

# GINA Pocket Guide

## Difficult to treat and severe asthma in adults and adolescents

V2.0 April 2019



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# Declaration of interest



- [PLEASE ADD YOUR DECLARATION OF INTEREST HERE]
- The work of GINA is supported only by the sale and licensing of GINA resources

## **International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma**

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# Limitations of current resources about severe asthma



- Guidelines are costly and time-consuming to develop, and to maintain
  - Typically, guidelines undergo a thorough initial development, with infrequent updates
- Conventional evaluation of evidence places a high importance on internal validity
  - Low importance is given to external validity, despite study populations being highly selected
  - Recommendations may not be generalizable to patients seen in normal clinical practice
- Guidelines are often written in academic language
  - Evidence is typically compiled as answers to individual PICOT\* questions
  - May have limited relevance to day-to-day clinical practice
- Much of current literature on severe asthma focuses on biologic therapies
  - There are many more patients with difficult-to-treat asthma than with severe asthma, and clinicians need practical advice about how to distinguish these patients, including in primary care
  - Advice is also needed by clinicians in areas where biologics are not available or affordable

*\*PICOT: a framework for constructing research questions – what is the Population, Intervention, Control, Outcome, Time period?*

# About the GINA strategy



- The GINA report is not a guideline, but an integrated evidence-based strategy focusing on translation into clinical practice
- Recommendations are framed, not as answers to isolated PICOT questions, but as part of an integrated strategy, in relation to:
  - The GINA goals of preventing asthma deaths and exacerbations, as well as improving symptom control
  - Current understanding of underlying disease processes
  - Human behavior (of health professionals and patients/carers)
  - Implementation in clinical practice
  - Global variation in populations, health systems and medication access
- GINA provides practical resources for clinicians
  - Figures and tables about implementation in clinical practice: not just 'what', but 'how to'
  - A survey of GINA Assembly members in 2017 strongly encouraged development of a practical resource about severe asthma

# Goals of asthma treatment



- Few asthma symptoms
  - No sleep disturbance
  - No exercise limitation
- } Symptom control
- Maintain normal lung function
  - Prevent flare-ups (exacerbations)
  - Prevent asthma deaths
  - Avoid medication side-effects
- } Risk reduction
- The patient's goals may be different from these
  - Symptoms and risk may be discordant – need to assess both

- Uncontrolled asthma
    - Frequent symptoms and/or flare-ups (exacerbations)
    - Many of these patients may potentially have mild asthma, i.e. their asthma could be well-controlled with low dose ICS, if taken regularly
  - Difficult-to-treat asthma
    - (not difficult patients!)
    - Asthma uncontrolled despite prescribing high dose preventer treatment
    - Contributory factors may include incorrect diagnosis, incorrect inhaler technique, poor adherence, comorbidities
  - Severe asthma
    - “Severe asthma” has had many different meanings (*Taylor, ERJ 2008; Reddel AJRCCM 2009*)
    - Now defined as asthma that is uncontrolled despite maximal optimised therapy and treatment of contributory factors, or that worsens when high dose treatment is decreased (*Chung, ERJ 2014*)
- i.e. relatively refractory to corticosteroids (rarely completely refractory)
- A retrospective definition, dependent on how thoroughly contributory factors are excluded

# Terminology



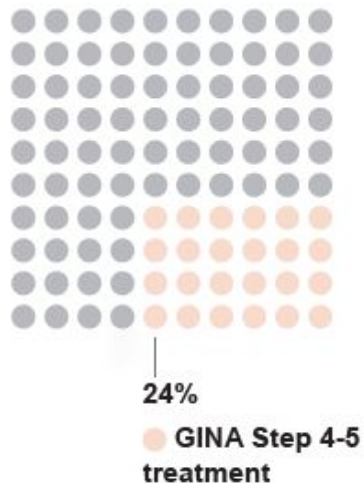
- **Phenotype:** The observable characteristics of a disease, such as morphology, development, biochemical or physiological properties, or behaviour.
  - Patients with an identified phenotype of obstructive lung disease may share a cluster of clinical, functional and/or inflammatory features, without any implication of a common underlying mechanism
  - Examples: allergic asthma, aspirin-exacerbated respiratory disease, severe eosinophilic asthma
- **Endotype:** A subtype of disease, defined functionally and pathologically by a distinct molecular mechanism or by distinct treatment responses (*Anderson, Lancet 2008*)
  - Among patients with obstructive lung disease, there are likely to be several specific endotypes associated with divergent underlying molecular causes, and with distinct treatment responses. These endotypes may or may not align with clinical or inflammatory phenotypes identified from studies limited to asthma or to COPD
  - Examples: emphysema due to alpha1-antitrypsin deficiency
- **Biomarker:** A defined characteristic measured as an indicator of normal biologic processes, pathogenic processes or response to an intervention
  - Potential examples: FeNO, blood eosinophils – but these may not meet quality criteria for biomarkers



# How common is severe asthma?



Box 1. What proportion of adults have difficult-to-treat or severe asthma?

