GINA Pocket Guide
Difficult to treat and severe asthma in adults and adolescents

V2.0 April 2019

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

Current severe asthma guidelines - 2014

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

Kian Fan Chung[1,2,21], Sally E. Wenzel[3,21], Jan L. Brozek[4], Andrew Bush[1,2], Mario Castro[5], Peter J. Sterk[6], Ian M. Adcock[1], Eric D. Bateman[7], Elisabeth H. Bel[6], Eugene R. Bleecker[8], Louis-Philippe Boulet[9], Christopher Brightling[10], Pascal Chanez[11], Sven-Erik Dahlen[12], Ratko Djukanovic[13], Urs Frey[14], Mina Gaga[15], Peter Gibson[16], Qutayba Hamid[17], Nizar N. Jajour[18], Thais Mauad[19], Ronald L. Sorkness[18] and W. Gerald Teague[20]

Chung et al, ERJ 2014

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

Terminology

- 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)

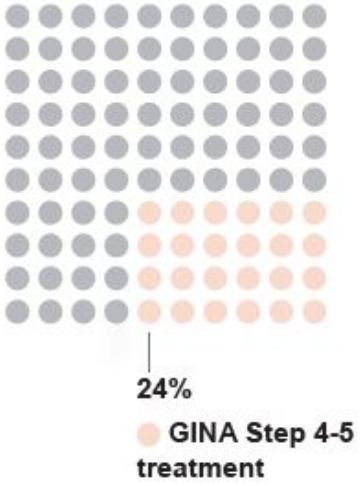
  A retrospective definition, dependent on how thoroughly contributory factors are excluded

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?

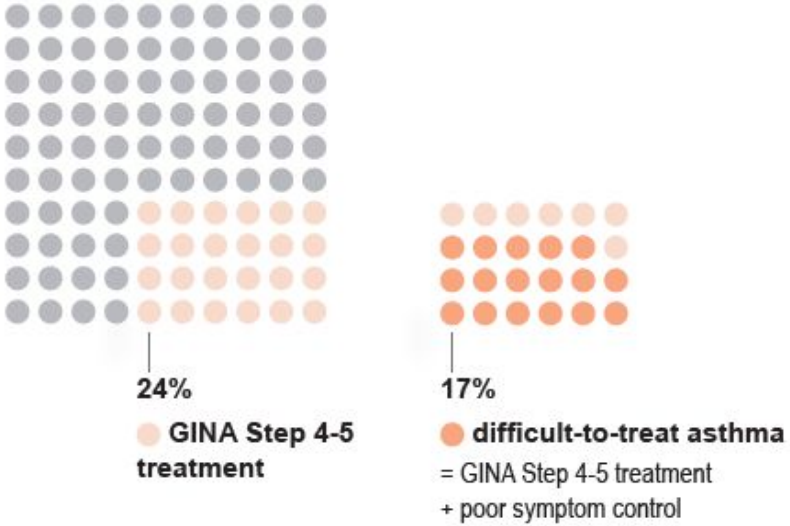
Box 1. What proportion of adults have difficult-to-treat or severe asthma?



These data are from a Dutch population survey of people ≥18 years with asthma[2]

How common is severe asthma?

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



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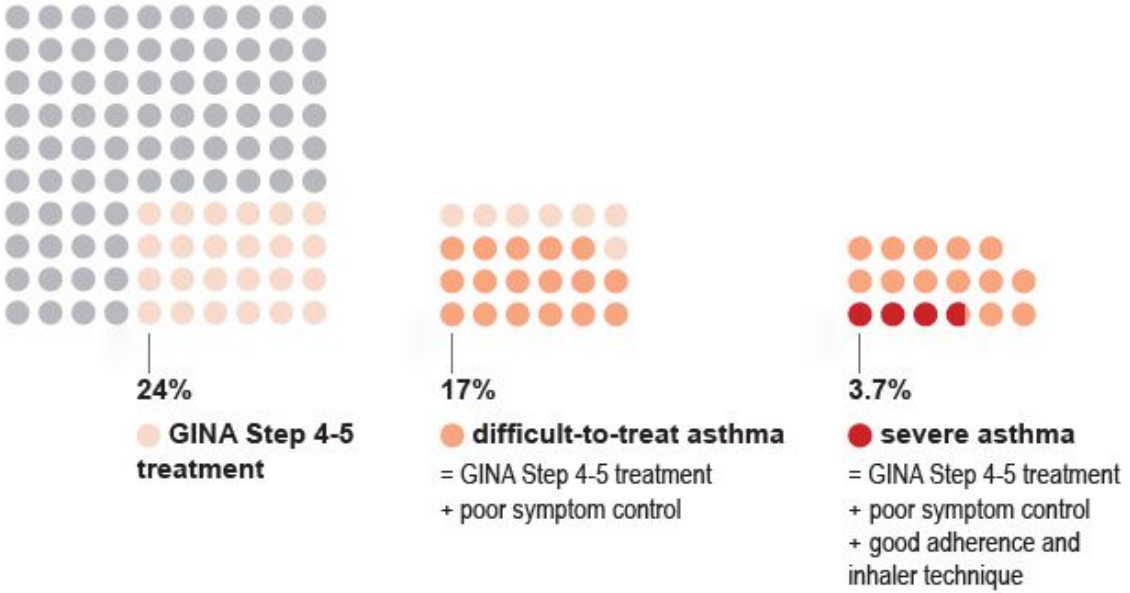

