A New Era for Treating and Preventing Asthma Exacerbations

Manuscript Summary for Webinar begins on the next page.

Learning Objectives:
After viewing this webinar, participants should be able to:

- Explain the potential for adverse outcomes of systemic corticosteroid overuse and SABA monotherapy for asthma treatment.
- Describe the benefits of ICS use with a fast-acting bronchodilator to prevent exacerbations in mild or moderate asthma.
- Apply asthma management principles consistent with GINA recommendations for asthma care.
- Discuss prescribing information and clinical evidence of a newly approved, combination, inhaled therapy for prevention and treatment of asthma exacerbations.

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Dr. Njira Lugogo discloses that she does research for and serves on advisory boards for Regeneron/Sanofi, Novartis, and Genentech. She does research for Janssen and serves as a consultant for Amgen. In addition, these are the companies for whom she does research, serves on an advisory board, serves as a consultant, and does talks: AstraZeneca, GSK and Teva.
Dr. Neil Skolnik discloses that he receives research support, serves on the advisory board as a consultant and serves as a speaker for: AstraZeneca, Sanofi Pasteur, Bayer, Novo Nordisk and GSK, He receives research support and serves on the advisory board as a consultant for Sanofi Diabetes. He serves on the advisory board as a consultant and as a speaker for Astellas, Lilly, and Boehringer-Ingelheim/Lilly. He serves as a speaker for Teva and Heartland, and as an advisory board member as a consultant for Genentech, Abbott and Idorsia.
Dr. Barbara Yawn discloses that she serves as a consultant and on the advisory board for GlaxoSmithKline, Boehringer Ingelheim, Teva, AstraZeneca. She serves as a consultant for Regeneron.
Austin Ulrich, PharmD, editorial support, and **Dr. Michael Hanak**, CME reviewer, have no disclosures to report. All conflicts of interest have been mitigated.

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Summary Manuscript for

"A New Era for Treating and Preventing Asthma Exacerbations"

PART ONE: Asthma Management for PCCs

Most patients with asthma are managed in the primary care setting. Although severe cases of asthma may be treated by specialists, such as pulmonologists or allergists, primary care clinicians (PCCs) are responsible for managing those with mild or moderate asthma, which are more prevalent than severe asthma. Approximately 60% of all asthma visits are conducted by PCCs (**FIGURE ONE**).

The Global Initiative for Asthma (GINA) report is published yearly and provides an international perspective on the management of asthma. The National Asthma Education and Prevention Program (NAEPP) guidelines were most recently published in 2020 and represent asthma guidelines for the United States (US). These two documents form the basis of evidence-based approaches for treating asthma, including assessment and diagnosis, initial therapy selection and therapy adjustment based on a stepwise approach, and assessment of asthma control and risk of exacerbations.

Since the GINA report is more recent than NAEPP, we'll review the stepwise treatment approach as recommended in the GINA 2023 report. **FIGURES TWO to FIVE** show the two "Tracks" that GINA recommends in the treatment approach. Consistent across both tracks is the emphasis on use of an inhaled corticosteroid whenever a reliever inhaler is taken to address underlying airway inflammation and reduce the risk of asthma-related death associated with short-acting beta-agonist (SABA)-only use.

It is helpful for PCCs to know when to refer patients to an asthma specialist. Common indications for referral of patients with asthma to a specialist include suspected alternative pulmonary diagnosis, inability to confirm asthma diagnosis by usual means, suspicion of occupational asthma, persistently uncontrolled disease, and severe disease requiring specialized therapy (**FIGURE SIX**).

As part of ongoing management of asthma, assessing asthma control is essential for optimizing therapy and achieving treatment goals. Validated tools for asthma assessment are acknowledged in GINA and NAEPP. They include the Asthma Control Test (ACT), Asthma Therapy Assessment Questionnaire (ATAQ), Asthma Control Questionnaire (ACQ), and Asthma Impairment and Risk Questionnaire (AIRQ) (**FIGURES SEVEN to TEN**).

Preventing exacerbations is a key goal in treating asthma. Fewer exacerbations leads to fewer visits to the emergency department, lower rates of hospitalization, lower mortality rates, and improvement in quality of life. Regular use of inhaled corticosteroids (ICS) leads to reductions in exacerbations across asthma severity levels. Adding a fast-acting bronchodilator to ICS as a rescue or maintenance and rescue therapy has demonstrated additional benefit. There may be a window of opportunity prior to an exacerbation in which treatment with ICS can mitigate exacerbation occurrence or severity (**FIGURE ELEVEN**).

PART TWO: Navigating Patient Access and Costs of Asthma Care

Asthma poses a substantial health and economic burden on individuals and populations worldwide, despite advances in guidance and treatments in recent years. Asthma is estimated to affect approximately 339 million people across the globe. In the US, about 25 million people live with asthma and many experience effects on quality of life (**FIGURE TWELVE**).

Projections of asthma costs in the US through 2038 estimate that 52% of asthma patient-years will be uncontrolled and total direct and indirect costs for asthma care will approach $1 trillion. However, much of the burden of uncontrolled asthma is preventable. Adherence to evidence-based management strategies by patients and clinicians can significantly reduce costs and improve quality of life.

Significant disparities in asthma and asthma care persist in the US. The burden of asthma uniquely affects patients across different age, socioeconomic, and minority groups. Black and/or Hispanic/Latinx individuals of Puerto Rican origin have the highest rates of asthma and the highest asthma death rates in the US. Black individuals are nearly 3 times more likely to die from asthma than White individuals. Refugees and other immigrants face unique barriers in accessing the health care system, such as language barriers, lack of familiarity with the health care system, and cultural barriers, such as misinformed fears of ICS being addictive. Addressing disparities in asthma involves efforts at the clinician, patient, and health care system levels (**FIGURES THIRTEEN to FIFTEEN**).

In looking at access to asthma care and treatments, there are a few concepts that can be helpful for clinicians practicing in primary care. Free clinics are often available to patients who are uninsured or underinsured. Many pharmaceutical companies offer financial assistance programs for asthma medications that have high out-of-pocket costs. Community-based asthma education programs can improve health literacy and cultural

competency. Adherence to therapy can be improved by having more frequent touchpoints through the use of digital health interventions and telemedicine.