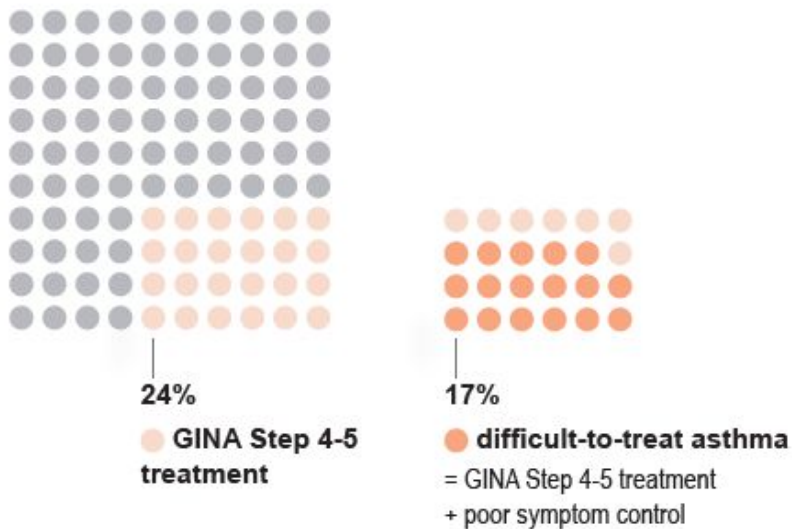


These data are from a Dutch population survey of people  $\geq 18$  years with asthma<sup>2</sup>

# How common is severe asthma?



Box 1. What proportion of adults have difficult-to-treat or severe asthma?

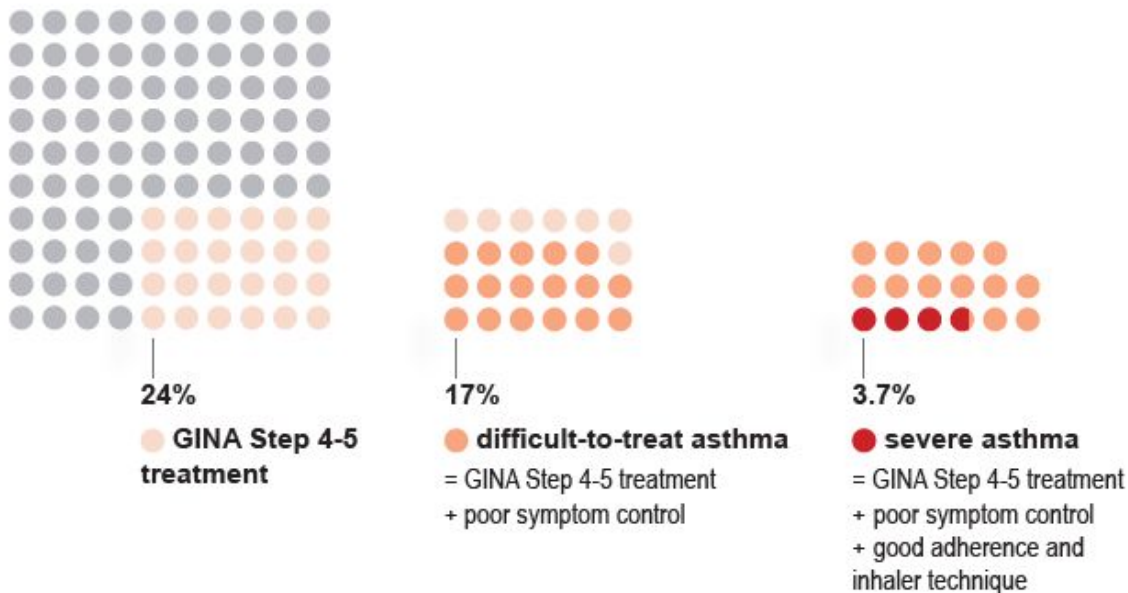


These data are from a Dutch population survey of people  $\geq 18$  years with asthma<sup>2</sup>

# How common is severe asthma?



Box 1. What proportion of adults have difficult-to-treat or severe asthma?



