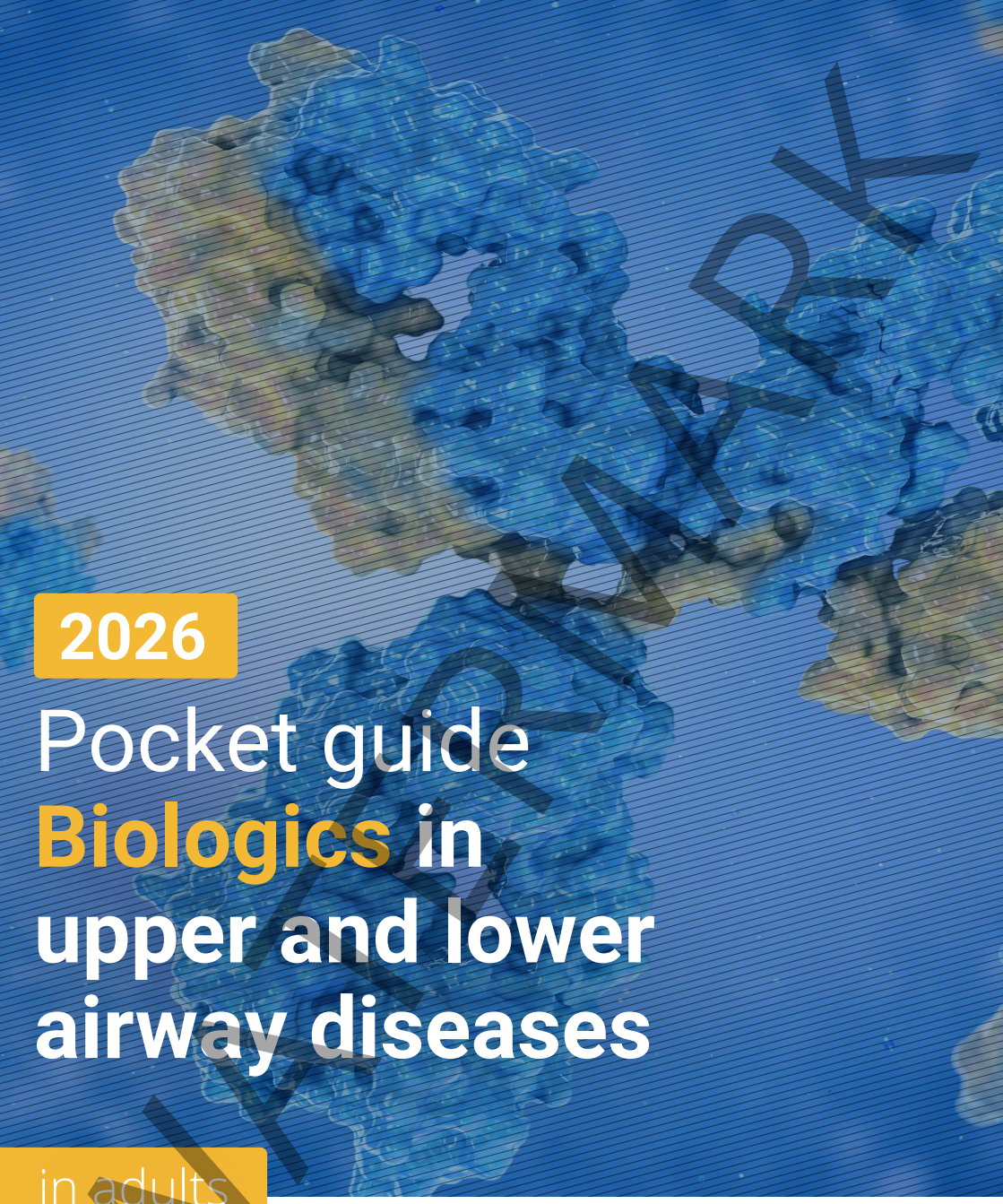


2026

Pocket guide **Biologics** in upper and lower airway diseases

in adults

DEVELOPED BY EUFOREA EXPERT TEAMS
BASED ON INTERNATIONAL GUIDELINES

EUFOREA

Biologics and their applications

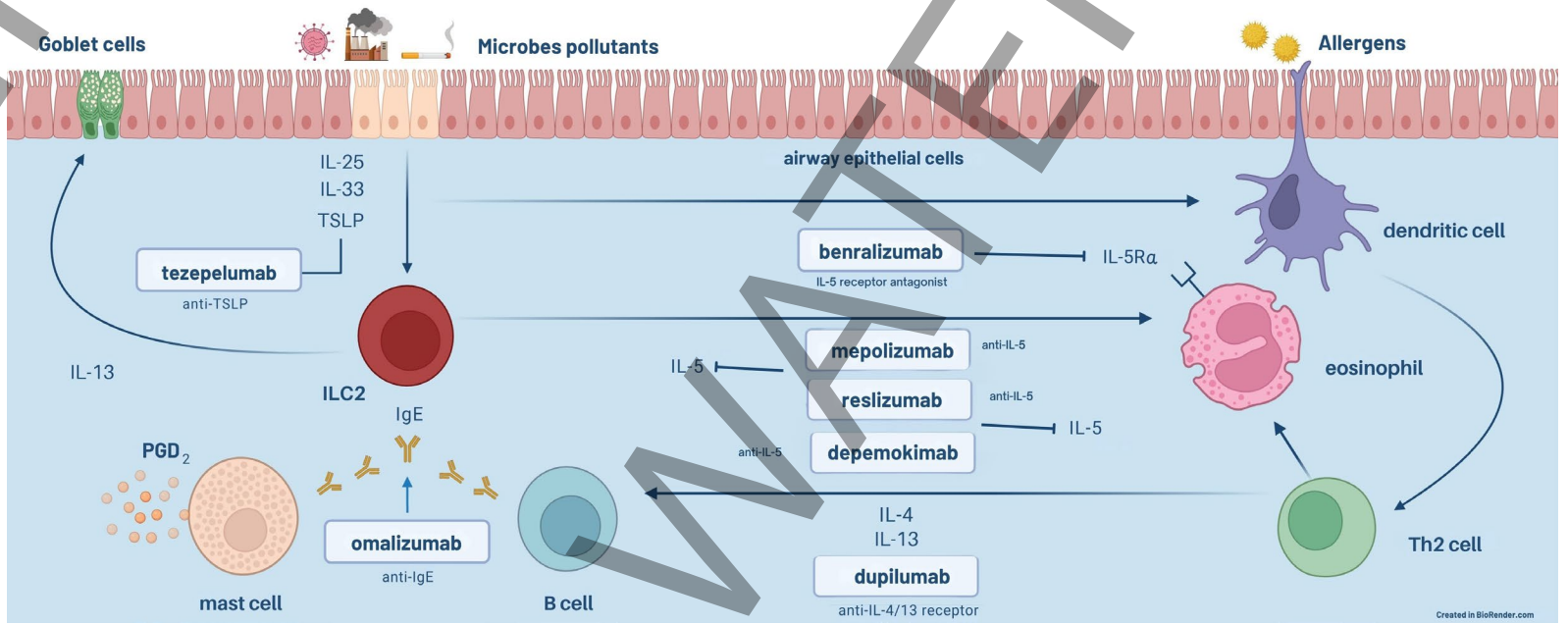
What are Biologics?

Biological therapeutics, also referred to as Biologics, are the class of medicines which are grown and then purified from large-scale cell cultures of bacteria or yeast, or plant or animal cells. In the context of Type 2 inflammatory diseases, biologics are targeted monoclonal antibodies that neutralize one or more type 2 inflammatory mediators or pathways in CRSwNP, asthma and/or eosinophilic COPD.

Key references:
EPOS/EUFOREA, Fokkens W. et al, *Rhinology* 2023, 61(3)
EPOS 2020, Fokkens W. et al, *Rhinology* 2020, 58 (S29)
GINA Strategy Report 2026, *Ginasthma.org*

Molecules	Target	Dose	Indication
Benralizumab	IL-5Rα	30 mg - SC / 4 - 8 wk	Asthma