We'll now review 3 brief case studies that illustrate situations that PCCs may encounter in practice, with a focus on improving access to optimal asthma care. Case #1 discusses a 48-year-old female with moderate asthma (GINA Step 4) and commercial insurance (**FIGURES SIXTEEN and SEVENTEEN**). Dr. Lugogo: "The first question I often have for a patient like this is whether she's taking the medication because, believe it or not, $50 can be a lot of money for patients that have other responsibilities. Many of our patients have children, elderly parents, and their own expenses. If it is an issue with prescription coverage, then we have strategies in the clinic, ancillary, care managers and other staff that can try to help the patient access the medication." Additionally, most manufacturers of brand-name inhalers offer a co-pay card/discount for patients with commercial insurance, which is usually freely available on the manufacturer's website and can drop co-pays to about $0–$15 per month. Patients may need some help getting this set up.

Case #2 discusses a 70-year-old Black female with mild asthma (GINA Step 2) and government insurance (**FIGURE EIGHTEEN**). Dr. Skolnik: "More often than we'd like, we learn that patients are unable to afford their medication. In this case, there's two medicines that she's on. She's on her ICS — and there is no inexpensive ICS out there. And she's on her less expensive albuterol, but that's still two co-pays. We could either recommend ICS-formoterol because there are clinicians who are comfortable recommending a non-FDA approved approach. Or we could, though it is a generalization from the available data, recommend an ICS-albuterol rescue therapy. We know that if she has mild intermittent disease, that would be acceptable and would get her that inhaled ICS when she needs it — and would be one rather than two medicines that she pays for. There's no ideal solution here, but those are two options."

Finally, Case #3 reviews the situation of a 35-year-old male with moderate asthma (GINA Step 3) without insurance (**FIGURE NINETEEN**). Being Hispanic and an immigrant, the patient has a higher risk of adverse asthma outcomes and other barriers in accessing health care. He may also have language barriers, cultural barriers, economic instability, and behaviors that increase his risk of disease symptoms/complications. Dr. Yawn: "This is also a case that all of us have seen, whether it was in a federally qualified health center (FQHC) or in our office that isn't an FQHC. I'm hoping that I do have

an excellent translator so I can communicate adequately with him so that we do talk about his cultural expectations, his financial abilities — all those things need to be covered. I'm probably going to try to start with a daily maintenance medication, an ICS at moderate dose. It's going to take some time, and I'm going to have to make sure that I spend the time with him, and I then also ask my social service colleague to help me figure out how we get the resources to help pay for these medications."

PART THREE: New FDA-Approved Options for Mild to Moderate Asthma Care

In PART THREE, we're going to focus on treating patients with mild to moderate asthma, or GINA Steps 1–4 (**FIGURE TWENTY**). As we learned in PART ONE, including ICS in rescue/reliever therapy for asthma is part of GINA recommendations across all severities of asthma.

When looking at the importance of ICS in rescue/reliever therapy, we know that ICS have both nongenomic and genomic anti-inflammatory effects. Both contribute to lowering airway inflammation related to an exacerbation. Nongenomic effects have a rapid onset (within seconds to minutes), which is contrary to previous views that ICS don't act quickly; genomic effects have a delayed onset of approximately 4 to 24 hours (**FIGURE TWENTY-ONE**).

Budesonide-formoterol is one example of an ICS + fast-acting bronchodilator that has been well-studied as maintenance and rescue therapy in patients with moderate-to-severe asthma and as rescue therapy in patients with mild and mild-to-moderate asthma. Of note, formoterol is technically considered a long-acting beta-agonist (LABA), though its onset if action is within 3 minutes, so it is fast acting. Compared with as-needed SABA, budesonide maintenance therapy, or budesonide-formoterol maintenance therapy with as-needed SABA, results in reduced ICS exposure, better symptom control, and improved lung function. Collectively, trials (including SYGMA 1 and SYGMA 2 [**FIGURE TWENTY-TWO**) demonstrate reductions in asthma exacerbations with as-needed budesonide-formoterol compared to as-needed SABA alone. However, budesonide-formoterol is not currently FDA-approved for as-needed use in the US.

Several recent studies have demonstrated the effectiveness of ICS + SABA combinations for patients with asthma (**FIGURES TWENTY-THREE to TWENTY-FIVE**). In the PREPARE trial, adults with moderate-to-severe asthma who were instructed to take ICS every time they used rescue therapy had a lower annualized rate of severe exacerbations than the control group.

In MANDALA, a novel as-needed fixed-dose combination of albuterol 180 mcg and budesonide 160 mcg was compared to as-needed albuterol 180 mcg, along with routine therapy in adults with moderate-to-severe asthma. Those in the albuterol-budesonide combination group experienced a 27% reduction in the risk of severe exacerbations, lower mean annualized total dose of systemic corticosteroids, improvement in asthma control, and improved asthma-related quality of life.

DENALI evaluated patients aged ≥12 years with mild-to-moderate asthma who were randomized to one of 4 rescue therapies or placebo, taken four times daily. Patients receiving a fixed-dose combination of albuterol/budesonide 180/160 mcg had greater improvement in baseline forced expiratory volume in 1 second (FEV_1) than those receiving individual components or placebo.

Based largely on the results of the MANDALA trial, as well as other trials of the combination inhaler, albuterol/budesonide was approved as the first as-needed ICS + fast-acting bronchodilator for asthma in the US. In January 2023, the FDA approved the combination inhaler albuterol/budesonide "for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older." The approved strength is albuterol 90 mcg and budesonide 80 mcg per inhalation, and dosing is 2 inhalations as needed for asthma symptoms. The maximum dose is 12 inhalations in 24 hours. This approval fills a long-time gap in asthma management in the US and will be an option for ensuring patients have an ICS with their rescue/reliever treatment.

PART FOUR: Comprehensive Case Studies in Asthma Care

In PART FOUR, we review 2 comprehensive case studies in asthma care that incorporate key points that we learned in the previous sections of the webinar.