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# **DIFFICULT-TO-TREAT & SEVERE ASTHMA**

**in adolescent and  
adult patients**

Diagnosis and Management

*A GINA Pocket Guide  
For Health Professionals*

November 2018



GINA

# **DIFFICULT-TO-TREAT & SEVERE ASTHMA**

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# Team who developed pocket guide



- Tomoko Ichikawa, Clinical Professor of Design, Information Designer, University of Illinois
- Hugh Musick, Associate Director, Program for Healthcare Delivery Design, University of Illinois
- Helen Reddel, Chair of GINA Science committee
- Members of the GINA Science Committee

# Methods used to develop v1.0 of pocket guide



## **Research:** (20+ hours)

- Familiarized with content area (read papers from prominent authors in the field)
- Developed interview protocols
- Interviewed key GINA members and external experts/GPs previously identified as advisors for input
- Transcribed interviews
- Aligned content with GINA's existing key messages
- Collected existing published guidelines for reference
- Researched printing possibilities and limitations

# Methods used to develop V1.0 of pocket guide



## **Decision tree prototype:** (60+ hrs, 20 versions)

- Synthesized content matter, structured into pocket guide outline provided by content expert
- Parsed textual outline into diagrammatic decision tree structures
- Integrated additional inputs from experts and literature
- Incorporated feedback from experts, iterated
- Incorporated color

## **Booklet design overall:** (20 hrs, 5 versions)

- Integrated decision tree to fit booklet format
- Formatted detailed text pages to complete the pocket guide
- Designed Table of Contents to represent at-a-glance algorithm
- Increased total length of pocket guide to 36 pages

## **V2.0 published in April 2019**

## Table of Contents

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Prevalence: how many people have severe asthma? .....	7
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### Investigate and manage adult and adolescent patients with difficult-to-treat asthma

GP OR SPECIALIST CARE	Decision Tree	Detail Pages
1 Confirm the diagnosis (asthma or differential diagnoses) .....	8	16
2 Look for factors contributing to symptoms, exacerbations and poor quality of life .....	8	17
3 Optimize management .....	8	18
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### Assess and treat severe asthma phenotypes

#### SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

5 Assess the severe asthma phenotype and factors contributing to symptoms, quality of life and exacerbations .....	10	20
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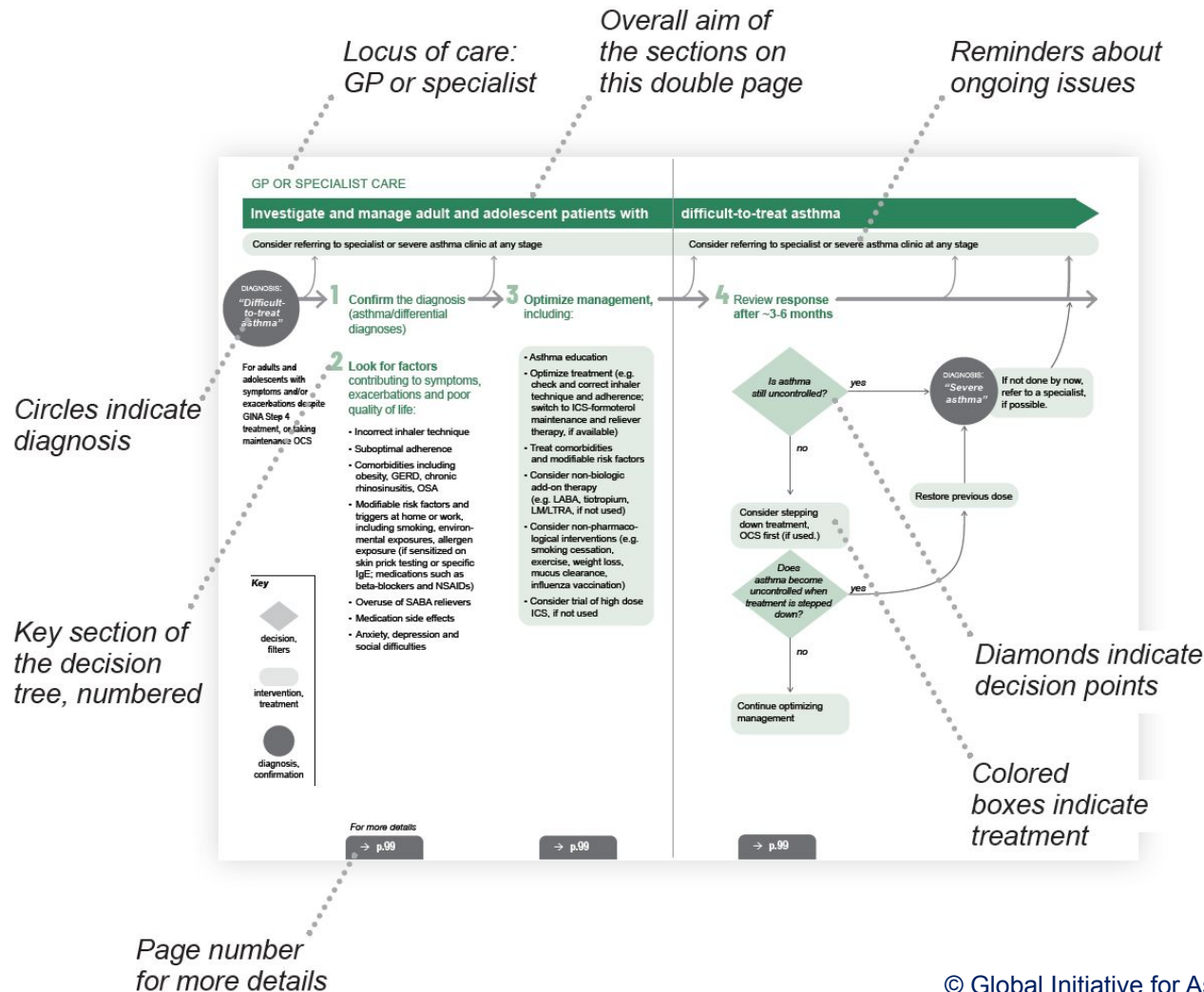
### Monitor / Manage severe asthma treatment

