Antimigraine Agents, Other Therapeutic Class Review

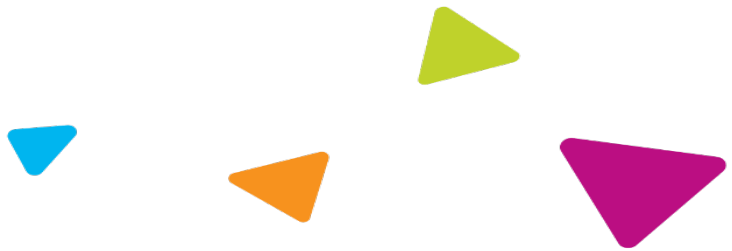
NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
MAY 12, 2022

Magellan Rx MANAGEMENT℠

Antimigraine Agents, Other

New Clinical Information

- New Drug Entity: Qulipta™ (atogepant)
- New Indication & Key Label Revisions: Nurtec ODT® (rimegepant)



Magellan Rx MANAGEMENT℠

Antimigraine Agents, Other

Qulipta (atogepant)

- **Indications:**
  - Calcitonin gene-related peptide antagonist indicated for the preventive treatment of episodic migraine in adults

- **Dosage/Availability:**
  - Tablets: 10 mg, 30 mg, and 60 mg
  - Taken orally once daily with or without food
  - Severe Renal Impairment or End-Stage Renal Disease: 10mg once daily

- **Contraindications/Warnings:**
  - None

Qulipta [package insert]. Dublin, Ireland; AbbVie; October 2021.

Qulipta (atogepant) cont.

- **Common Adverse Drug Reactions (incidence at least 4%):**
  - Nausea, constipation, and fatigue
- **Drug Interactions:**
  - Strong CYP3A4 Inhibitor: 10 mg once daily
  - Strong and Moderate CYP3A4 Inducers: 30 mg or 60 mg once daily
  - OATP Inhibitors: 10 mg or 30 mg once daily
- **Specific Populations:**
  - Pregnancy: Based on animal data, may cause fetal harm
  - Avoid use in patients with severe hepatic impairment
  - Pediatrics: Safety and efficacy has not been established
- **Clinical Comparative Studies (within class):**
  - None available

Qulipta [package insert]. Dublin, Ireland; AbbVie; October 2021.

Antimigraine Agents, Other

Nurtec ODT® (rimegepant) orally disintegrating tablets

- **New Indication:**
  - FDA approved for preventative treatment of episodic migraine in adults; previously approved only for acute treatment of migraine with or without aura in adults
  - Recommended dosage for preventive treatment of episodic migraine: 75 mg taken orally every other day

- **Key Label Revisions:**
  - There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to NURTEC ODT during pregnancy
  - A lactation study was conducted, and the results have established a relative infant dose of less than 1% of the maternal weight-adjusted dose and the milk-to-plasma ratio of 0.20
  - Avoid another dose of NURTEC ODT within 48 hours when it is concomitantly administered with potent inhibitors of P-gp
  - Concomitant administration of NURTEC ODT with BCRP inhibitors is not expected to have a clinically significant impact on rimegepant exposures

Nurtec ODT [package insert]. New Haven, CT; Biohaven Pharmaceuticals; April 2022.

New York State Medicaid Drug Utilization Review Board Meeting – May 12, 2022
Preferred Drug Program – Drug Class Review

<table>
<tr><th>Preferred Drugs</th><th>Non-Preferred Drugs</th><th>Prior Authorization/Coverage Parameters</th></tr>
<tr><td colspan="3">Antimigraine Agents, Other ST, F/Q/D</td></tr>
<tr><td>Ajovy®
Emgality®</td><td>Aimovig®
Emgality® 100mg syringe
Nurtec™ ODT
Qulipta™
Reyvow™
Ubrelvy™</td><td>STEP THERAPY (ST)
Acute treatment of migraine
• Trial of a product from the Antimigraine Agents-Triptan class
Prevention of migraine
• Trial of 2 FDA approved migraine prevention products from other drug classes

FREQUENCY/QUANTITY/DURATION (F/Q/D)
<table>
<tr><th>Agent</th><th>F/Q/D</th></tr>
<tr><td>Aimovig</td><td>1 syringe/30 days</td></tr>
<tr><td>Emgality 120mg</td><td>2 syringes/30 days</td></tr>
<tr><td>Emgality 100mg</td><td>3 syringes/30 days</td></tr>
<tr><td>Ajovy</td><td>3 syringes/90 days</td></tr>
<tr><td>Reyvow</td><td>8 units/30 days</td></tr>
<tr><td>Ubrelvy</td><td>16 units/30 days</td></tr>
<tr><td>Nurtec™ ODT</td><td>18 units/30 days</td></tr>
<tr><td>Qulipta</td><td>30 units/30 days</td></tr>
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Acne Agents, Topical Therapeutic Class Review

NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
MAY 12, 2022

Magellan Rx MANAGEMENT℠

Acne Agents, Topical

New Clinical Information

- New Drug Entity: Winlevi® (clascoterone)

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Acne Agents, Topical

Winlevi (clascoterone)

- **Indications:**
  - Androgen receptor inhibitor indicated for the topical treatment of acne vulgaris in patients 12 years of age and older

- **Dosage/Availability:**
  - 1% cream
  - Apply a thin layer to affected area twice daily (morning and evening)

- **Contraindications/Warnings:**
  - Local irritation: Pruritus, burning, skin redness, or peeling may be experienced with Winlevi cream. Discontinue or reduce frequency of application if occurs.
  - Hypothalamic-pituitary-adrenal (HPA) axis suppression: withdraw use if develops
  - Pediatric patients may be more susceptible to systemic toxicity
  - Hyperkalemia: elevated potassium levels were observed in some subjects during the clinical trials

Winlevi [package insert]. Cranbury, NJ; Sun Pharma; September 2021.

Winlevi (clascoterone) cont.

- **Common Adverse Drug Reactions:**
  - Erythema/reddening, pruritus, and scaling/dryness (incidence 7 to 12%)
  - Edema, stinging, and burning (incidence >3%)

- **Drug Interactions:**
  - None reported

- **Specific Populations:**
  - Pregnancy: no available data on use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes
  - Pediatrics: Safety and efficacy established for 12 years of age and older

- **Clinical Comparative Studies (within class):**
  - None available

Winlevi [package insert]. Cranbury, NJ; Sun Pharma; September 2021.

Preferred Drugs	Non-Preferred Drugs	Prior Authorization/Coverage Parameters
Acne Agents, Topical		
adapalene/benzoyl peroxide (generic for Epiduo) adapalene cream Differin® OTC (1% gel) Retin-A® cream CC, BLTG tazarotene cream CC tretinoin gel (generic Avita, Retin-A) CC	adapalene (Rx gel, gel pump) adapalene/benzoyl peroxide (gen Epiduo® Forte) Aklief® CC Altreno® CC Amzeeq™ F/Q/D Arazlo™ CC Atralin® CC Avita® CC clindamycin / tretinoin CC dapsone Differin® (Rx gel, solution, lotion, cream) Epiduo® Forte Fabior® CC Retin-A® gel CC Retin-A Micro® CC tazarotene foam (generic Fabior®) CC tretinoin cream, gel CC (generic Atralin) tretinoin micro CC Twyneo® F/Q/D, CC Winlevi® Ziana® CC	**CLINICAL CRITERIA** • Confirm diagnosis of FDA-approved, compendia-supported, and Medicaid-covered indication **FREQUENCY/QUANTITY/DURATION (F/Q/D)** • **Amzeeq™ (minocycline), Twyneo® (tretinoin/benzoyl peroxide)** – maximum quantity: 30 grams per month

Growth Hormones Therapeutic Class Review

NEW YORK MEDICAID
DRUG UTILIZATION REVIEW BOARD MEETING
MAY 12, 2022

Magellan Rx MANAGEMENT℠

Growth Hormones

New Clinical Information

- New Drug Entity: Skytrofa® (lonapegsomatropin-tcgd)

Magellan Rx MANAGEMENT℠

Growth Hormones

Skytrofa (lonapegsomatropin-tcgd)

- **Indications:**
  - Human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone

- **Dosage/Availability:**
  - For injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg lyophilized powder in single-dose, dual-chamber, prefilled cartridges
  - Administered subcutaneously to the abdomen, buttock, or thigh with regular rotation of the injection sites once-weekly

Skytrofa [package insert]. Palo Alto, CA; Ascendis Pharma; April 2022

Skytrofa (lonapegsomatropin-tcgd) cont.