Case #1 describes a 54-year-old female who presents to her PCC for an asthma follow-up visit (**FIGURES TWENTY-SIX to THIRTY-THREE**). Dr. Yawn reviews the case information as shown in the figures and discusses how the AIRQ assessment (**FIGURE TWENTY-EIGHT**) may seem like a lot (10 questions), but the questions are all yes or no questions that move quickly. This assessment can remind PCCs to ask all of the relevant questions about asthma control and risk of exacerbations. Dr. Skolnik discusses that many primary care offices do not use validated tools, but if you don't use one of these tools, you still need to ask in detail about these concepts for asthma assessment.

Dr. Skolnik: “In discussing her treatment, I'm going to talk to her about the fact that she has found the rescue therapy very helpful. And what would she think if we could add the anti-inflammatory to her rescue therapy and focus primarily on that as her major therapy? I try to align my goals with the patient's goals and I try to understand why they are making the choices that they are making. We can actually talk to our patients quite extensively about their preferences and then try to meet them where they are, because if they buy in, they have a better tendency to follow through and also to tell you when they don't intend to follow through, which is quite helpful to know.”

Case #2 describes a 36-year-old male with asthma who presents to his PCC in October for a routine visit (**FIGURES THIRTY-FOUR to THIRTY-EIGHT**). Dr. Skolnik: “You know, what I love about this is that this really does clarify that just saying, ‘how are you doing’ in general is not sufficient. We have to drill down.” Dr. Lugogo: “Someone who has relatively few symptoms but still two exacerbations is at risk for poor outcomes. In fact, if you look at people who have died of asthma, about 16% had no symptoms three months before having that fatal episode. Because the disease is episodic in some people and driven by exposure, some outcomes can't be predicted, and we really need to have some vigilance and not assume that someone who's relatively asymptomatic now is not at risk for having a poor outcome.”

After the patient returns for follow-up, he is facing challenges with access to therapy (**FIGURE THIRTY-EIGHT**). Dr. Yawn: “What I'm going to have to do is try to look at some of the pharmaceutical coupon programs. I'm going to look at what kind of insurance he might be able to get, public insurance, suggesting he might feel more comfortable if he doesn't want to pay the co-pay to come in and see me, which I'm glad he did. I do have the ability to refer him to social services locally in my clinic; he doesn't have to go anywhere else. And I think that's really important.”

To receive credit for reading this summary manuscript, visit https://www.pcrg-us.org/survey/post/neweraman or use the QR code to the right.

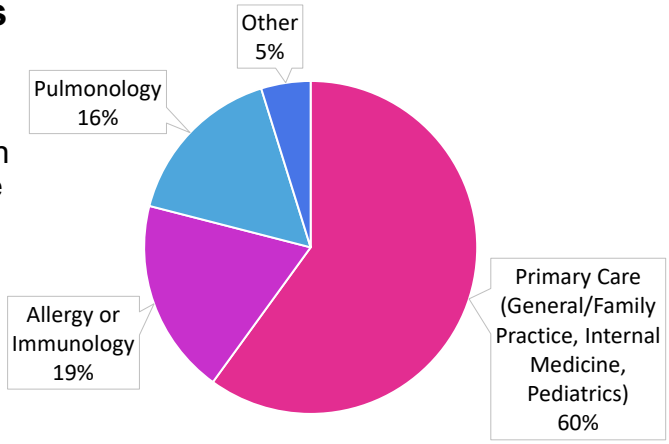
END

FIGURE ONE

Asthma – The Role of PCCs

60% of all asthma visits conducted by PCCs

- The majority of patients with asthma can successfully be managed by PCCs



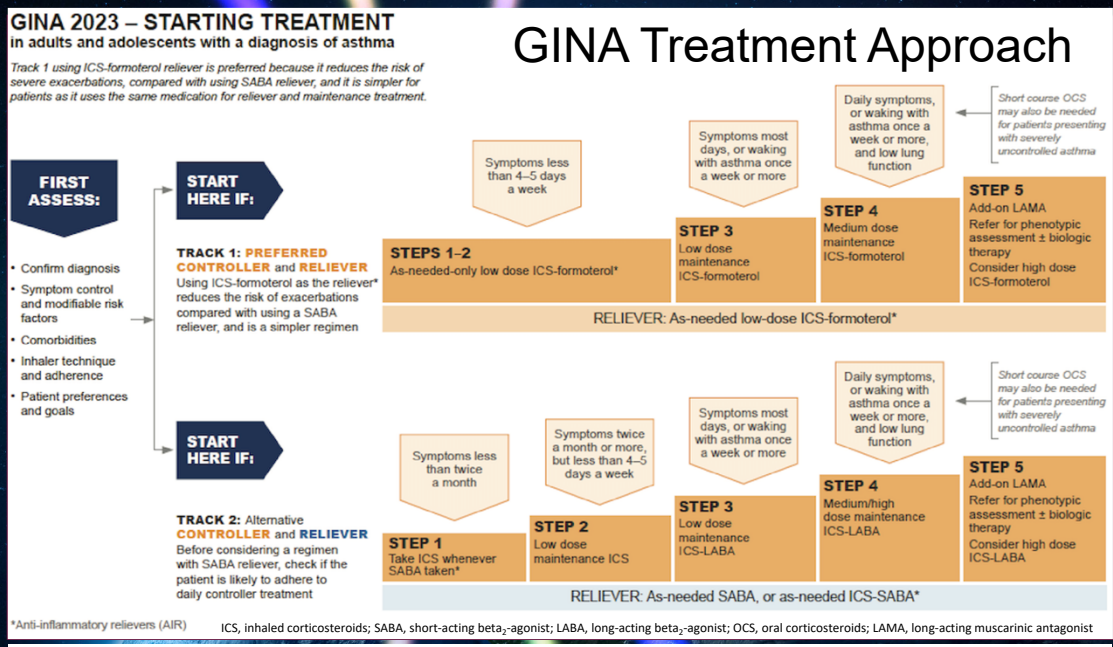
PCCs, primary care clinicians

Akinbami LJ, et al. *Natl Health Stat Report*. 2019;128:1-20. Wu TD, et al. *Med Clin North Am*. 2019;103(3):435-452.