#### SPECIALIST AND PRIMARY CARE IN COLLABORATION

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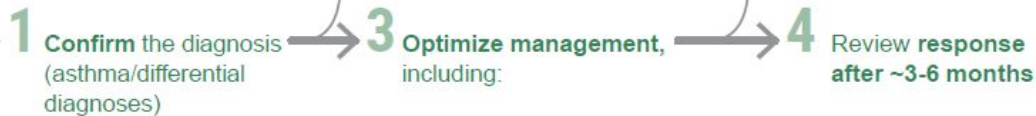
GP OR SPECIALIST CARE

## Investigate and manage adult and adolescent patients with difficult-to-treat asthma

Consider referring to specialist or severe asthma clinic at any stage

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS:  
"Difficult-to-treat asthma"



SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

## Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

→ **5** Assess the **severe asthma phenotype** and factors contributing to symptoms, quality of life and exacerbations

→ **6a** Consider *non-biologic* treatments

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

### Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

→ **6b** Consider *add-on biologic Type 2*  
targeted treatments

SPECIALIST AND PRIMARY CARE IN COLLABORATION

## Monitor / Manage severe asthma treatment

Continue to optimize management



## Investigate and manage adult and adolescent patients with

## difficult-to-treat asthma



Consider referring to specialist or severe asthma clinic at any stage

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS:

*"Difficult-to-treat asthma"*

For adolescents and adults with symptoms and/or exacerbations despite GINA Step 4 treatment, or taking maintenance OCS

## Key

decision,  
filtersintervention,  
treatment

## Investigate and manage adult and adolescent patients with

## difficult-to-treat asthma



Consider referring to specialist or severe asthma clinic at any stage

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS:  
"Difficult-  
to-treat  
asthma"

**1** Confirm the diagnosis  
(asthma/differential  
diagnoses)

**2** Look for factors  
contributing to symptoms,  
exacerbations and poor  
quality of life:

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers at home or work, including smoking, environmental exposures, allergen exposure (if sensitized on skin prick testing or specific IgE); medications such as beta-blockers and NSAIDs
- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties

For adolescents and adults with symptoms and/or exacerbations despite GINA Step 4 treatment, or taking maintenance OCS

## Key



decision,  
filters



intervention,  
treatment

## Investigate and manage adult and adolescent patients with difficult-to-treat asthma



Consider referring to specialist or severe asthma clinic at any stage

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS:  
"Difficult-to-treat asthma"

**1** Confirm the diagnosis (asthma/differential diagnoses)

**3** Optimize management, including:

**2** Look for factors contributing to symptoms, exacerbations and poor quality of life:

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers at home or work, including smoking, environmental exposures, allergen exposure (if sensitized on skin prick testing or specific IgE); medications such as beta-blockers and NSAIDs
- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties

- Asthma education
- Optimize treatment (e.g. check and correct inhaler technique and adherence; switch to ICS-formoterol maintenance and reliever therapy, if available)
- Treat comorbidities and modifiable risk factors
- Consider non-biologic add-on therapy (e.g. LABA, tiotropium, LM/LTRA, if not used)
- Consider non-pharmacological interventions (e.g. smoking cessation, exercise, weight loss, mucus clearance, influenza vaccination)
- Consider trial of high dose ICS, if not used

## Key



decision, filters



intervention, treatment



## Investigate and manage adult and adolescent patients with difficult-to-treat asthma



Consider referring to specialist or severe asthma clinic at any stage

Consider referring to specialist or severe asthma clinic at any stage

DIAGNOSIS:  
"Difficult-to-treat asthma"

**1** Confirm the diagnosis (asthma/differential diagnoses)

**3** Optimize management, including:

**4** Review response after ~3-6 months

For adolescents and adults with symptoms and/or exacerbations despite GINA Step 4 treatment, or taking maintenance OCS

**2** Look for factors contributing to symptoms, exacerbations and poor quality of life:

- Incorrect inhaler technique
- Suboptimal adherence
- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
- Modifiable risk factors and triggers at home or work, including smoking, environmental exposures, allergen exposure (if sensitized on skin prick testing or specific IgE); medications such as beta-blockers and NSAIDs
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- Consider trial of high dose ICS, if not used