- **Contraindications/Warnings:**
  - Acute critical illness
  - Hypersensitivity to somatropin or any of the excipients
  - Children with closed epiphyses
  - Active malignancy
  - Active proliferative or severe non-proliferative diabetic retinopathy
  - Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment due to risk of sudden death
  - Severe Hypersensitivity
  - Increased Risk of Neoplasms
  - Glucose Intolerance and Diabetes Mellitus: May be unmasked
  - Intracranial Hypertension
  - Fluid Retention (i.e., edema, arthralgia, carpal tunnel syndrome)
  - Hypoadrenalism
  - Hypothyroidism: May first become evident or worsen
  - Slipped Capital Femoral Epiphysis: May develop
  - Progression of Preexisting Scoliosis: May develop
  - Pancreatitis

Skytrofa [package insert]. Palo Alto, CA; Ascendis Pharma; April 2022

Skytrofa (lonapegsomatropin-tcgd) cont.

- **Common Adverse Drug Reactions (≥5%) :**
  - Viral infection, pyrexia, cough, nausea and vomiting, hemorrhage, diarrhea, abdominal pain, and arthralgia and arthritis
- **Drug Interactions:**
  - Replacement Glucocorticoid Treatment
  - Pharmacologic Glucocorticoid Therapy and Supraphysiologic Glucocorticoid Treatment
  - Cytochrome P450-Metabolized Drugs
  - Oral Estrogen
  - Insulin and/or Other Antihyperglycemic Agents
- **Specific Populations:**
  - Pregnancy: no available data on use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes
  - Pediatrics: Safety and efficacy established for 1 years of age and older who weigh at least 11.5 kg

Skytrofa [package insert]. Palo Alto, CA; Ascendis Pharma; April 2022

Skytrofa (lonapegsomatropin-tcgd) cont.

- **Clinical Comparative Studies (within class):**
  - Treatment-Naïve Pediatric Patients with Growth Hormone Deficiency (NCT02781727) compared Skytrofa with daily somatropin
  - A multi-center randomized, open-label, active-controlled, parallel-group phase 3 study was conducted in 161 treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD)
    - 105 subjects received once-weekly Skytrofa, and 56 received daily somatropin
    - Dose in both arms was 0.24mg/kg/week
  - Primary efficacy endpoint was annualized height velocity at Week 52
    - Treatment with once-weekly Skytrofa resulted in an annualized height velocity of 11.2 cm/year
    - Treatment with daily somatropin achieved an annualized height velocity of 10.3 cm/year
  - Height SDS (change from baseline) was 1.1 in the Skytrofa arm and 0.96 in the daily somatropin arm at Week 52

Skytrofa [package insert]. Palo Alto, CA; Ascendis Pharma; April 2022

New York State Medicaid Drug Utilization Review Board Meeting – May 12, 2022
Preferred Drug Program – Drug Class Review

Preferred Drugs	Non-Preferred Drugs	Prior Authorization/Coverage Parameters
Growth Hormones CC, CDRP		
Genotropin® Norditropin®	Humatrope® Nutropin AQ® Omnitrope® Saizen® Skytrofa® Zomacton® Zorbtive®	**CLINICAL DRUG REVIEW PROGRAM (CDRP)** • Prescribers or their authorized agents may call or submit a fax request for a PA for beneficiaries 18 years of age or older **CLINICAL CRITERIA (CC)** • Patient-specific considerations for drug selection include concerns related to use of a non-preferred agent for FDA-approved indications that are not listed for a preferred agent. • Confirm diagnosis of FDA-approved or compendia-supported indication

Spravato® (esketamine) Nasal Spray

May 12, 2022
DURB Meeting

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

Background

- The aim of the DURB review is to provide recommendations for the management of esketamine in the Medicaid program.

Spravato® (esketamine Nasal Spray) Schedule III Controlled Substance

FDA-approved indications	In conjunction with an oral antidepressant for the treatment of adults with treatment resistant depression (TRD) and depressive symptoms associated with acute suicidal ideation or behavior in adults with major depressive disorder (MDD).
FDA-approval date	March 5, 2019
Manufacturer	Janssen Pharmaceutical Companies
Limitation of use	• The effectiveness of esketamine in preventing suicide or reducing suicidal ideation or behavior has not been demonstrated. Additionally, the use of esketamine does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose. • Esketamine is not approved as an anesthetic agent.
Dosing regimen	**TRD:** Induction Phase, Weeks 1 to 4: • Day 1 starting dose: 56 mg IN • Administer IN twice per week for subsequent doses: 56 mg or 84 mg Maintenance Phase: • Weeks 5 to 8: Administer IN once weekly, 56 mg or 84 mg • Week 9 and beyond: Administer IN every 2 weeks or once weekly, 56 mg or 84 mg (dosing is based on response) **MDD with acute suicidal ideation or behavior:** • 84 mg IN twice per week for 4 weeks. • The dosage may be reduced to 56 mg twice per week based on tolerability. • The use of esketamine, in conjunction with an oral antidepressant, >4 weeks has not been systematically evaluated in treating depressive symptoms in patients with MDD with acute suicidal ideation or behavior.

Spravato® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2020

Spravato® (esketamine Nasal Spray), Continued

Availability and storage	Each nasal spray device contains a total of 28 mg of esketamine. Each nasal spray device delivers 2 sprays containing a total of 28 mg of esketamine. • The drug should be stored at room temperature (e.g., 68° to 77°F). • The drug is a Schedule III controlled substance and must be handled with adequate security, accountability, and proper disposal, per facility procedure and applicable federal, state, and local regulations.
Administration	• 1 spray/nostril self-administered by the patient. • The patient must wait 5 minutes after each 28 mg dose so that the drug can be absorbed. • Once the total dose has been self-administered, the patient must be monitored for at least 2 hours by a healthcare provider. • A baseline BP must be measured, and then 40 minutes after administration of the drug, another BP must be taken and recorded. • Before the patient receives the drug, the healthcare provider must instruct the patient not to engage in potentially hazardous activities, such as driving a motor vehicle or operating machinery, until the next day after a restful sleep. • Patients should not eat for 2 hours or drink 30 minutes before administering the drug. • Patients who require a nasal corticosteroid or nasal decongestant on a dosing day should administer these medications at least 1 hour before esketamine.
Spravato® REMS	• Inpatient and outpatient healthcare settings and pharmacies not associated with an inpatient healthcare setting must be certified under the Spravato® REMS to treat patients with esketamine. In addition, pharmacies operating under the same Drug Enforcement Administration license and located within the inpatient healthcare setting are considered certified under the inpatient healthcare setting. • Patients must be enrolled in the Spravato® REMS to receive esketamine in an outpatient medical office or clinic. • The product must never be dispensed directly to a patient for home use.

Spravato® [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; 2020
Spravato® REMS (Risk Evaluation and Mitigation Strategy). Available at: https://www.spravatorems.com/.

Major Depressive Disorder (MDD)

- MDD is a prevalent condition, affecting individuals of all ages.
  - Data from the 2020 National Survey on Drug Use and Health, published by the Substance Abuse and Mental Health Services Administration (SAMHSA), indicate that among individuals aged 18 years or older, 8.4% had a major depressive episode.

- The disease course is variable.
  - Some individuals rarely experience remission, defined as a period of ≥2 months with no symptoms or only 1-2 mild symptoms;
  - Others experience lengthy periods of remission between episodes or complete symptom resolution.

Depressive disorders. In: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.

MDD (Continued)

- Suicidal behavior can occur at all times during major depressive episodes.
- Risk factors are:
  - history of suicide attempts/threats,
  - male sex,
  - living alone, and
  - presence of prominent feelings of hopelessness.

Depressive disorders. In: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.

Treatment-Resistant Depression (TRD)

- There is no consensus definition for TRD.
- The most widely accepted definition appears to be **failure to achieve remission after 2 trials of a medication of adequate dose and duration**.
- Clinical risk factors for the development of TRD have been identified and include:
  - Symptom severity of the current episode,
  - Frequent and recurrent depressive episode,
  - Long duration of illness,
  - Bipolar features,
  - Current psychosocial stressors and comorbidities – specifically anxiety, psychotic features, personality disorders, and substance use disorders,
  - Failed psychotherapy trials, failed electroconvulsive therapy, and greater number of hospitalizations.

Depressive disorders. In: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association; 2013.