1

FIGURE TWO

GINA Treatment Approach



From GINA ©2023 Global Initiative for Asthma, reprinted with permission. Available from www.ginasthma.org

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FIGURE THREE

GINA Treatment Approach – Initial Assessment

FIRST ASSESS:

- Confirm diagnosis
- Symptom control and modifiable risk factors
- Comorbidities
- Inhaler technique and adherence
- Patient preferences and goals

GINA 2023 – STARTING TREATMENT

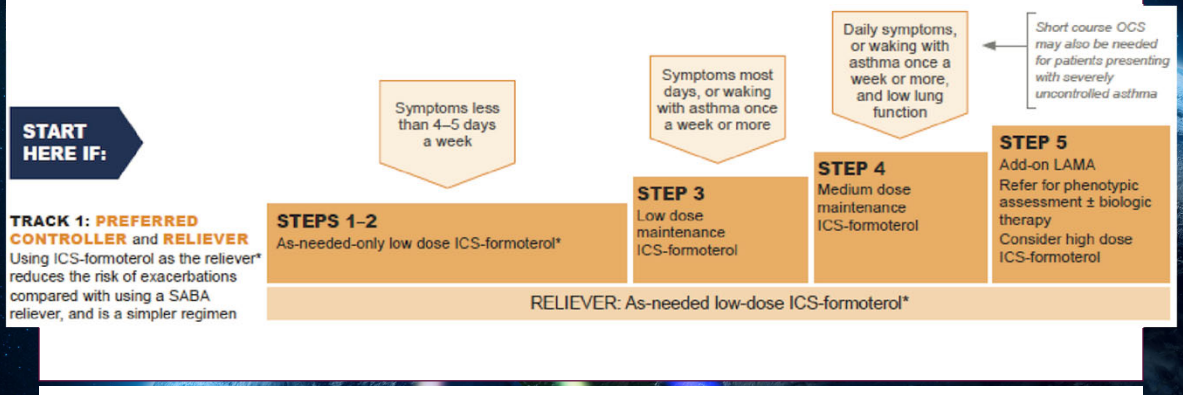
in adults and adolescents with a diagnosis of asthma

Track 1 using ICS-formoterol reliever is preferred because it reduces the risk of severe exacerbations, compared with using SABA reliever, and it is simpler for patients as it uses the same medication for reliever and maintenance treatment.

3

FIGURE FOUR

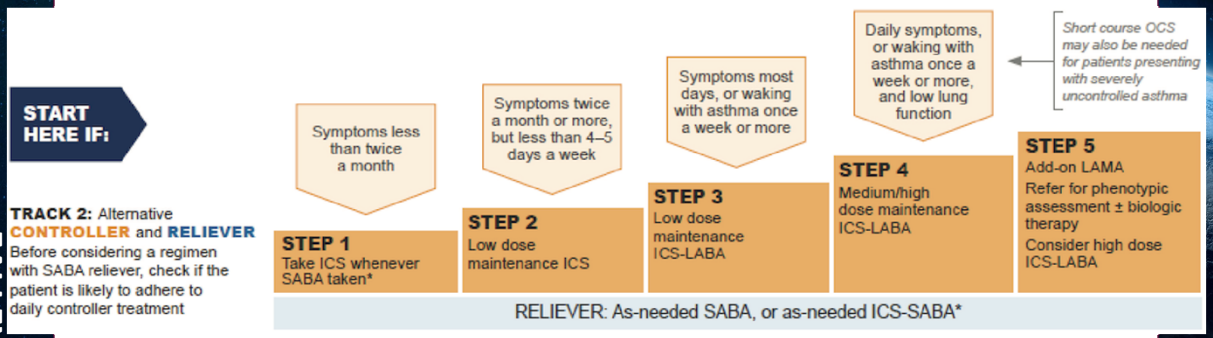
GINA Treatment Approach – Track 1



4

FIGURE FIVE

GINA Treatment Approach – Track 2



From GINA ©2023 Global Initiative for Asthma, reprinted with permission. Available from www.ginasthma.org

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FIGURE SIX

Asthma – When to Refer

- While many patients with asthma can be successfully managed in primary care, it requires adequate training and equipment
- Specialist referral is warranted in some cases
  - Involving specialists (pulmonologists, allergists) can lead to improved outcomes for certain patients

Common Reasons for Specialist Referral
Suspected alternative pulmonary diagnosis
Unable to confirm asthma diagnosis by usual means
Suspicion of occupational asthma
Persistently uncontrolled disease
Severe disease requiring specialized therapy

Wu TD, et al. *Med Clin North Am*. 2019;103(3):435-452.

6

FIGURE SEVEN

Validated Asthma Assessment Tools

Assessment Tool	Description
Asthma Control Test (ACT)	• Scores range from 5-25 with higher scores indicating better control • Score of 20-25 indicates well-controlled asthma, and the maximum clinically important difference is 3 points

Nathan RA, et al. *J Allergy Clin Immunol*. 2004;113(1):59-65. Schatz M, et al. *J Allergy Clin Immunol*. 2009;124(4):719-723.

7

FIGURE EIGHT

Validated Asthma Assessment Tools (cont.)

Assessment Tool	Description
Asthma Therapy Assessment Questionnaire (ATAQ)	• 4-question assessment with scores ranging from 0-4 • Higher score indicates worse asthma control

Vollmer WM, et al. *Am J Respir Crit Care Med*. 1999;160(5):1647-1652.

8

FIGURE NINE

Validated Asthma Assessment Tools (cont.)

Assessment Tool	Description
Asthma Control Questionnaire (ACQ)	• Includes 5 symptom questions • SABA rescue use included in ACQ-6 and pre-bronchodilator forced expiratory volume in 1 second (FEV1) included in ACQ-7 • Scores range from 0-6, with higher scores indicating worse asthma control • Total score is an average of individual items

Juniper EF, et al. *Eur Respir J.* 1999;14(4):902-907.