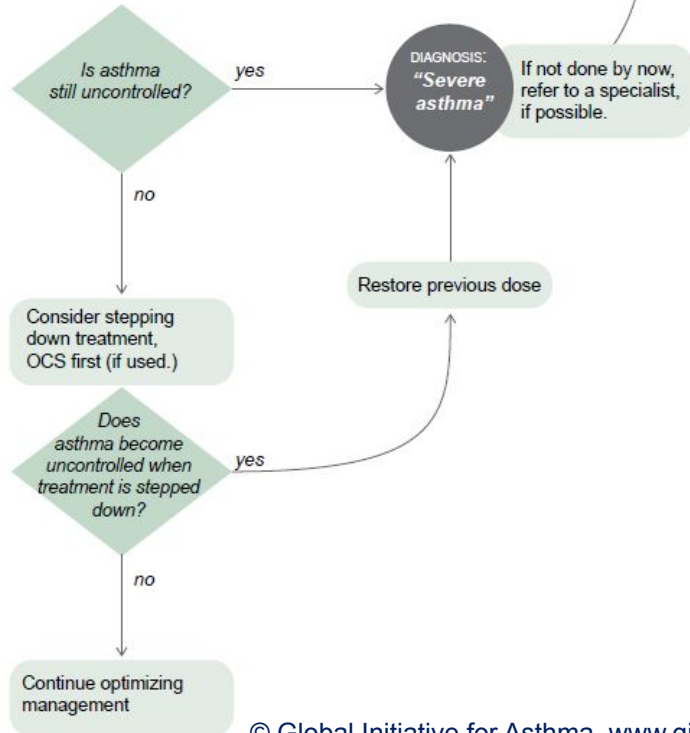
## Key



decision,  
filters



intervention,  
treatment



## Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)



- Assess the **severe asthma phenotype** during high dose ICS treatment (or lowest possible dose of OCS)

### Type 2 inflammation

Could patient have Type 2 airway inflammation?

*Note: these are not the criteria for add-on biologic therapy (see 6b)*

- Blood eosinophils  $\geq 150/\mu\text{l}$  and/or
- FeNO  $\geq 20$  ppb and/or
- Sputum eosinophils  $\geq 2\%$ , and/or
- Asthma is clinically allergen-driven and/or
- Need for maintenance OCS  
(Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)

- Investigate for comorbidities/differential diagnoses and treat/refer as appropriate
  - Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion
- Consider need for social/psychological support
- Involve multidisciplinary team care (if available)
- Invite patient to enroll in registry (if available) or clinical trial (if appropriate)

## Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

**5** Assess the **severe asthma phenotype** and factors contributing to symptoms, quality of life and exacerbations

**6a** Consider **non-biologic** treatments

**Assess the severe asthma phenotype during high dose ICS treatment (or lowest possible dose of OCS)**

### Type 2 inflammation

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- Need for maintenance OCS (Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)

*Note: these are not the criteria for add-on biologic therapy (see 6b)*

yes

no

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis (clinical Type 2 phenotypes with specific add-on treatment)

**Investigate for comorbidities/differential diagnoses and treat/refer as appropriate**

- Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
- Skin prick testing or specific IgE for relevant allergens, if not already done
- Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion

**Consider need for social/psychological support**

**Involve multidisciplinary team care (if available)**

**Invite patient to enroll in registry (if available) or clinical trial (if appropriate)**

### If no evidence of Type 2 inflammation:

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
- Consider add-on treatments
  - Trial of tiotropium or macrolide\* (if not already tried)
  - Consider add-on low dose OCS, but implement strategies to minimize side-effects
  - Stop ineffective add-on therapies
- Consider bronchial thermoplasty (+ registry)

## Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

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- Need for maintenance OCS (Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)

yes

no

Note: these are not the criteria for add-on biologic therapy (see 6b)

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- Skin prick testing or specific IgE for relevant allergens, if not already done
- Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion

• Consider need for social/psychological support

• Involve multidisciplinary team care (if available)

• Invite patient to enroll in registry (if available) or clinical trial (if appropriate)

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis (clinical Type 2 phenotypes with specific add-on treatment)

Is add-on Type 2 biologic therapy available/affordable?

no

**If add-on Type 2 biologic therapy is NOT available/affordable**

- Consider higher dose ICS, if not used
- Consider non-biologic add-on therapy (e.g. LABA, tiotropium, LMLTRA, macrolide\*)
- Consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

**If no evidence of Type 2 inflammation:**

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
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- Consider bronchial thermoplasty (+ registry)

Not currently eligible for biologics



## Assess and treat severe asthma phenotypes

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

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**Assess the severe asthma phenotype during high dose ICS treatment (or lowest possible dose of OCS)**