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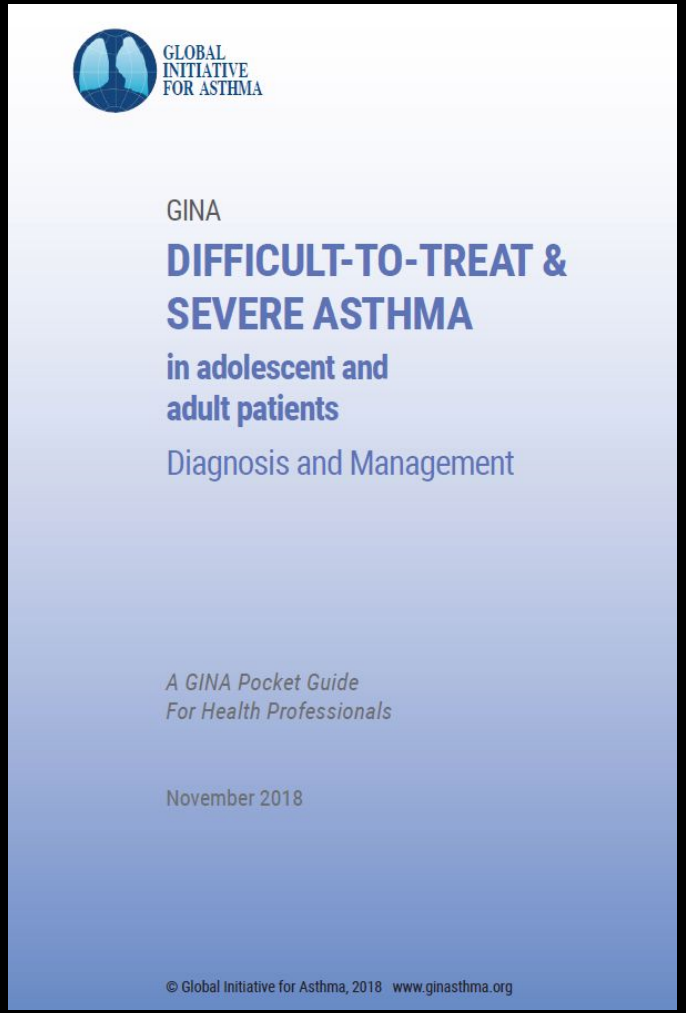
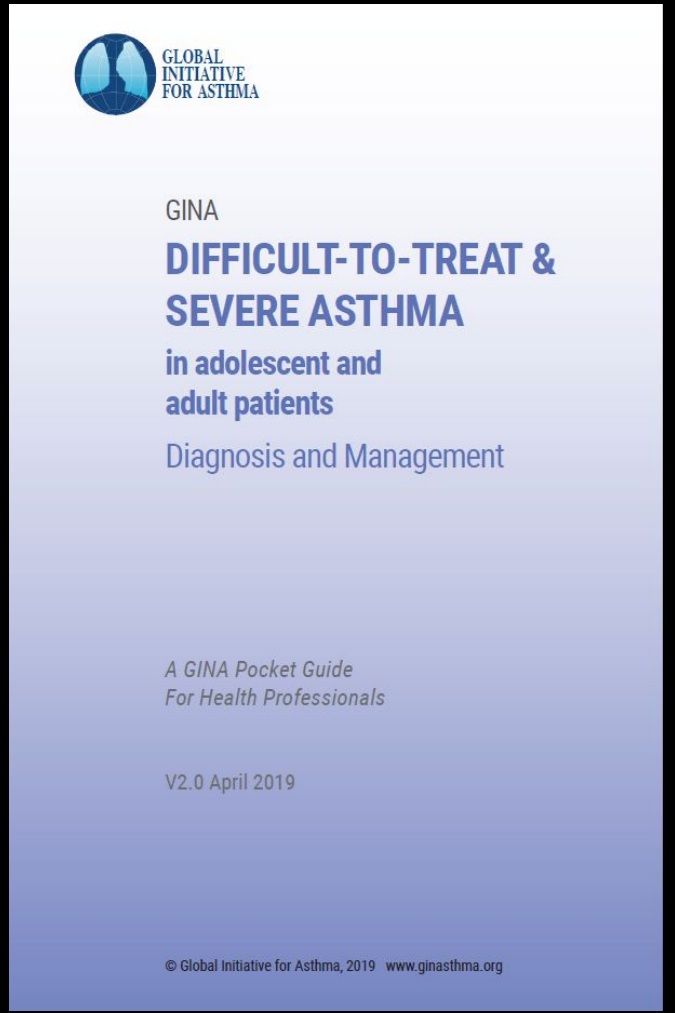




