an appropriate therapeutic option for individuals with moderate to severe persistent asthma, but the reviewed data suggest that the use of ICS-formoterol for maintenance and reliever therapy has superior efficacy, ease of use (because it is administered in a single inhaler rather than two separate inhalers), and perhaps safety as a result of reduced corticosteroid exposure. Other LABAs, including newer agents with a rapid onset, may be effective and safe to use for both maintenance and reliever therapy, but their efficacy and safety will need to be demonstrated in clinical studies. The number of studies available and the consistency of the evidence led the Expert Panel to make a strong recommendation to use ICS-formoterol in a single inhaler as both daily controller and reliever therapy.

Data were insufficient to compare ICS-formoterol as single maintenance and reliever therapy with same-dose ICS for daily controller therapy along with SABA for quick-relief therapy in individuals ages 4 years and older. However, multiple studies have demonstrated that adding any LABA to the same ICS dose is more effective than ICS therapy alone.[12] Thus, the lack of comparisons data on ICS-formoterol as single maintenance and reliever therapy vs. same-dose ICS and SABA for quick-relief therapy is of minimal clinical importance.

Recommendation 13: In individuals ages 12 years and older with moderate to severe persistent asthma, the Expert Panel conditionally recommends ICS-formoterol in a single inhaler used as both daily controller and reliever therapy compared to higher-dose ICS-LABA as daily controller therapy and SABA for quick-relief therapy.

Conditional recommendation, high certainty of evidence

Implementation Guidance

Clinician's Summary:

In individuals ages 12 years and older, the preferred Step 4 therapy is single-inhaler ICS-formoterol used both daily and as needed. The maximum total daily dose of formoterol should not exceed 12 puffs (54 mcg) for ages 12 and older. The recommended alternate therapy of maintenance ICS-LABA along with SABA as quick-relief therapy does not need to be changed if it is providing adequate control. However, individuals whose asthma is uncontrolled on such therapy should receive the preferred SMART if possible before stepping up their treatment to a higher step of therapy.