9

FIGURE TEN

Validated Asthma Assessment Tools (cont.)

Assessment Tool	Description
Asthma Impairment and Risk Questionnaire (AIRQ)	• Incorporates both impairment and risk assessment • Scores range from 0-10, with a score of 0-1 indicating well-controlled asthma and higher scores representing worsening asthma control • Follow-up version of AIRQ available intended to assess control with a 3-month recall period, in between annual visits

Murphy KR, et al. *J Allergy Clin Immunol Pract.* 2020;8(7):2263-2274. Chipps BE, et al. *Ann Allergy Asthma Immunol.* 2022;128(5):544-552.

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FIGURE ELEVEN

Preventing Asthma Exacerbations: The Window of Opportunity

10-14 days before an exacerbation:

- Peak expiratory flow worsens
  - (inverse relationship shown in figure)
- Symptoms increase
- SABA use increases

The time leading up to an exacerbation may offer a window of opportunity to mitigate exacerbation occurrence or severity with anti-inflammatory therapy (ICS)

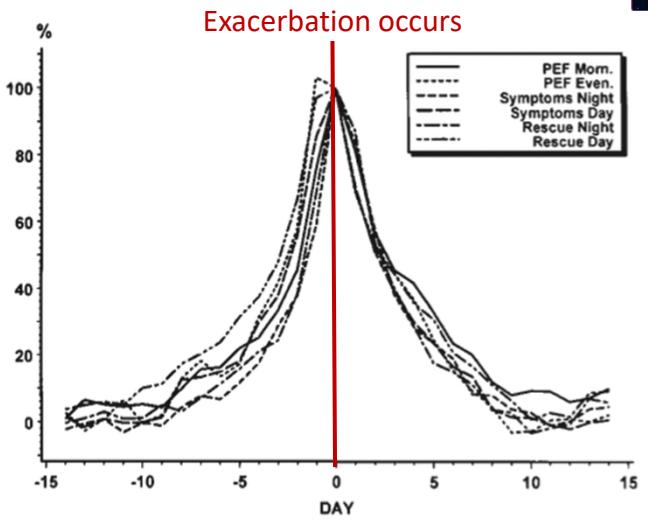

FIGURE TWELVE

Asthma in the US – By the Numbers

- **24.9** million people living with asthma
- **39%** experience at least 1 asthma attack per year
- **986** thousand emergency department visits per year due to asthma
- **3.5** thousand deaths per year
- **7.9** million missed school days per year
- **10.9** million missed days of work per year

Centers for Disease Control and Prevention. Most Recent National Asthma Data. Updated May 10, 2023. Accessed September 12, 2023. https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm; American Lung Association. Asthma Trends and Burden. Accessed September 12, 2023. https://www.lung.org/research/trends-in-lung-disease/asthma-trends-brief/trends-and-burden

FIGURE THIRTEEN

Addressing Disparities – Challenges and Solutions

Clinicians

Challenges
- Availability of asthma specialist care
- Linguistic and cultural competency
- Limitations from payors

Solutions
- Assess access of specialist asthma care
- Telemedicine and technology use
- Improve medication coverage

Nanda A, et al. *J Allergy Clin Immunol*. 2023;151(4):869-880.

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FIGURE FOURTEEN

Addressing Disparities – Challenges and Solutions

Patients

Challenges
- Treatment preferences
- Adherence issues
- Limited health literacy
- Social environment
- Economic instability
- Health behavior
- Risk behavior

Solutions
- Telemedicine
- Care coordination
- Referral to local services
- Improve opportunities for higher education and employment
- Improve access to social work services

Nanda A, et al. *J Allergy Clin Immunol*. 2023;151(4):869-880.

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FIGURE FIFTEEN

Addressing Disparities – Challenges and Solutions

Health Care System

Challenges
- Medication coverage
- Asthma health literacy
- Limited access to quality asthma services
- Inequitable receipt of care

Solutions
- Care coordination
- Collaborate with pharmaceutical agencies
- Combat implicit and explicit bias
- Address health equity
- Enhance community-based programming
- Telemedicine

Nanda A, et al. *J Allergy Clin Immunol.* 2023;151(4):869-880.

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FIGURE SIXTEEN

Case #1 – Patient with commercial insurance

48-year-old female with moderate asthma (GINA Step 4)

- Insured commercially through her employer-sponsored insurance
  - Prescription insurance coverage
  - $50 co-pay for preferred brand medications
- Currently prescribed medium-dose maintenance ICS-LABA
- Presents with complaints of worsening shortness of breath
- Asks for a refill of her albuterol inhaler

What might contribute to problems with medication access for this patient?

How could her asthma regimen be optimized to better align with current evidence?

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FIGURE SEVENTEEN

Case #1 – Patient with commercial insurance

48-year-old female with moderate asthma (GINA Step 4)

- Insured commercially through her employer-sponsored insurance
  - Prescription insurance coverage
  - $50 copay for preferred brand medications
- Currently prescribed medium-dose maintenance ICS-LABA
- Presents with complaints of worsening shortness of breath
- Asks for a refill of her albuterol inhaler
- Further investigation finds that she only uses her ICS-LABA 2-3 times a week because she doesn't like paying $50 every time she picks up the ICS-LABA inhaler, and albuterol is less expensive

What could you do to improve this patient's medication access for the ICS-LABA inhaler?

FIGURE EIGHTEEN

Case #2 – Patient with government insurance

70-year-old Black female with mild asthma (GINA Step 2)

- Has Medicare Part D prescription insurance
  - $50 copay for preferred brand medications
- Currently prescribed low-dose ICS and as-needed SABA
  - Instructed to take her ICS when she uses her SABA
  - Says she follows her regimen as prescribed
- She states that she's having trouble affording her ICS inhaler because she's on a fixed income

What asthma care disparities does this patient have (or is at risk for)?

How could you improve her access to her asthma treatments?