Depemokimab	IL-5	100 mg – SC/ 6m	CRSwNP Asthma
Dupilumab	IL-4Rα/ IL-13	300 mg- SC / 2 wk	CRSwNP Asthma Eos COPD
Mepolizumab	IL-5	100 mg - SC / 4wk	CRSwNP Asthma Eos COPD
Omalizumab	IgE	Body weight and pre-treatment total IgE SC / 2-4wk	CRSwNP Asthma
Reslizumab	IL-5	3 mg/kg body weight i.v./4 wk	Asthma
Tezepelumab	TSLP	210 mg - SC / 4wk	CRSwNP Asthma

Mechanisms of action of biologics in type 2 inflammation



Diagnosis of Chronic Rhinosinusitis (CRS)

- ✓ **Two or more symptoms suggestive of CRS for ≥ 3 months**
  - Nasal congestion / obstruction
  - Nasal secretions (rhinorrhoea and/or post-nasal drip)
  - Smell loss (hyposmia or anosmia)
  - Facial pain / headache
- ✓ **Abnormalities at:**
  - Nasal endoscopy (polyps, purulence, mucosal edema)
  - OR CT scan of paranasal sinuses (Lund-Mackay score ≥ 4)
- ✓ **Markers of type 2 inflammation:**
  - Eosinophils in blood/tissue/secretions and IgE in blood