Team who developed pocket guide

- 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

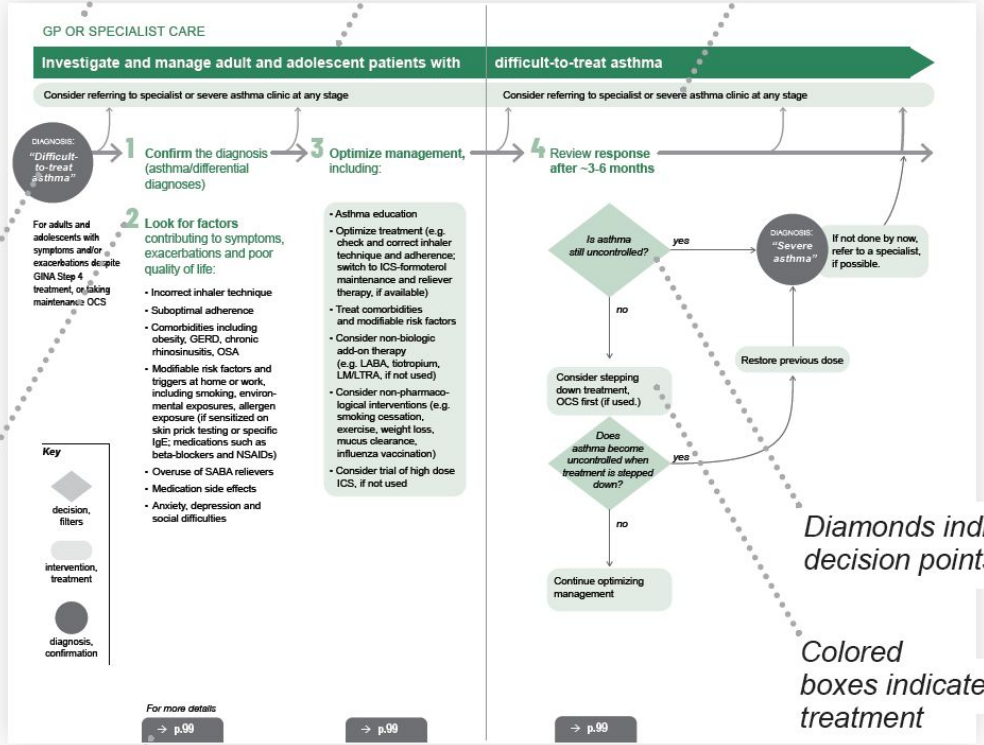
V2.0 published in April 2019

Table of Contents

Locus of care: GP or specialist

Overall aim of the sections on this double page

Reminders about ongoing issues



Circles indicate diagnosis

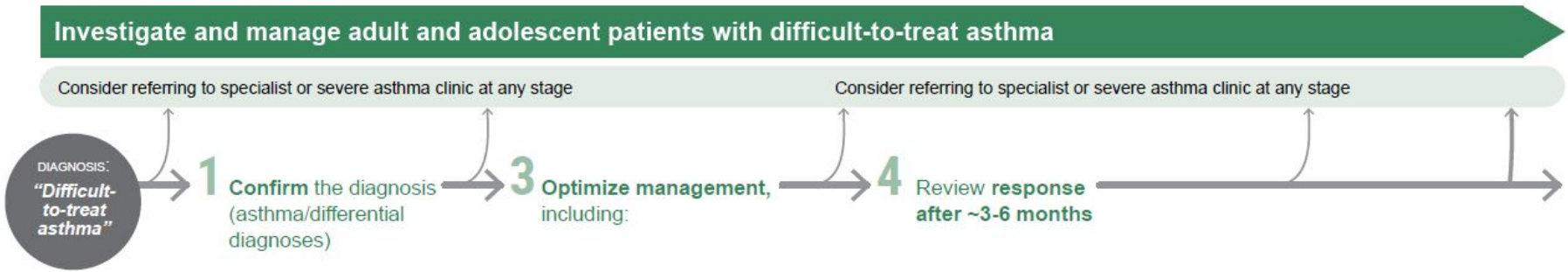
Key section of the decision tree, numbered