FIGURE NINETEEN

Case #3 – Patient without insurance

35-year-old Hispanic male with moderate asthma (GINA Step 3)

- Presents to your federally-qualified health center (FQHC) to establish care; he has been in the US for about 3 years
- His asthma has not been well-managed previously
  - Several emergency department visits in the last 3 months
- He's currently not taking any asthma medication because his inhalers have all run out, including those he received at the hospital

What asthma care disparities does this patient have (or is at risk for)?

What regimen might you consider for this patient's asthma, and how could you help ensure access to treatments?

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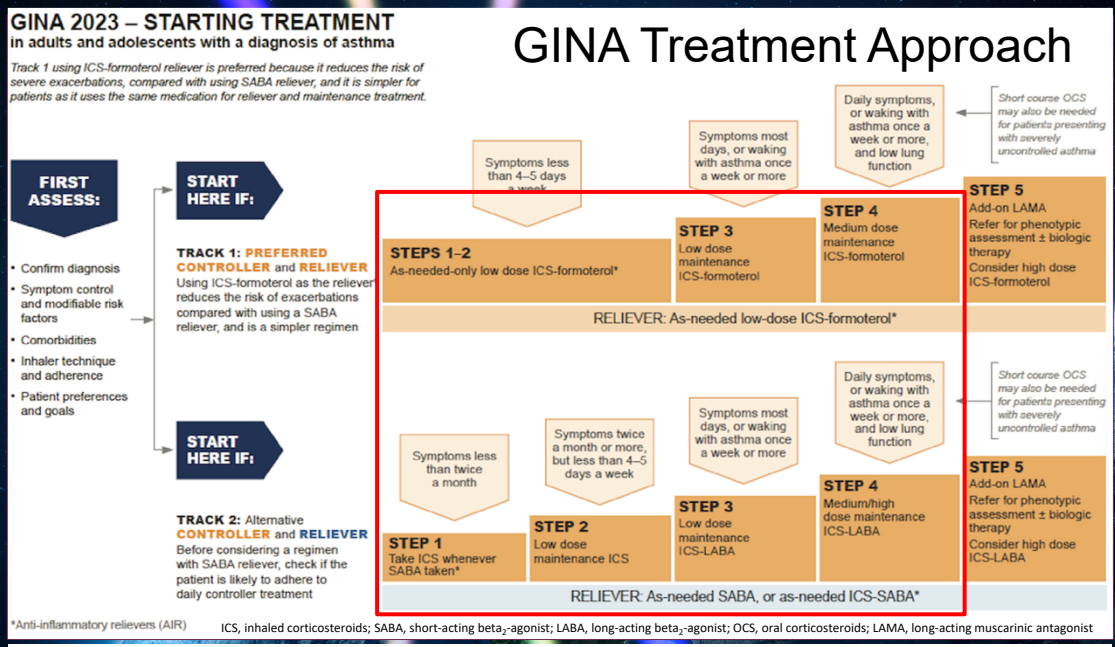
FIGURE TWENTY

GINA Treatment Approach



From GINA ©2023 Global Initiative for Asthma, reprinted with permission. Available from www.ginasthma.org

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FIGURE TWENTY-ONE

The Importance of ICS in Rescue/Reliever Therapy

ICS have both nongenomic and genomic anti-inflammatory effects

- Both contribute to role for lowering airway inflammation related to an exacerbation

Nongenomic Effects (Rapid onset – seconds to minutes)	Genomic Effects (Delayed onset – 4–24 hours)
Decreased airway mucosal blood flow	Increased transcription of anti-inflammatory genes
Decreased airway edema	Decreased transcription of inflammatory genes
Immune cell activity modulation	
Potentiation of bronchodilator effects	

Panettiere RA, et al. *Trends Pharmacol Sci.* 2019;40(1):38-49. Alangari AA. *Ann Thorac Med.* 2010;5(3):133-139.

FIGURE TWENTY-TWO

The Role of ICS + Fast-acting Bronchodilator

Select budesonide-formoterol studies

SYGMA Trials (mild asthma)

SYGMA 1

- 65% reduction in annualized exacerbation rate compared to PRN terbutaline
- Equally effective as budesonide maintenance therapy for preventing exacerbations
- Post-hoc analysis: a single day of treatment with ≥2 PRN inhalations of budesonide-formoterol reduced short-term risk of severe exacerbations

SYGMA 2

- Equally effective compared to budesonide maintenance therapy for preventing exacerbations
- 75% reduction of inhaled corticosteroid exposure

Note: Although most maintenance and rescue therapy studies of ICS + fast-acting bronchodilator were conducted with budesonide-formoterol, mometasone-formoterol is also an ICS + fast-acting bronchodilator combination inhaler. It also lacks approval for PRN use in the US.

O'Byrne PM, et al. *N Engl J Med.* 2018;378(20):1865-1876. O'Byrne PM, et al. *Lancet Respir Med.* 2021;9(2):149-158. Bateman ED, et al. *N Engl J Med.* 2018;378(20):1877-1887.

FIGURE TWENTY-THREE

ICS + SABA Studies

PREPARE Trial

Adults with moderate-to-severe asthma
Randomly assigned to: • Patient-activated ICS + SABA for rescue therapy along with usual maintenance therapy or • Usual maintenance or SABA for rescue therapy along with usual maintenance therapy
Patients who were instructed to take ICS every time they used rescue therapy had a **lower annualized rate of severe exacerbations** than the control group (HR 0.85; 95% CI 0.72–0.999; *P* = .048)
Intervention group also had better asthma control and fewer missed days of work, school, and usual activities

Israel E, et al. *N Engl J Med*. 2022;386(16):1505-1518.

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FIGURE TWENTY-FOUR

ICS + SABA Studies

MANDALA Trial

Note: all data are from the pre-planned efficacy analysis

3132 adolescent and adult patients with moderate-to-severe asthma
Key patient groups: • PRN fixed-dose combination of albuterol 180 mcg + budesonide 160 mcg along with routine therapy • PRN albuterol 180 mcg along with routine therapy
Patients in the fixed-dose group compared to albuterol-alone group experienced: • 27% reduction in risk of severe exacerbations (HR 0.73; 95% CI 0.61–0.88) • Lower mean annualized total dose of SCS (86.2 ± 262.9 mg prednisone equivalents versus 129.3 ± 657.2 mg) • Improvement in asthma control (ACQ; OR, 1.22; 95% CI, 1.02 to 1.47) • Improved asthma-related quality of life (AQLQ+12; OR, 1.23; 95% CI 1.02–1.48)

AQLQ+12, Asthma Quality of Life Questionnaire validated for persons ≥12 years of age

Papi A, et al. *N Engl J Med*. 2022;386(22):2071-2083.