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- Asthma is clinically allergen-driven and/or
- Need for maintenance OCS (Repeat blood eosinophils and FeNO up to 3x, on lowest possible OCS dose)

yes

no

*Note: these are not the criteria for add-on biologic therapy (see 6b)*

- Investigate for comorbidities/differential diagnoses and treat/refer as appropriate
  - Consider: CBC, CRP, IgG, IgA, IgM, IgE, fungal precipitins; CXR and/or HRCT chest; DLCO
  - Skin prick testing or specific IgE for relevant allergens, if not already done
  - Other directed testing (e.g. ANCA, CT sinuses, BNP, echocardiogram) based on clinical suspicion
- Consider need for social/psychological support
- Involve multidisciplinary team care (if available)
- Invite patient to enroll in registry (if available) or clinical trial (if appropriate)

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
- Consider AERD, ABPA, chronic rhinosinusitis, nasal polyposis, atopic dermatitis (clinical Type 2 phenotypes with specific add-on treatment)

Is add-on Type 2 biologic therapy available/affordable?

yes

no

**If add-on Type 2 biologic therapy is NOT available/affordable**

- Consider higher dose ICS, if not used
- Consider non-biologic add-on therapy (e.g. LABA, tiotropium, LMLTRA, macrolide\*)
- Consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

**If no evidence of Type 2 inflammation:**

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
- Avoid exposures (tobacco smoke, allergens, irritants)
- Consider investigations (if available and not done)
  - Sputum induction
  - High resolution chest CT
  - Bronchoscopy for alternative/additional diagnoses
- Consider add-on treatments
  - Trial of tiotropium or macrolide\* (if not already tried)
  - Consider add-on low dose OCS, but implement strategies to minimize side-effects
  - Stop ineffective add-on therapies
- Consider bronchial thermoplasty (+ registry)

Not currently eligible for biologics

**Assess and treat severe asthma phenotypes** *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

**6b**Consider **add-on biologic Type 2**  
targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:<sup>1</sup>
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider local payer eligibility criteria<sup>1</sup> and predictors of response when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

<sup>1</sup> Check local eligibility criteria for specific biologic therapies as these may vary from those listed

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)



6b

Consider *add-on biologic Type 2*  
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  - have eosinophilic or allergic biomarkers, or
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- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic  
is appropriate to  
start first?

## Anti-IgE

Is the patient eligible for *anti-IgE* for severe allergic asthma?

- Sensitization on skin prick testing or specific IgE<sup>1</sup>
- Total serum IgE and weight within dosage range<sup>1</sup>
- Exacerbations in last year<sup>1</sup>

no  
↑  
no

## Anti-IL5 / Anti-IL5R

Is the patient eligible for *anti-IL5 / anti-IL5R* for severe eosinophilic asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 300/\mu\text{l}$ <sup>1</sup>

no  
↑  
no

## Anti-IL4R

Is the patient eligible for *anti-IL4R* ... for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 150/\mu\text{l}$ <sup>1</sup> or FeNO  $\geq 25$  ppb<sup>1</sup>
- ... or because of need for maintenance OCS<sup>1</sup>?

Eligible for none?  
Return to section 6a<sup>1</sup> Check local eligibility criteria for specific biologic therapies as these may vary from those listed

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)



6b

Consider **add-on biologic Type 2**  
targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
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- Consider local payer eligibility criteria<sup>1</sup> and predictors of response when choosing between available therapies
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Which biologic  
is appropriate to  
start first?**Anti-IgE**Is the patient eligible for *anti-IgE*  
for severe allergic asthma?

- Sensitization on skin prick testing or specific IgE<sup>1</sup>
- Total serum IgE and weight within dosage range<sup>1</sup>
- Exacerbations in last year<sup>1</sup>

What factors may predict good  
asthma response to *anti-IgE*?

- Blood eosinophils  $\geq 260/\mu\text{l}$  ++
- FeNO  $\geq 20$  ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no  
↑  
no**Anti-IL5 / Anti-IL5R**Is the patient eligible for *anti-IL5 / anti-IL5R*  
for severe eosinophilic asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 300/\mu\text{l}$ <sup>1</sup>

What factors may predict good  
asthma response to *anti-IL5/5R*?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no  
↑  
no**Anti-IL4R**Is the patient eligible for *anti-IL4R*  
... for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 150/\mu\text{l}$ <sup>1</sup> or FeNO  $\geq 25$  ppb<sup>1</sup>
- ... or because of need for maintenance OCS<sup>1</sup>?

What factors may predict good  
asthma response to *anti-IL4R*?