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Definitions in Chronic Rhinosinusitis (CRS)

- **Type 2 endotype in CRS:** CRS characterized by elevated blood eosinophils (≥150 cells/μL) or tissue eosinophils (≥10/HPF) or total IgE ≥100 IU/ml.
- **Chronic rhinosinusitis with nasal polyps (CRSwNP):** chronic rhinosinusitis as defined above and bilateral, endoscopically visualised polyps in middle meatus. Predominant type 2 endotype of CRS.
- **Chronic rhinosinusitis without nasal polyps (CRSsNP):** chronic rhinosinusitis as defined above and no visible polyps in middle meatus. Predominant non-type 2 endotype of CRS.

Diagnosis of Asthma

- ✓ **Suggestive clinical and/or family history of:**
  - Cough
  - Chest tightness
  - Shortness of breath
  - Wheezing
- ✓ **Lung function test (LFT): variable expiratory airflow limitation:**
  - FEV1 or FVC reversibility (to SABA)
  - PEF variability
  - Bronchial challenge test: Increased reactivity to direct or indirect stimuli (methacholine, mannitol, exercise, hypertonic saline)
- ✓ **Markers of inflammation:**
  - Blood/sputum eosinophils
  - FeNO

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Definitions in Asthma

- **Type 2-high asthma:** asthma characterized by type 2 inflammation. Common and if early onset, usually presents with either allergy with or without prominent eosinophilia or, if late onset, with non-allergic eosinophilic inflammation.
  - **Allergic asthma:** asthma in patients with sensitisation to allergens that trigger asthma symptoms
  - **High eosinophilic asthma:** adult-onset asthma with high blood eosinophils (≥500 cells/μL)
  - **Very high eosinophilic asthma:** ≥1000 cells/μL
- **Type 2-low asthma:** asthma characterised by the absence of high blood eosinophils and high FeNO after ruling out other chronic obstructive airway diseases.

Treatment of Chronic Rhinosinusitis (CRS)

- **Step 1: Basic (maintenance) treatment**
  - Saline rinses and/or nasal corticosteroid spray or drops or rinses
  - Identify treatable traits and treat accordingly
- **Step 2**
  - Add short-course oral corticosteroids and/or antibiotics
  - If no improvement: complete Endoscopic Sinus Surgery (ESS)
  - Re-identify treatable traits and treat accordingly
- **Step 3: Endo-typing by nasal endoscopy, blood tests and/or histology**
  - Type 2: biologics, revision surgery, steroid-eluting implants. In AERD, aspirin treatment after desensitization (ATAD) can be considered
  - Non-type 2: long-term antibiotics, revision surgery, xylitol, steroid-eluting implants

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Key definitions in CRSwNP

Well-controlled CRSwNP	Defined as the absence of bothersome CRS symptoms for ≥4 weeks with: VAS ≤ 4 for total CRS-related and individual symptoms (smell loss, nasal obstruction) AND/OR SNOT-22 score ≤20 (with individual nasal obstruction and smell scores <3) AND no use of systemic corticosteroids or need for sinus surgery in the preceding 12 months.
Uncontrolled CRSwNP	Patient-reported lack of control and the presence of clinically relevant sinonasal symptoms of active disease (defined as overall symptom severity, nasal obstruction and smell).
Clinical remission in CRSwNP (on or off treatment):	Defined as sustained disease control ≥12 months (on or off treatment) with all of the following: Control according to the above 'control' criteria AND absence of exacerbations AND absence of signs of active disease evaluated by nasal endoscopy: nasal polyp score of maximum 1 on each side and absence of coloured secretions and crusting.
Complete (pathophysiological) remission (on or off treatment):	Clinical remission of CRSwNP, including normal smell and inflammatory markers.
CRSwNP cure (off treatment):	Sustained remission off treatment for ≥ 5 years.