Guidelines

- Few guidelines address the use of esketamine and/or focus on the management of TRD
- SAMHSA includes information about esketamine in its Treatment Improvement Protocol 42
  - States that esketamine was FDA-approved in 2019 for TRD
  - Does not make recommendations regarding use of esketamine

Substance Abuse and Mental Health Services Administration. TIP 42: Substance use treatment for persons with co-occurring disorders. https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004. Accessed February 26, 2022.

Guidelines Focusing on TRD

Organization, Year	Canadian expert group, 2021	Polish National Consultant, 2021
Objectives	To determine a standard definition, model, and assessment of TRD	To determine strategies for management of TRD
Selected findings/ recommendations	TRD definition: agreement on requirement for 2 treatment failures; • Lack of agreement on definition of adequate dose/duration and outcome measures • Failure usually defined as <50% reduction in symptom severity; duration of trials ranged from 4-12 weeks • Varying opinions on effectiveness of switching antidepressants and use of agents in the same or different classes	Five approaches: 1) Optimize dose and duration of antidepressant therapy 2) Change the antidepressant to one of a different class 3) Use combination therapy - antidepressants with differing mechanisms of action 4) Augment therapy with lithium, thyroid hormones, atypical antipsychotics, CNS stimulants, or esketamine 5) Consider non-pharmacologic therapies

Rybak YE et al. *Depress Anxiety*. 2021;38:456. doi:10.1002/da.23135.
Gałecki P. *Psychiatr Pol*. 2021;55:7. doi:10.12740/PP/OnlineFirst/115208.

Guidelines on Treatment of MDD

- Several guidelines have been published on the treatment of MDD. Examples:
  - Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016
  - American College of Physicians (ACP) 2016
  - British Association for Psychopharmacology (BAP) 2015
  - World Federation of Societies of Biological Psychiatry (WFSBP) 2013, 2015 (2 parts)
- All have recommendations on initial therapy, switching therapy, and combination therapy.
- Similarities:
  - Consider switching therapy in patients with poor tolerance or lack of response to initial/current therapy
  - Consider combination therapy in patients with lack of response to initial/current therapy (no tolerability issues)
  - Choice of augmentation therapy: first and second-line agents generally include quetiapine, aripiprazole, olanzapine, lithium, triiodothyronine, and mirtazapine

Kennedy SH et al. *Can J Psychiatry*. 2016;61:540. doi:10.1177/0706743716659417.
Qaseem A et al. *Ann Intern Med*. 2016;164:350. doi:10.7326/M15-2570.
Cleare A et al. *J Psychopharmacol*. 2015;29:459. doi:10.1177/0269881115581093.
Bauer M et al. *World J Biol Psychiatry*. 2015;16:76. doi:10.3109/15622975.2014.1001786; World J Biol Psychiatry. 2013;14:334. doi:10.3109/15622975.2013.804195.

Guidelines on Treatment of MDD (Continued)

- Recommendations addressing patients with inadequate response or resistant depression not available in all aforementioned guidelines
- Available recommendations differ. Examples:
  - Consider longer evaluation periods and less emphasis on symptom reduction / more emphasis on improvement in functioning and quality of life (CANMAT, 2016)
  - Consider multiple combinations concurrently (BAP, 2015)
  - Consider longer-term maintenance therapy (≥3 years) (WFSBP, 2015)
  - Consider maximizing antidepressant doses, switching antidepressants, combining antidepressants from different classes, augmenting therapy, or combining antidepressants with nonpharmacologic therapy (WFSBP, 2013)

Kennedy SH et al. *Can J Psychiatry*. 2016;61:540. doi:10.1177/0706743716659417.
Qaseem A et al. *Ann Intern Med*. 2016;164:350. doi:10.7326/M15-2570.
Cleare A et al. *J Psychopharmacol*. 2015;29:459. doi:10.1177/0269881115581093.
Bauer M et al. *World J Biol Psychiatry*. 2015;16:76. doi:10.3109/15622975.2014.1001786; World J Biol Psychiatry. 2013;14:334. doi:10.3109/15622975.2013.804195.

Esketamine: Drug Development Trials

- Four phase 2 and four phase 3 efficacy studies were submitted to the FDA
  - Two phase 3 trials were considered sufficiently supportive of the efficacy of esketamine for TRD: TRANSFORM-2 and SUSTAIN-1
  - TRD: lack of clinically meaningful improvement after treatment with ≥2 different antidepressant drugs prescribed in adequate doses for adequate durations during the current depressive episode
  - All subjects were randomized to receive esketamine or placebo in addition to a newly initiated oral antidepressant
    - Duloxetine, escitalopram, sertraline, or venlafaxine XR

Food and Drug Administration. Center for Drug Evaluation and Research. Application number: 211243Orig1s000 – summary review. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/211243Orig1s000SumR.pdf. Accessed February 27, 2022.
Popova V et al. Am J Psychiatry. 2019;176:428. doi:10.1176/appi.ajp.2019.19020172.
Daly EJ et al. JAMA Psychiatry. 2019;76:893. doi:10.1001/jamapsychiatry.2019.1189.

Esketamine: Drug Development Trials (Continued)

Reference	Design, duration	Population	Interventions	Primary Endpoint	Results
TRANSFORM-2	R, DB, MC, PG, PC 4-week treatment phase, 24-week follow-up	n=324 adults with TRD, ages 18-64 years	Esketamine 56 mg or 84 mg (flexible doses) IN, twice weekly or Placebo 1:1 randomization	Change from baseline in MADRS total score at week 4	LS mean change (95% CI) from placebo at week 4: -4.0 (-7.31 to -0.64), p=0.020
SUSTAIN-1	R, DB, MC, PC withdrawal study Event-driven	n=705 adults with TRD, ages 18-64 years Subjects had received 16 weeks of esketamine treatment and were stable responders or stable remitters	Esketamine, 56 or 84 mg IN (continued dose from previous study or OL treatment) or Placebo	Time to relapse (HR)	HR (95% CI) In remitters: 0.49 (0.29 to 0.84), p=0.003 In responders: 0.30 (0.16 to 0.55), p<0.001

CI=confidence interval; DB=double-blind; HR=hazard ratio; IN=intranasal; LS=least-squares; MADRS=Montgomery-Asberg depression rating scale; MC=multicenter; OL=open-label; PC=placebo-controlled; PG=parallel-group; R=randomized; TRD=treatment-resistant depression

Popova V et al. Am J Psychiatry. 2019;176:428. doi:10.1176/appi.ajp.2019.19020172.
Daly EJ et al. JAMA Psychiatry. 2019;76:893. doi:10.1001/jamapsychiatry.2019.1189.

Esketamine: Drug Development Trials (Continued)

Reference	Design, duration	Population	Interventions	Primary Endpoint	Results
ASPIRE I	R, DB, MC, PG, PC 4-week treatment phase, 9-week follow-up	n=226 adults ages 18-64 years with MDD based on DSM-5 criteria, active suicidal ideation with intent, and need for psychiatric hospitalization	Esketamine 84 mg IN, twice weekly or Placebo 1:1 randomization All patients received comprehensive standard-of-care treatment and were initially hospitalized for 5 days	Change in MADRS total score from baseline to 24 hours post-first dose	LS mean change (95% CI) from placebo at 24 hours: -3.8 (-6.56 to -1.09), p=0.006
ASPIRE II		n=230 adults, same inclusion criteria as ASPIRE I			LS mean change (95% CI) from placebo at 24 hours: -3.9 (-6.60 to -1.11), p=0.006

CI=confidence interval; DB=double-blind; DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition; IN=intranasal; LS=least-squares; MADRS=Montgomery-Asberg depression rating scale; MC=multicenter; MDD=major depressive disorder; PC=placebo-controlled; PG=parallel-group; R=randomized;

Fu et al. J Clin Psychiatry. 2020;81:19m13191. doi:10.4088/JCP.19m13191.
Ionescu DF et al. *Int J Neuropsychopharmacol*. 2021;24:22. doi:10.1093/ijnp/pyaa068.

Esketamine: Drug Development Trials (Continued)

- In phase 3 trials involving patients with **TRD**:
  - Significant improvements in MADRS scores were observed with esketamine from baseline to 4 weeks.
  - FDA noted changes in scores were comparable to those observed with other FDA-approved antidepressants.

- In phase 3 trials involving patients with **MDD and acute suicidal ideation or behavior**:
  - Significant reductions in MADRS scores were observed from baseline to 24 hours post-first dose and remained low through follow-up.