- Higher blood eosinophils +++
- Higher FeNO +++

*Anti-IL4R may also be used to treat*

- Moderate/severe atopic dermatitis
- Nasal polyposis

Eligible for none?  
Return to section 6a

<sup>1</sup> Check local eligibility criteria for specific biologic therapies as these may vary from those listed



Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)



6b

Consider **add-on biologic Type 2**  
targeted treatments

- Consider add-on Type 2-targeted biologic for patients with exacerbations or poor symptom control on high dose ICS-LABA, who:
  - have eosinophilic or allergic biomarkers, or
  - need maintenance OCS
- Consider local payer eligibility criteria<sup>1</sup> and predictors of response when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

**Anti-IgE**Is the patient eligible for *anti-IgE* for severe allergic asthma?

- Sensitization on skin prick testing or specific IgE<sup>1</sup>
- Total serum IgE and weight within dosage range<sup>1</sup>
- Exacerbations in last year<sup>1</sup>

no ↑ no

What factors may predict good asthma response to *anti-IgE*?

- Blood eosinophils  $\geq 260/\mu\text{l}$  ++
- FeNO  $\geq 20$  ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

**Anti-IL5 / Anti-IL5R**Is the patient eligible for *anti-IL5 / anti-IL5R* for severe eosinophilic asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 300/\mu\text{l}$ <sup>1</sup>

no ↑ no

What factors may predict good asthma response to *anti-IL5/5R*?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

**Anti-IL4R**Is the patient eligible for *anti-IL4R* ... for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 150/\mu\text{l}$ <sup>1</sup> or FeNO  $\geq 25$  ppb<sup>1</sup>
- ... or because of need for maintenance OCS<sup>1</sup>?

Eligible for none?

Return to section 6a

What factors may predict good asthma response to *anti-IL4R*?

- Higher blood eosinophils +++
- Higher FeNO +++

*Anti-IL4R may also be used to treat*

- Moderate/severe atopic dermatitis
- Nasal polyposis

Choose one if eligible; trial for at least 4 months and assess response

Extend trial to 6-12 months

unclear

Good asthma response?

yes  
Good response to T2-targeted therapy

no

<sup>1</sup> Check local eligibility criteria for specific biologic therapies as these may vary from those listed

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section 3 (including inhaler technique, adherence, comorbidities)

6b

Consider **add-on biologic Type 2**  
targeted treatments

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- Total serum IgE and weight within dosage range<sup>1</sup>
- Exacerbations in last year<sup>1</sup>

no ↑ no

What factors may predict good asthma response to *anti-IgE*?

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- FeNO  $\geq 20$  ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

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- Exacerbations in last year<sup>1</sup>
- Blood eosinophils  $\geq 300/\mu\text{l}$ <sup>1</sup>

no ↑ no

What factors may predict good asthma response to *anti-IL5/5R*?

- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

**Anti-IL4R**Is the patient eligible for *anti-IL4R* ... for severe eosinophilic/Type 2 asthma?

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What factors may predict good asthma response to *anti-IL4R*?

- Higher blood eosinophils +++
- Higher FeNO +++

*Anti-IL4R* may also be used to treat

- Moderate/severe atopic dermatitis
- Nasal polyposis

Choose one if eligible; trial for at least 4 months and assess response

Extend trial to 6-12 months

unclear

Good asthma response?

yes  
Good response to T2-targeted therapy

no

**STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible

no

Little/no response to T2-targeted therapy

Eligible for none?  
Return to section 6a

<sup>1</sup> Check local eligibility criteria for specific biologic therapies as these may vary from those listed

## Monitor / Manage severe asthma treatment

Continue to optimize management



### 7 Review response

- Asthma: symptom control, exacerbations, lung function
- Type 2 comorbidities  
e.g. nasal polyposis, atopic dermatitis
- Medications: treatment intensity, side-effects, affordability
- Patient satisfaction


## Monitor / Manage severe asthma treatment

Continue to optimize management

### 7 Review response

- Asthma: symptom control, exacerbations, lung function
- Type 2 comorbidities  
e.g. nasal polyposis, atopic dermatitis
- Medications: treatment intensity, side-effects, affordability
- Patient satisfaction

#### *If good response to Type 2-targeted therapy*

- Re-evaluate the patient every 3-6 months 
- For oral treatments: consider decreasing/stopping OCS first, then stopping other add-on medication
- For inhaled treatments: consider decreasing after 3-6 months; continue at least moderate dose ICS
- Re-evaluate need for ongoing biologic therapy
- Order of reduction of treatments based on observed benefit, potential side-effects, cost and patient preference

yes →


## Monitor / Manage severe asthma treatment

Continue to optimize management

### 7 Review response →

- Asthma: symptom control, exacerbations, lung function
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#### *If good response to Type 2-targeted therapy*