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FIGURE TWENTY-FIVE

ICS + SABA Studies

DENALI Trial

989 patients aged ≥ 12 years with mild-to-moderate asthma

Patients were randomized 1:1:1:1:1 for 12 weeks to receive four-times-daily:

- Fixed-dose combination of albuterol 180 mcg + budesonide 160 mcg
- Fixed-dose combination of albuterol 180 mcg + budesonide 80 mcg
- Albuterol 180 mcg
- Budesonide 160 mcg
- Placebo

- Change from baseline in FEV_1 $AUC_{0\text{-}6h}$ over 12 weeks was greater with albuterol-budesonide 180/160 mcg vs budesonide 160 mcg ($P = .003$)
- Change in trough FEV_1 at week 12 was greater with albuterol-budesonide 180/160 and 180/80 µg vs albuterol 180 µg ($P < .001$)
- Both monocomponents contributed to albuterol-budesonide lung function efficacy

FEV1, forced expiratory volume in 1 second; AUC, area under the curve

Chipps BE, et al. *Chest*. 2023;164(3):585-595.

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FIGURE TWENTY-SIX

Case #1

A 54-year-old female presents to her PCC for an asthma follow-up visit

- Busy accountant
- Currently taking a medium-dose ICS maintenance inhaler (two doses per day) along with an albuterol rescue inhaler
- Has had two urgent care visits in the last year for asthma exacerbations, one of which was during a concomitant upper respiratory infection

What additional information do you need to assess this patient's asthma control?

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FIGURE TWENTY-SEVEN

Case #1 – Initial Assessment

A 54-year-old female presents to her PCC for an asthma follow-up visit

- Currently taking a medium-dose ICS maintenance inhaler (two doses per day) along with an albuterol rescue inhaler
- Has had two urgent care visits in the last year for asthma exacerbations, one of which was during a concomitant upper respiratory infection
- She initially states that she is adherent to her medications
- She acknowledges that she often skips 1 of the 2 doses of her maintenance inhaler, and sometimes misses using the inhaler all together
- She says that the albuterol inhaler seems to really help her breathe better, so she carries this with her and uses it most days of the week

How would you assess this patient's asthma control?

FIGURE TWENTY-EIGHT

AIRQ Assessment Tool

In the past 2 weeks, has coughing, wheezing, shortness of breath, or chest tightness:

1. Bothered you during the day on **more than 4 days**? Yes / No
2. Woke you up from sleep **more than 1 time**? Yes / No
3. Limited the activities you want to do **every day**? Yes / No
4. Caused you to use your rescue inhaler or nebulizer **every day**? Yes / No

Primatene® MIST (Amphastar Pharmaceuticals) or Epinephrine | ProAir RespiClick® (Teva Respiratory, LLC) or Albuterol sulfate | Proventil® HFA (Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.) or Albuterol sulfate | Ventolin® HFA (GlaxoSmithKline) or Albuterol sulfate | Xopenex HFA® (Sunovion Pharmaceuticals Inc.) or Levalbuterol tartrate | Albuterol sulfate or Xopenex® (Sunovion Pharmaceuticals Inc.) or Levalbuterol HCl

Please see all prescribing information for all products.

In the past 2 weeks:

5. Did you have to limit your social activities (such as visiting with friends/relatives or playing with pets/children) because of your asthma? Yes / No
6. Did coughing, wheezing, shortness of breath, or chest tightness limit your ability to exercise? Yes / No
7. Did you feel that it was difficult to control your asthma? Yes / No

In the past 12 months, has coughing, wheezing, shortness of breath, or chest tightness:

8. Caused you to take steroid pills or shots, such as prednisone or Medrol®*? Yes / No
9. Caused you to go to the emergency room or have unplanned visits to a health care provider? Yes / No
10. Caused you to stay in the hospital overnight? Yes / No

Total YES Answers ☐

AIRQ, Asthma Impairment and Risk Questionnaire

FIGURE TWENTY-NINE

Case #1 – AIRQ Results

A 54-year-old female presents to her PCC for an asthma follow-up visit

- The patient's AIRQ score is 4, indicating not well-controlled

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FIGURE THIRTY

Case #1 – Treatment Approach

A 54-year-old female presents to her PCC for an asthma follow-up visit

- Currently taking a medium-dose ICS maintenance inhaler (two doses per day) along with an albuterol rescue inhaler
- Has had two urgent care visits in the last year for asthma exacerbations, one of which was during a concomitant upper respiratory infection
- She initially states that she is adherent to her medications
- She acknowledges that she often skips 1 of the 2 doses of her maintenance inhaler, and sometimes misses using the inhaler all together
- She says that the albuterol inhaler seems to really help her breathe better, so she carries this with her and uses it most days of the week

How would you approach discussing the patient's treatment regimen?

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FIGURE THIRTY-ONE

Case #1 – Evaluating Treatment Response

A 54-year-old female presents to her PCC for an asthma follow-up visit

- You decide to continue the medium-dose ICS maintenance inhaler and prescribe ICS-SABA instead of her albuterol inhaler for improved symptom control and to reduce the risk of severe exacerbations

- She comes back for a follow-up visit 3 months later

How would you assess the patient's response to therapy?