Food and Drug Administration. Center for Drug Evaluation and Research. Application number: 211243Orig1s000 – summary review. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/211243Orig1s000SumR.pdf. Accessed February 27, 2022.
Fu et al. J Clin Psychiatry. 2020;81:19m13191. doi:10.4088/JCP.19m13191.
Ionescu DF et al. *Int J Neuropsychopharmacol*. 2021;24:22. doi:10.1093/ijnp/pyaa068.

Additional Literature on Esketamine

- Random-effects meta-analysis
- Objective: to determine the relative efficacy and tolerability of different therapies, used in combination with antidepressants:
  - Second-generation antipsychotics
  - Lithium
  - Esketamine
- Included randomized controlled trials with duration ≤12 weeks
- Response rates summarized using odds ratios and 95% CI

Vazquez GH et al. *J Psychopharmacol*. 2021;35:890. doi:10.1177/02698811211013579.

Additional Literature on Esketamine (Continued)

- Results:
  - Esketamine efficacy deemed "intermediate"

Adjunctive therapy	OR (95% CI)
Second-generation antipsychotics	1.59 (1.44 to 1.75)
Esketamine	**1.94 (1.52 to 2.46)**
Lithium	2.22 (1.44 to 3.43)

  - Number-needed-to-treat estimates did not differ significantly among the individual drugs and classes

Vazquez GH et al. *J Psychopharmacol*. 2021;35:890. doi:10.1177/02698811211013579.

Management of Esketamine Intranasal

- In the fee-for-service (FFS) program, esketamine intranasal is available as a medical benefit which requires providers to purchase and then bill for the drug via a code.

- A survey of the 15 NYS Medicaid MCOs was conducted and only 1 MCO had not established clinical criteria for esketamine intranasal.

- A review of other state Medicaid programs was conducted.
  - Of the 7 state Medicaid programs reviewed, 5 of the programs had established clinical criteria for esketamine intranasal.

- A retrospective analysis of NYS Medicaid Spravato® (esketamine) nasal spray pharmacy and medical claims was conducted for the timeframe of January 1, 2020, through December 31, 2021.
  - A total of 81 unique members (FFS+MC) received esketamine nasal spray, resulting in 1,047 total claims for the 2-year timeframe.

UB Recommendations

- Require prior authorization for Spravato® (esketamine) nasal spray requests to confirm FDA-approved and Compendia-supported uses.

- Require providers attest that before initiating esketamine intranasal therapy, they obtained a baseline score on a clinical assessment tool (e.g., 17-item Hamilton Rating Scale for Depression [HAMD17], 16-item Quick Inventory of Depressive Symptomatology [QIDS-C16], 10-item Montgomery-Asberg Depression Rating Scale [MADRS]).

- Establish clinical criteria to require the use of at least 2 oral antidepressants for an adequate duration and at an adequate dose with or without adjunctive therapy before initiating Spravato® (esketamine) nasal spray.

- Establish clinical criteria to require the concomitant use of an oral antidepressant with Spravato® (esketamine) nasal spray.

<u>Renewal Criteria</u>

- Utilizing the same clinical assessment tool that was used at baseline, the provider attests that esketamine intranasal therapy has resulted in an improvement in depressive symptoms for the patient.

- The provider attests to monitoring for signs of potential drug abuse or misuse.

Asthma Update:

Use of inhaled corticosteroid / long-acting beta agonist combinations for maintenance and reliever therapy

For: Drug Utilization Review Board

May 12, 2022

NEW YORK STATE | Department of Health | Office of Health Insurance Programs
SUNY The State University of New York

Purpose

- The primary objective is to review updates to asthma treatment guidelines related to the use of inhaled corticosteroid (ICS) / long-acting beta agonist (LABA) combinations as both maintenance and reliever therapy and discuss implications for the New York State (NYS) Medicaid program.
- Utilization of ICS-LABA combinations across the entire NYS Medicaid population, including the fee-for-service (FFS) program and managed care (MC) organizations will also be reviewed.

Background

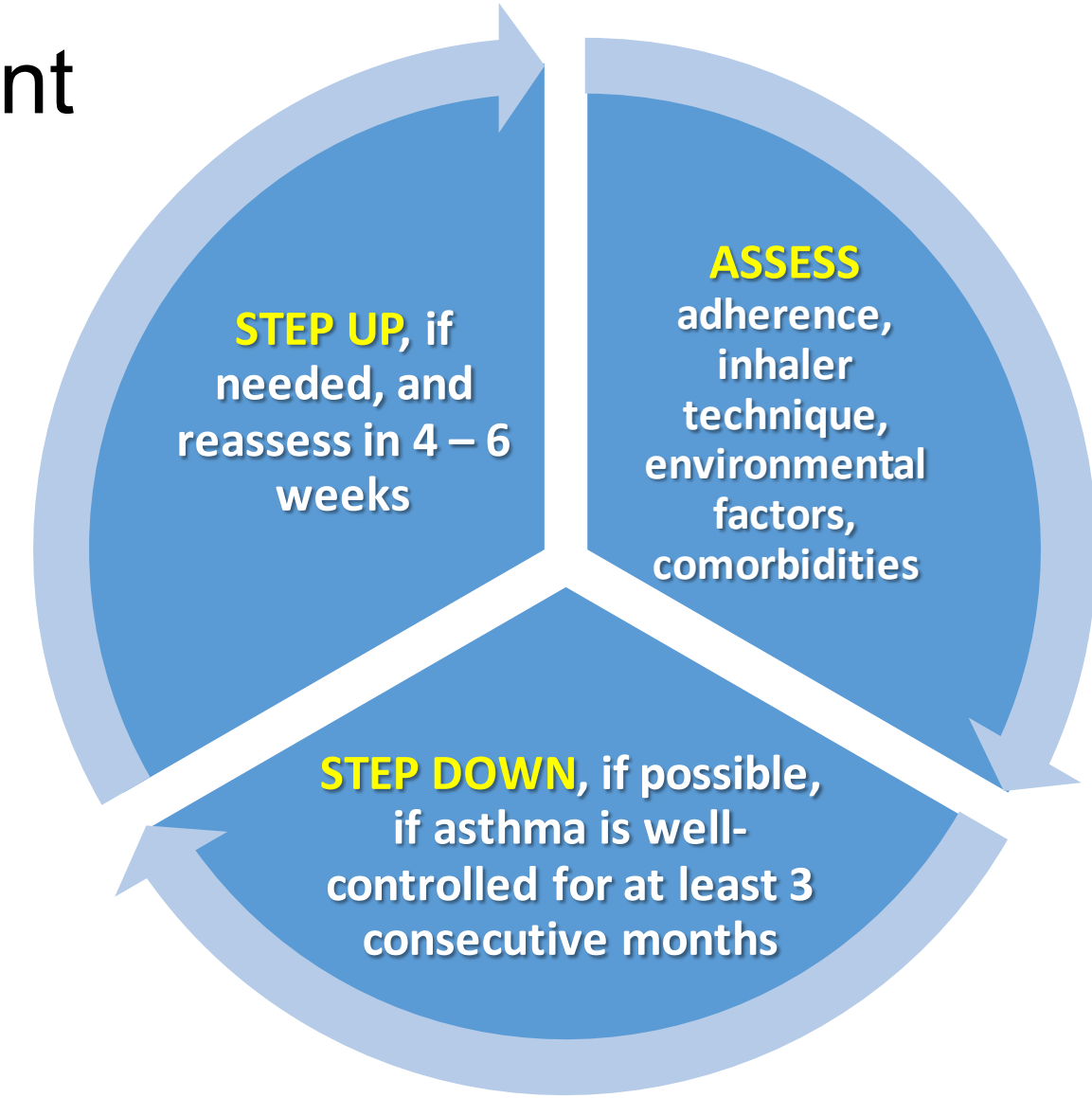
- The National Asthma Education and Prevention Program (NAEPP) guidelines for treatment of asthma, sponsored by the National Heart Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH), were updated in December 2020.
- The previous update occurred in 2007 with the Expert Panel Report (EPR)-3.
- The 2020 update was not a complete update of EPR-3 but focused on specific questions about 6 priority topics, including intermittent use of ICS. The Agency for Healthcare Research and Quality (AHRQ) conducted systematic reviews to address these questions.

Background

- In addressing intermittent use of ICS, the NAEPP 2020 focused updates include recommendations for use of select ICS-LABA medications as both maintenance and reliever therapy.
- Global Initiative for Asthma (GINA) guidelines have included recommendations for use of select ICS-LABA as both maintenance and reliever therapy for several years.
- Food and Drug Administration (FDA)-approved labeling for ICS-LABA products does not include use as reliever therapy, however such use is included in official compendia.