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- For oral treatments: consider decreasing/stopping OCS first, then stopping other add-on medication
- For inhaled treatments: consider decreasing after 3-6 months; continue at least moderate dose ICS
- Re-evaluate need for ongoing biologic therapy
- Order of reduction of treatments based on observed benefit, potential side-effects, cost and patient preference

yes →

#### *If no good response to Type 2-targeted therapy*

- Stop the biologic therapy
- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects, emotional support
- Consider high resolution chest CT (if not done)
- Reassess phenotype and treatment options
  - Induced sputum (if available)
  - Consider add-on macrolide\*
  - Consider add-on low dose OCS, but implement strategies to minimize side-effects
  - Consider bronchoscopy for alternative/additional diagnoses
  - Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies
- Do not stop ICS

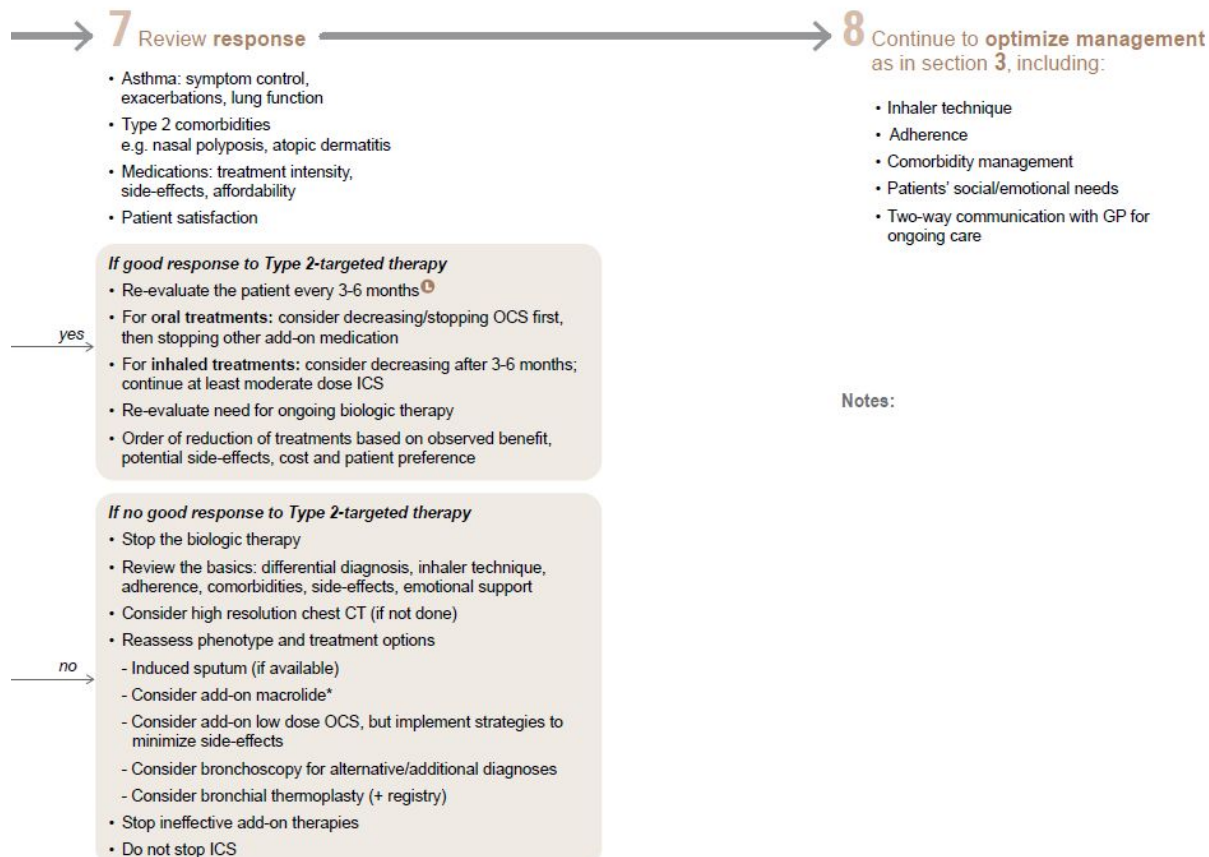
no →

\* Off-label



## Monitor / Manage severe asthma treatment

Continue to optimize management



Notes:

\* Off-label

# Severe Asthma Pocket Guide v2.0: key changes



- Section 5: “Could patient have Type 2 airway inflammation?”
  - Criteria for blood/sputum eosinophils and FeNO listed here are the lowest levels associated with good response to any of the included biologics
  - These are not the criteria for individual biologic therapies, which come later in the decision tree, and for which local regulator/payer criteria need to be checked
  - Addition of need for maintenance OCS, as this may have suppressed evidence of T2 inflammation
- Section 6b: Additional class of T2-targeted treatment: anti-IL4 receptor alpha (dupilumab)
  - For patients with severe eosinophilic asthma or need for maintenance OCS
- Section 6b: review response to initial trial of biologic
  - Consider increasing trial of biologic to 6-12 months if initial response is unclear
- Section 7: review response
  - Process of reviewing need for add-on therapy in patients with good and poor response to biologic therapy has been clarified