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FIGURE THIRTY-TWO

Follow-up AIRQ

In the past 2 weeks, has coughing, wheezing, shortness of breath, or chest tightness:

1. Bothered you during the day on more than 4 days?	Yes / No
2. Woke you up from sleep more than 1 time?	Yes / No
3. Limited the activities you want to do every day?	Yes / No
4. Caused you to use your rescue inhaler or nebulizer every day?	Yes / No

Primatene® MIST (Amphastar Pharmaceuticals) or Epinephrine

ProAir RespiClick® (Teva Respiratory, LLC) or Albuterol sulfate

Proventil® HFA (Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.) or Albuterol sulfate

Ventolin® HFA (GlaxoSmithKline) or Albuterol sulfate

Xopenex HFA® (Sunovion Pharmaceuticals Inc.) or Levalbuterol tartrate

Albuterol sulfate or Xopenex® (Sunovion Pharmaceuticals Inc.) or Levalbuterol HCl

Please see all prescribing information for all products.

In the past 2 weeks:

5. Did you have to limit your social activities (such as visiting with friends/relatives or playing with pets/children) because of your asthma?	Yes / No
6. Did coughing, wheezing, shortness of breath, or chest tightness limit your ability to exercise?	Yes / No
7. Did you feel that it was difficult to control your asthma?	Yes / No

In the past 3 months, has coughing, wheezing, shortness of breath, or chest tightness:

8. Caused you to take steroid pills or shots, such as prednisone or Medrol**?	Yes / No
9. Caused you to go to the emergency room or have unplanned visits to a health care provider?	Yes / No
10. Caused you to stay in the hospital overnight?	Yes / No

Total YES Answers ☐

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Case #1 – Follow-up AIRQ Results

A 54-year-old female presents to her PCC for an asthma follow-up visit

- The patient's AIRQ score is 1, indicating well-controlled

FIGURE THIRTY-THREE

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Case #2 – Initial Assessment

A 36-year-old male with asthma presents to his PCC in October for a routine visit.

- He is adherent to his inhaler regimen (low-dose ICS daily) with good inhaler technique.
- He notes that he's feeling great and has had no trouble with his breathing recently.
- His AIRQ score today is 2 (steroids in the past 12 months and emergency room visit for breathing symptoms), indicating "not well-controlled" asthma.
- Upon further discussion, he adds that he gets "asthma attacks" when he exercises during allergy seasons (fall and spring) and so he always uses his albuterol inhaler before jogging (5 times/week) during these times of the year.

How would you classify the patient's asthma?

FIGURE THIRTY-FOUR

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FIGURE THIRTY-FIVE

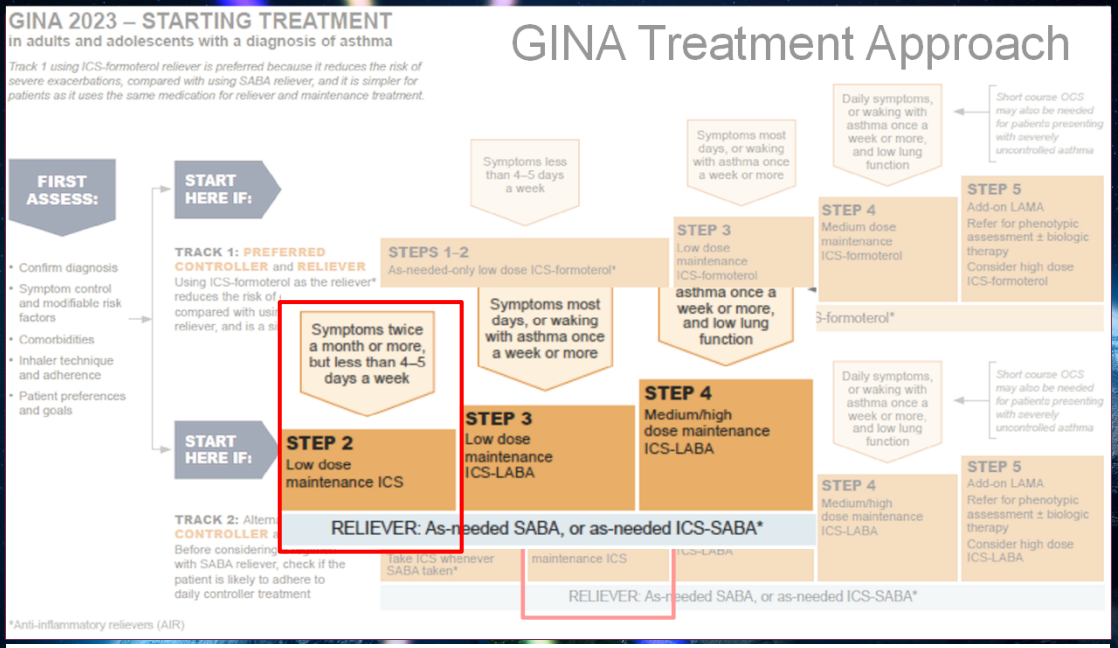

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FIGURE THIRTY-SIX

Case #2 – Initial Assessment

A 36-year-old male with asthma presents to his PCC in October for a routine visit.

- He is adherent to his inhaler regimen (low-dose ICS daily) with good inhaler technique.
- He notes that he's feeling great and has had no trouble with his breathing recently.
- His AIRQ score today is 2 (steroids in the past 12 months and emergency room visit for breathing symptoms), indicating "not well-controlled" asthma.
- Upon further discussion, he adds that he gets "asthma attacks" when he exercises during allergy seasons (fall and spring) and so he always uses his albuterol inhaler before jogging (5 times/week) during these times of the year.

Is the patient at risk for asthma adverse outcomes or exacerbations?

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FIGURE THIRTY-SEVEN

Case #2 – Treatment Approach

A 36-year-old male with asthma presents to his PCC in October for a routine visit.

- You decide to recommend taking his ICS inhaler every time he uses his SABA
- The patient agrees

- He returns 3 months later (January) for follow up

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FIGURE THIRTY-EIGHT

Case #2 – Treatment Access

A 36-year-old male with asthma presents to his PCC in January for a follow-up visit.

- He reports that he recently lost his job and has trouble affording his inhalers now
- He has run out of both inhalers
- He currently doesn't have prescription drug insurance
- His AIRQ score has worsened to 4, indicating "not well-controlled" likely due to nonadherence

What would you recommend to improve this patient's access to medication?

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