Pharmacologic management

- Both NAEPP and GINA recommend assessment of asthma control using objective measures on an ongoing basis, prior to any regimen changes.
- Both list preferred therapies and alternative therapies at each step based on what is supported by the evidence.
- There are slight differences in number of steps and age brackets.



NAEPP asthma severity and pharmacologic steps

- The 2020 update continued to use the step pharmacologic approach to asthma management based on asthma severity defined in EPR-3

Asthma severity	Intermittent	Mild Persistent	Moderate Persistent	Severe Persistent
Symptom frequency when not on controller medication	Symptoms ≤2 days/week	Symptoms >2 days/week but not daily	Symptoms daily	Symptoms throughout the day
Pharmacologic treatment step	Step 1	Step 2	Steps 3 & 4*	Steps 5 & 6
Level of control based on symptoms when on controller medication	Well-controlled	Not well-controlled	Not well-controlled	Very poorly controlled

*Treatment steps 3 & 4 are referred to as moderate-to-severe persistent asthma in NAEPP 2020 update

NHLBI NAEPP EPR-3; 2007.

NAEPP 2020 grading of recommendations

Definitions of strength:

- **Strong recommendation for** = benefits of the intervention outweigh risks and most individuals would want and should receive it
- **Conditional recommendation for** = an appropriate course of action for different individuals based on values and preferences; most will want it but many will not
- **Conditional recommendation against** = most individuals will not want it but some will and it may be appropriate for some
- **Strong against** = most should not receive it but some will want it

Expert Panel Working Group of NHLBI. *J Allergy Clin Immunol,* 2020.

NAEPP 2020: implications of strong and conditional recommendations

Implications	Strong Recommendation	Conditional Recommendation
For individuals with asthma	Most would want the recommended course of action and only a small proportion would not.	Most would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values or preferences.	Different choices will be appropriate for individuals consistent with their values and preferences. Use shared decision making…
For policymakers	The recommendation can be adapted as policy or performance measure in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Policy making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision making is documented.
For researchers	The recommendation is supported by credible research…additional research is unlikely to alter the recommendation…	The recommendation is likely to be strengthened (for future updates or adaptation) by additional research…

Excerpted from Table 1E. Expert Panel Working Group of NHLBI. *J Allergy Clin Immunol,* 2020.

NAEPP 2020: ICS-LABA for SMART

Question:

What is the comparative effectiveness of ICS with LABA used as both controller and quick-relief therapy compared to ICS with or without LABA used as controller therapy in individuals aged 5 years and older with persistent asthma?

Recommendations:

The Expert Panel recommends ICS-formoterol in a single inhaler used as both daily controller and reliever therapy, i.e., "single maintenance and reliever therapy" (SMART) for individuals aged ≥4 years with moderate to severe persistent asthma

- **Strong recommendation** with high certainty of evidence for ages ≥12 years and moderate certainty of evidence for ages 4-11 when compared to higher-dose ICS + PRN SABA or same-dose ICS-LABA + PRN SABA
- **Conditional recommendation** with high certainty of evidence for ages ≥12 years compared to higher-dose ICS-LABA + PRN SABA

Expert Panel Working Group of NHLBI. *J Allergy Clin Immunol,* 2020.

Evidence supporting SMART

Systematic review and meta-analysis sponsored by AHRQ:

- Searched for randomized clinical trials and observational studies
  - MEDLINE, EMBASE, and Cochrane database through November 2017
- Interventions
  - SMART vs ICS ± LABA as controller and PRN SABA as reliever therapy
- Population
  - Patients aged ≥5 years of age with persistent asthma
- Main outcome
  - Asthma exacerbations

Sobieraj et al. *JAMA*, 2018.

SMART meta-analysis results

Age group	Overall sample	Comparators	Asthma exacerbations
≥12 years 16 studies	N = 22,524 Mean age 42 years 65% female	SMART vs same daily dose ICS alone + PRN SABA	RD = -8.1% (-11.5% to -4.5%) RR = 0.64 (0.53 to 0.78)
		SMART vs same daily dose ICS-formoterol + PRN SABA	RD = -6.4% (-10.2% to -2.6%) RR = 0.68 (0.58 to 0.80)
		SMART vs higher daily dose ICS-formoterol + PRN SABA	RD = -2.8% (-5.2% to -0.3%) RR = 0.77 (0.60 to 0.98)
4 – 11 years 1 study	N = 341 Mean age 8 years 31% female	SMART vs higher daily dose ICS alone + PRN SABA	RD = -12.0% (-22.5% to -1.5%) RR = 0.55 (0.32 to 0.94)
		SMART vs same daily dose ICS-formoterol + PRN SABA	RD = -23.2% (-33.6% to -12.1%) RR = 0.38 (0.23 to 0.63)

N=number of patients; RD=absolute risk difference (95% confidence interval); RR=risk ratio (95% confidence interval)

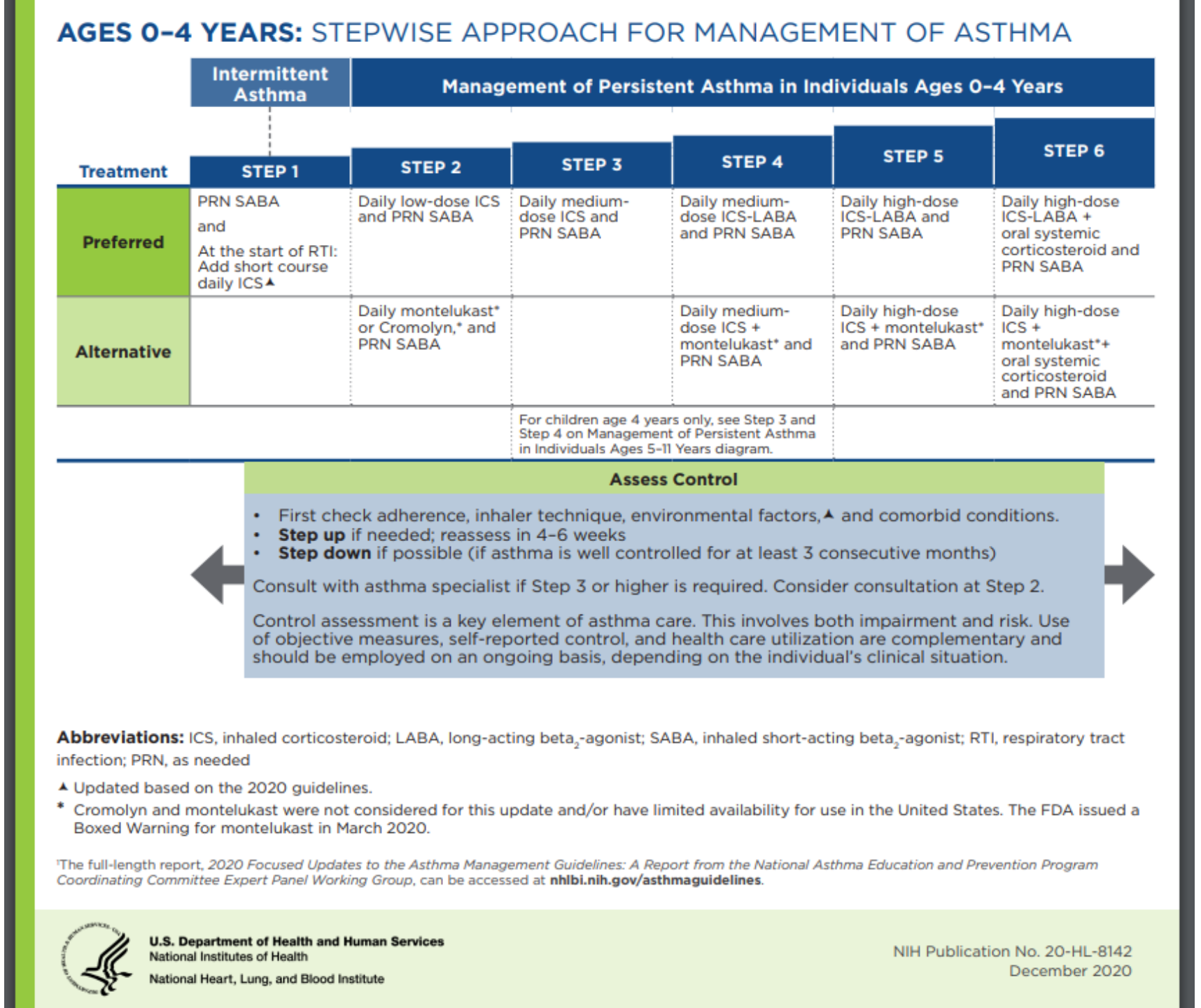
- In 15/16 studies (including pediatric subgroup study), budesonide-formoterol was used for SMART; beclomethasone-formoterol was used in 1 study
- Conclusion: SMART reduced the risk of asthma exacerbations compared to conventional therapy

Sobieraj et al. *JAMA*, 2018.