Diamonds indicate decision points

Colored boxes indicate treatment

Page number for more details

GP OR SPECIALIST CARE



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

7 Review **response** → 8 Continue to **optimize management**

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"

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

Key

decision, filters

intervention, treatment

GP OR SPECIALIST CARE

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

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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

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

Key

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- Overuse of SABA relievers
- Medication side effects
- Anxiety, depression and social difficulties

3 Optimize management, including:

- 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

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

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

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

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

- Incorrect inhaler technique
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- Comorbidities including obesity, GERD, chronic rhinosinusitis, OSA
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- 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

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

Is asthma still uncontrolled?

yes

DIAGNOSIS: *"Severe asthma"*

If not done by now, refer to a specialist, if possible.

no

Consider stepping down treatment, OCS first (if used.)

Restore previous dose

Does asthma become uncontrolled when treatment is stepped down?

yes

no

Continue optimizing management

Key

decision, filters

intervention, treatment

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

- ***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?	• Blood eosinophils ≥150/µl and/or • FeNO ≥20 ppb and/or • Sputum eosinophils ≥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)
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)***

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

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- Blood eosinophils ≥150/µl and/or
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- Sputum eosinophils ≥2%, and/or
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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

- 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)

no

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)

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

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(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

- 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, LM/LTRA, macrolide*)
- Consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

no

If no evidence of Type 2 inflammation:

- Review the basics: differential diagnosis, inhaler technique, adherence, comorbidities, side-effects
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Not currently eligible for biologics

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
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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)

Off-label

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

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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)

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

yes

- Consider adherence tests
- Consider increasing the ICS dose for 3-6 months
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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, LM/LTRA, macrolide*)
- Consider add-on low dose OCS, but implement strategies to minimize side-effects
- Stop ineffective add-on therapies

no

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

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Not currently eligible for biologics

*Off-label

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

- 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** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Check local eligibility criteria for specific biologic therapies as these may vary from those listed

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

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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
- Total serum IgE and weight within dosage range
- Exacerbations in last year

no / *no*

Anti-IL5 / Anti-IL5R

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

- Exacerbations in last year
- Blood eosinophils ≥300/µl

no / *no*

Anti-IL4R

*Is the patient eligible for **anti-IL4R***

… for severe eosinophilic/Type 2 asthma?

- Exacerbations in last year
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

Eligible for none?

Return to section **6a**

Check local eligibility criteria for specific biologic therapies as these may vary from those listed

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

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

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

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

- Blood eosinophils ≥260/µl ++
- FeNO ≥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
- Blood eosinophils ≥300/µl

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
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

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**

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SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

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- Exacerbations in last year
- Blood eosinophils ≥300/µl

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
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

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**

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

Good asthma response?

unclear → Extend trial to 6-12 months

yes → Good response to T2-targeted therapy

no

Check local eligibility criteria for specific biologic therapies as these may vary from those listed

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

- 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** 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
- Total serum IgE and weight within dosage range
- Exacerbations in last year

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

- Blood eosinophils ≥260/µl ++
- FeNO ≥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
- Blood eosinophils ≥300/µl

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
- Blood eosinophils ≥150/µl or FeNO ≥25 ppb

… or because of need for maintenance OCS?

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**

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

Good asthma response?

- *yes* → Good response to T2-targeted therapy
- *unclear* → Extend trial to 6-12 months
- *no* → **STOP add-on**: Consider switching to a different Type 2-targeted therapy, if eligible
  - *no* → Little/no response to T2-targeted therapy

Check local eligibility criteria for specific biologic therapies as these may vary from those listed

SPECIALIST AND PRIMARY CARE IN COLLABORATION

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

SPECIALIST AND PRIMARY CARE IN COLLABORATION

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

yes →

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

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

yes →

If good response to Type 2-targeted therapy

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- 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

no →

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

**Off-label*

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

yes →

- 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

If no good response to Type 2-targeted therapy

no →

- 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)
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  - Consider bronchoscopy for alternative/additional diagnoses
  - Consider bronchial thermoplasty (+ registry)
- Stop ineffective add-on therapies
- Do not stop ICS

*Off-label

8 Continue to **optimize management** as in section 3, including:

- Inhaler technique
- Adherence
- Comorbidity management
- Patients' social/emotional needs
- Two-way communication with GP for ongoing care

Notes:

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