NAEPP considerations with SMART

- **Recommendation is specific to ICS-formoterol**
  - Formoterol has been the only LABA reported for SMART; it has a rapid onset of action and can be used more than twice daily
  - Regular daily use = 1-2 inhalations once or twice daily
  - PRN use = 1-2 inhalations every 4 hours PRN for asthma symptoms
  - Maximum daily formoterol inhalations = 8 for ages 4 – 11 and 12 for ages 12 and up
- Individuals with an asthma exacerbation in the previous year may be particularly good candidates
- ICS-formoterol should not be used as reliever in patients using ICS-salmeterol for maintenance (unknown safety profile)
- Patients adequately controlled with daily ICS-LABA + PRN SABA do not need to be switched

Expert Panel Working Group of NHLBI. *J Allergy Clin Immunol,* 2020.



AGES 0–4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily medium-dose ICS and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting $beta_2$-agonist; SABA, inhaled short-acting $beta_2$-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

* Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

[1]The full-length report, *2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group*, can be accessed at **nhlbi.nih.gov/asthmaguidelines**.

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

NIH Publication No. 20-HL-8142
December 2020

2020 NAEPP focused updates to asthma management guidelines: At-a-glance guide

Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.

2020 NAEPP focused updates to asthma management guidelines: At-a-glance guide

AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

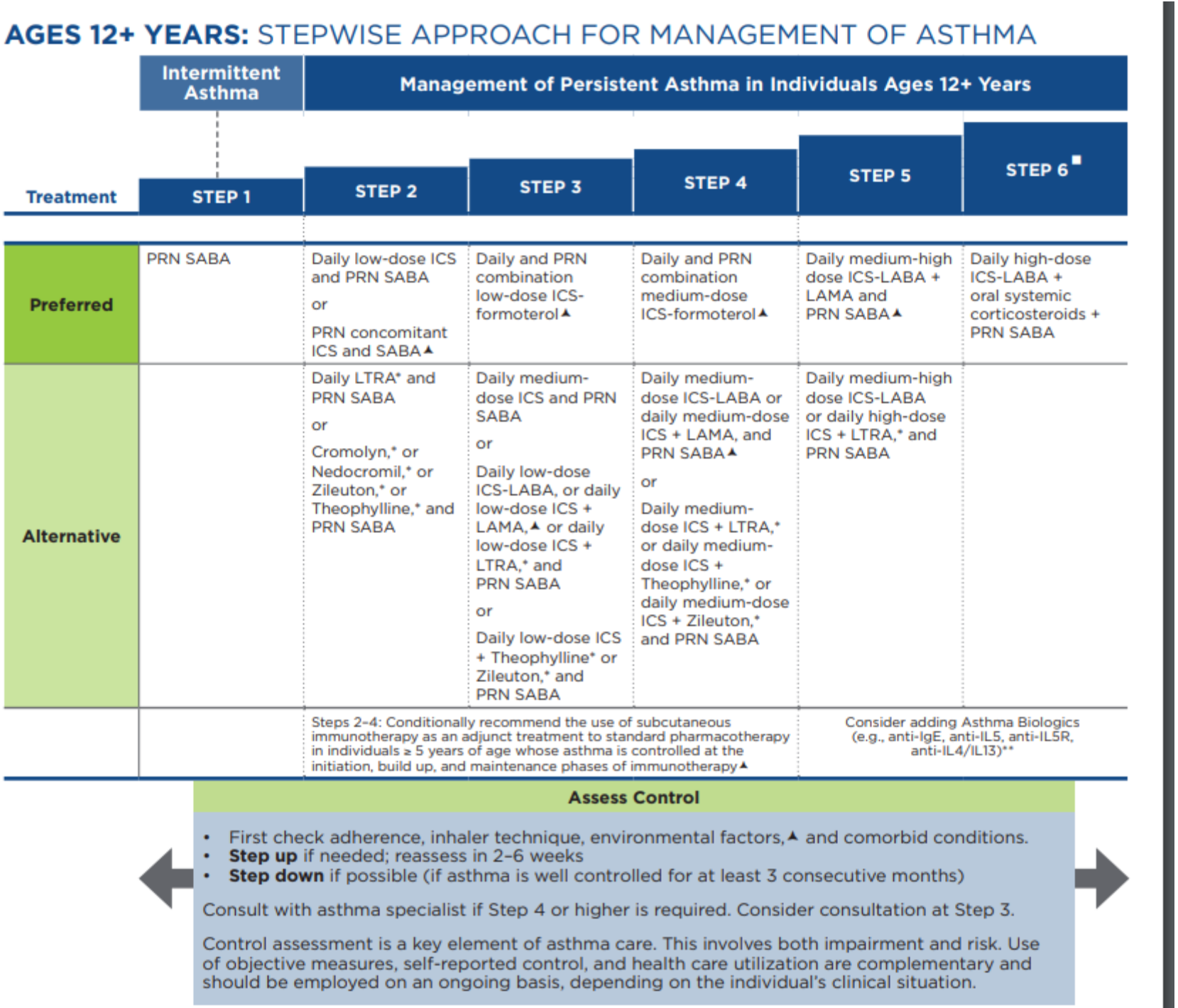
Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** Omalizumab is the only asthma biologic currently FDA-approved for this age range.

Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.



AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

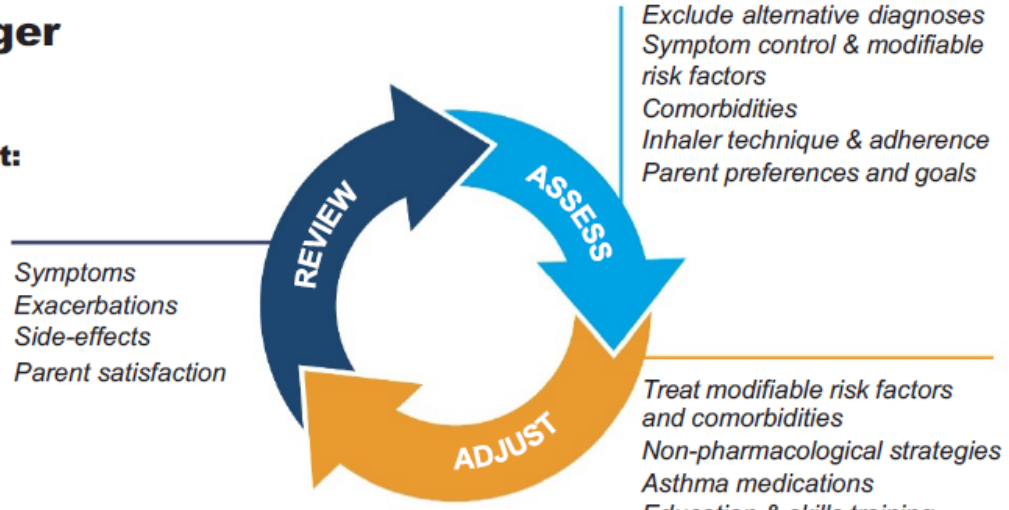
Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

2020 NAEPP focused updates to asthma management guidelines: At-a-glance guide

Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.

Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



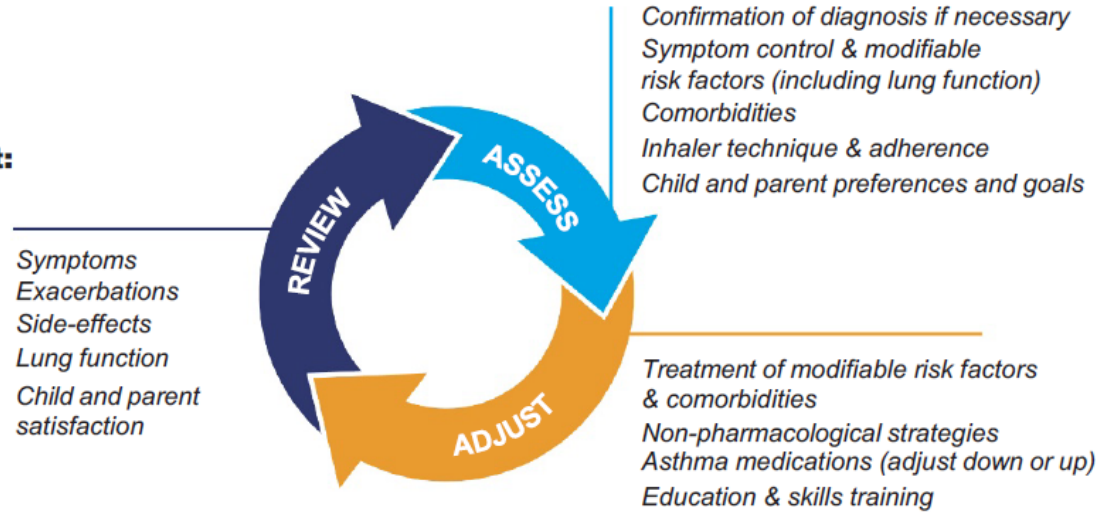
Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS	Continue controller & refer for specialist assessment
Other controller options		*Daily leukotriene receptor antagonist (LTRA), or intermittent short courses of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	*As-needed short-acting β_2-agonist*			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral.	Asthma diagnosis, and asthma not well-controlled on low dose ICS	Asthma not well-controlled on double ICS
		Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

GINA 2021. Box 6-5 Asthma management, children 5 years and younger

Children 6-11 years

Personalized asthma management:
Assess, Adjust, Review



Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose* ICS-formoterol maintenance and reliever (MART)	Medium dose ICS-LABA, OR low dose† ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE
Other controller options	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken*	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*Add-on anti-IL5, or add-on low dose OCS, but consider side-effects*
RELIEVER	*As-needed short-acting beta2-agonist (or ICS-formoterol reliever for MART as above)*				

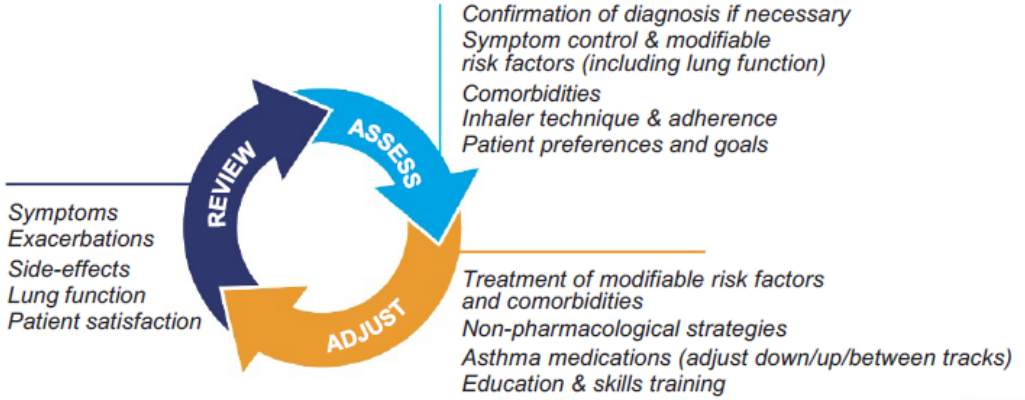
*Very low dose: BUD-FORM 100/6 mcg
†Low dose: BUD-FORM 200/6 mcg (metered doses).

GINA 2021, Box 3-5B

Adults & adolescents 12+ years

Personalized asthma management

Assess, Adjust, Review
for individual patient needs



CONTROLLER and PREFERRED RELIEVER
(Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-formoterol
RELIEVER: As-needed low-dose ICS-formoterol			

CONTROLLER and ALTERNATIVE RELIEVER
(Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for phenotypic assessment ± anti-IgE, anti-IL5/5R, anti-IL4R Consider high dose ICS-LABA
RELIEVER: As-needed short-acting β2-agonist				

Other controller options for either track

	Low dose ICS whenever SABA taken, or daily LTRA, or add HDM SLIT	*Medium dose ICS, or add LTRA, or add HDM SLIT*	*Add LAMA or LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA; add low dose OCS but consider side-effects*

GINA 2021, Box 3-5A

FDA-approved indications for ICS-formoterol

Drug	FDA indications	Dosage
Budesonide-formoterol (Symbicort® and generic) metered-dose inhaler	Treatment of asthma in patients ≥12 years of age	2 inhalations twice daily 80/4.5 mcg or 160/4.5 mcg
	Treatment of asthma in patients 6 to <12 years of age	2 inhalations twice daily 80/4.5 mcg
	Maintenance treatment of chronic obstructive pulmonary disease	2 inhalations twice daily 160/4.5 mcg
Mometasone-formoterol (Dulera®) inhalation aerosol	Treatment of asthma in patients ≥12 years of age	2 inhalations twice daily 100/5 mcg or 200/5 mcg
	Treatment of asthma in patients 5 to <12 years of age	2 inhalations twice daily 50/5 mcg

- Important limitation for both drugs: not indicated for relief of acute bronchospasm
- Contraindication for both drugs: primary treatment of status asthmaticus or acute episodes of asthma requiring intensive measures

Symbicort® package insert. AstraZeneca; 2019.
Dulera® package insert. Kindeva; 2021.

Compendia-supported use

- Under FDA use for asthma:
  - “Combination ICS-formoterol, preferably in a single inhaler, is appropriate as SMART in individuals 4 years or older with moderate to severe persistent asthma. Maintenance therapy is delivered as 1 to 2 puffs once or twice daily and then 1 to 2 puffs are taken as-needed for asthma symptom control”
  - “SMART should be offered in moderate to severe persistent asthma (Step 3, low-dose ICS; Step 4, medium-dose ICS) that is uncontrolled on current therapy before moving on to a higher step of therapy”

Budesonide/formoterol FDA uses in Micromedex; 2022.
Mometasone/formoterol FDA uses in Micromedex; 2022.

Comparator state Medicaid programs

State	PDL Status	Age Limits	F/Q/D Limits
CA	Dulera® & Symbicort® on CDL	None listed	None listed
CO	Dulera® & Symbicort® preferred	None listed	None listed
FL	Dulera® & Symbicort® preferred	Minimum 5 years	1 inhaler/30 days
IL	Dulera® & Symbicort® preferred	None listed	None listed
MA	Dulera® & Symbicort® preferred	None listed	None listed
MI	Dulera® preferred Symbicort® preferred	None listed	1 inhaler/30 days 2 inhalers/30 days
PA	Dulera® & Symbicort® preferred	None listed	1 inhaler/month
TX	Dulera® & Symbicort® preferred	None listed	None listed
WA	Dulera® & Symbicort® preferred	None listed	None listed

CA=California; CDL=contract drugs list; CO=Colorado; FL=Florida; IL=Illinois; MA=Massachusetts; MI=Michigan; PA=Pennsylvania; PDL=Preferred Drug List; TX=Texas; WA=Washington

NYS Medicaid FFS Preferred Drug Program

Preferred	Non-preferred	Additional coverage parameters	
Dulera® (mometasone/ formoterol) Symbicort® (budesonide/ formoterol)	Budesonide/ formoterol (generic Symbicort)	PA required for all new LABA prescriptions for members under FDA or compendia-supported age limits: Dulera® 50 mcg ≥5 yrs Dulera® 100 or 200 mcg ≥12 yrs Symbicort® 80/4.5 mcg ≥6 yrs Symbicort® 160/4.5 mcg ≥12 yrs	F/Q/D limit: 1 inhaler every 30 days Dulera® Symbicort®

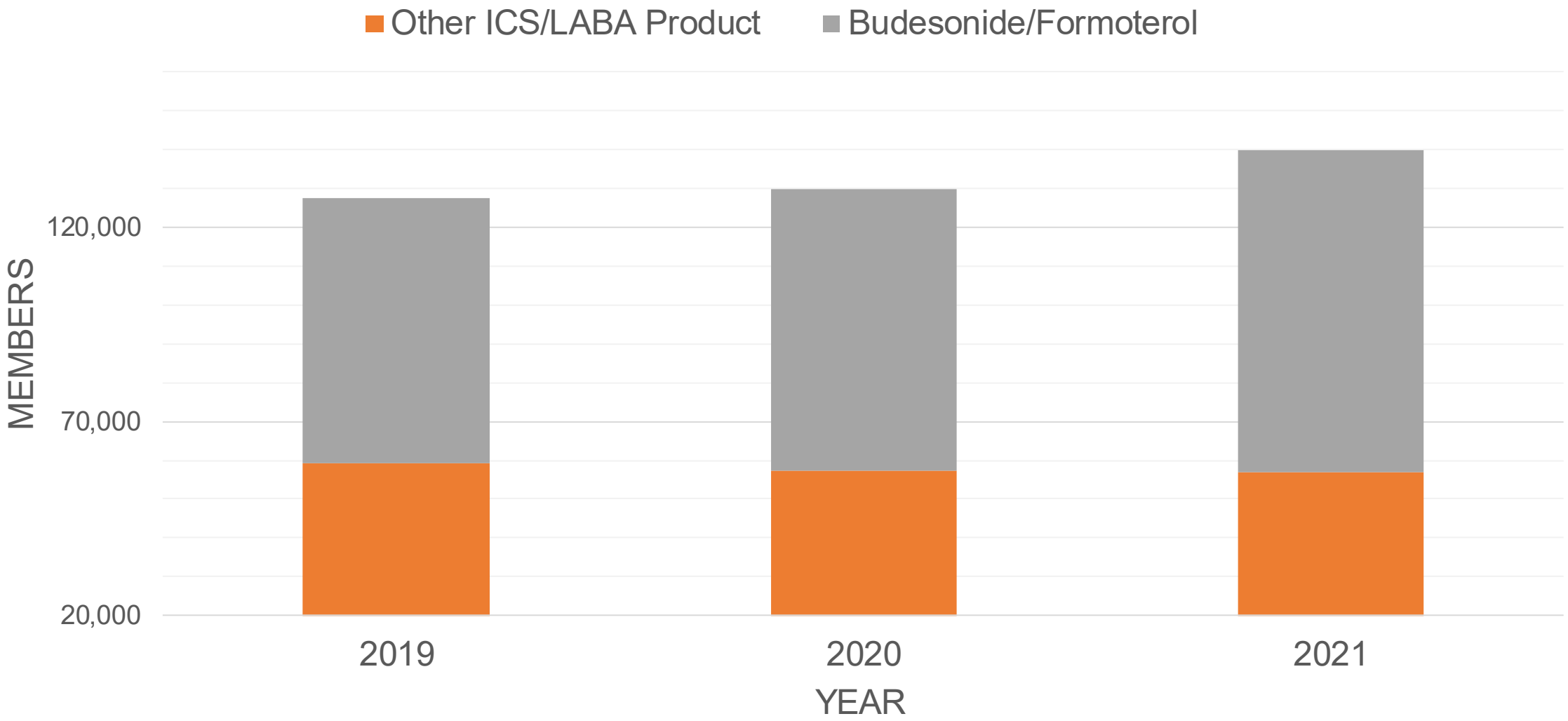
FDA=Food and Drug Administration; FFS=fee for service; F/Q/D=frequency/quantity/duration; ICS=inhaled corticosteroid; LABA=long-acting beta agonist; NYS=New York State; PA=prior authorization

NYS Medicaid FFS PDP PDL; March 22, 2022

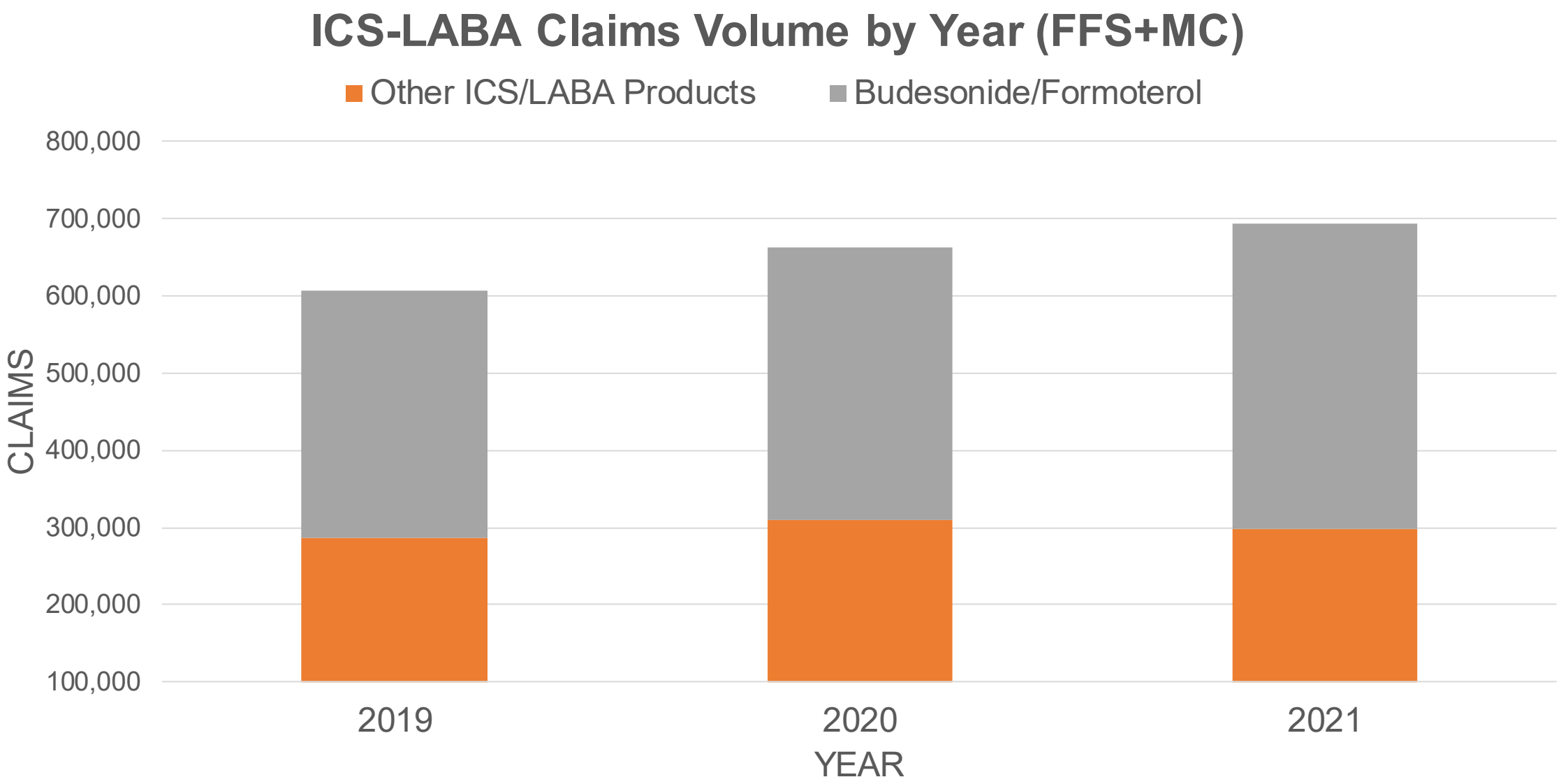
Utilization analysis methods

- A retrospective analysis was conducted using the Medicaid Data Warehouse (MDW)
- Timeframe: January 1, 2019 through December 31, 2021
- Sample: Members with a pharmacy claim for an ICS-LABA
- Limitations:
  - While time periods analyzed take into account inherent delays in claim/encounter submissions, data may not be fully complete
  - Other limiting factors: changing eligibility of Medicaid members and subjective nature of reporting diagnosis codes

Members Utilizing an ICS-LABA Product (FFS+MC)



Source: MDW, 1/1/2019 – 12/31/21



Source: MDW, 1/1/2019 – 12/31/21

Summary

- The 2020 NAEPP guideline updates include a strong recommendation for use of ICS-formoterol as SMART in patients ≥4 years of age with moderate to severe asthma
  - Strong recommendations "can be adapted as policy or performance measures in most situations"
- Though FDA labeling for ICS-formoterol products states they are not indicated for treatment of acute bronchospasm, the guideline recommendations for SMART are included with FDA uses in official compendia
- Overall FFS+MC utilization of ICS-LABA (both members and claims) has increased from 2019 through 2021

Considerations

- The guideline recommendation for use of ICS-formoterol as SMART in patients ≥4 years of age presents the following considerations for NYS Medicaid FFS members:
  - Symbicort® and Dulera® are both preferred drugs on the FFS PDL
  - PA is required for all new LABA prescriptions, including Dulera® and Symbicort®, for members under FDA- or compendia-supported age limits
    - Dulera® is FDA-approved for treatment of asthma in patients aged ≥5 years
    - Symbicort® is FDA-approved for treatment of asthma in patients aged ≥6 years
    - Both drugs appear to be compendia-supported for use as SMART in ages ≥4 years
  - F/Q/D limits for both products are currently 1 inhaler every 30 days
    - Higher quantities and/or more frequent refills may be needed for SMART

References

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