Treatment of Asthma

- **Step 1: Basic (maintenance) treatment:**
  - Standard care (ICS, ICS+LABA, LTRA)
  - Identify treatable traits and treat accordingly
- **Step 2:**
  - Adjust pharmacological treatment (increase ICS, add LABA/LAMA, LTRA, immunotherapy, long-term antibiotics, ATAD)
  - Re-identify treatable traits and treat accordingly
- **Step 3: Choose biologic based on phenotype/endotype**
  - Type 2-high asthma (anti-IL4R, anti-TSLP, anti-IL-5)
  - Allergic asthma (anti-IgE, SLIT)
  - Eosinophilic asthma (anti-IL5/IL5R, anti-TSLP)
  - Type 2-low asthma after ruling out other chronic obstructive airway diseases (anti-TSLP)

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Key definitions in asthma

Well- controlled asthma	Current control of asthma symptoms (i.e. no daytime asthma symptoms and no night wakening due to asthma and no need for reliever medication and no activity limitation) PLUS low future risk of adverse outcomes.
Uncontrolled asthma	Persistent asthma symptoms (3-4 of the following: frequent daytime asthma symptoms, night wakening due to asthma, frequent need for reliever medication, activity limitation) OR history of ≥2 mild-to-moderate or ≥1 severe exacerbation in the previous year.
Clinical remission in asthma (on treatment):	Long-term well-controlled asthma without asthma symptoms, without exacerbations, without use of (maintenance or burst) systemic corticosteroids and stable or improving lung function.
Complete (pathophysiological) remission (on or off treatment):	Clinical remission of asthma, also including normal or stabilized lung function, normalization of airway responsiveness and/or inflammatory markers.
Asthma cure off treatment):	Long-term complete remission of asthma, off treatment.

What to discuss with the patient?

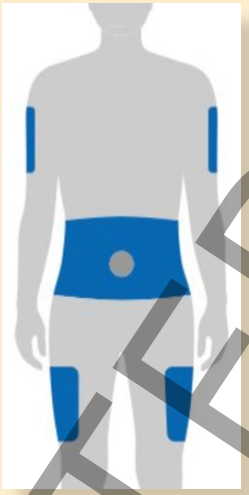
- Add-on treatment to maintenance therapy
- Treatment is a regular self-injection (for dosing, see previous figure in this pocket guide)
- Onset effect can be in weeks – months, often progressive
- Potential local and general adverse events
- When to alert the health care professional
- Treatment has to be taken long-term but sometimes interval between injections can be prolonged on indication

The first injection(s)

- Most biologics come with an auto-injector
- Administration under medical supervision for the first two injections is required for omalizumab because of training and small risk of anaphylaxis.
  For other available biologics, home initiation is acceptable.

How to train the patient?

- ☐ Prepare the medication
- ☐ Wash hands thoroughly and use an alcohol wipe to clean the injection site
- ☐ Inject under skin in abdomen, thigh, or upper arm with auto-injector or with pre-filled syringe



Sites of subcutaneous injection

What should the physician do when considering a biologic?

General considerations (CRSwNP & Asthma)

- ☐ Re-evaluate the diagnosis
- ☐ Define the severity of disease
- ☐ Define the level of disease control
- ☐ Evaluate the impact on quality of life
- ☐ Review previous therapies, adherence, technique and treatable traits
- ☐ Assess history of allergies and type 2 comorbidities
- ☐ Skin prick testing or specific IgE in case of suspicion of sensitization
- ☐ Endotype the disease (blood/tissue eosinophils and total/specific IgE)
- ☐ Consider sampling of mucus/tissue for inflammatory profiling

CRSwNP-specific considerations

- ☐ Perform nasal endoscopy including nasal polyp scoring
- ☐ Assess olfactory function
- ☐ Recent (<5y) imaging (CT/MRI) of the paranasal sinuses

Asthma-specific considerations

- ☐ Perform lung function testing (spirometry ± bronchodilator reversibility)
- ☐ Measure FeNO
- ☐ Consider bronchial provocation testing if indicated
- ☐ Consider additional imaging for excluding pulmonary comorbidities (e.g. bronchiectasis)

Indications for Biologics*

CRSwNP

≥ 3 out of 5 of the criteria below in patients that had at least one sinus surgery (or cannot be operated)

1/ Evidence of type 2 inflammation (blood eosinophil ≥ 150 cells/µL or tissue eosinophilia ≥ 10/hpf)

2/ Need for systemic corticosteroids or contraindication to systemic corticosteroids

3/ Significant impaired quality of life

4/ Significant loss of smell

5/ Diagnosis of comorbid asthma

ASTHMA / COPD

Uncontrolled severe asthma/unstable COPD with recurrent exacerbations and type 2 inflammation

Blood eosinophil ≥ 150 cells/µL (for COPD > 300 cells/µL) (all but omalizumab)

Need for systemic corticosteroids or contraindication to systemic corticosteroids

Sensitization to inhaled perennial allergens (omalizumab)

***Today there are no indications for biologics for patients with non-type 2 CRS or allergic rhinitis but they are expected in the coming years.**

Reimbursement of biologics depends on the local situation.

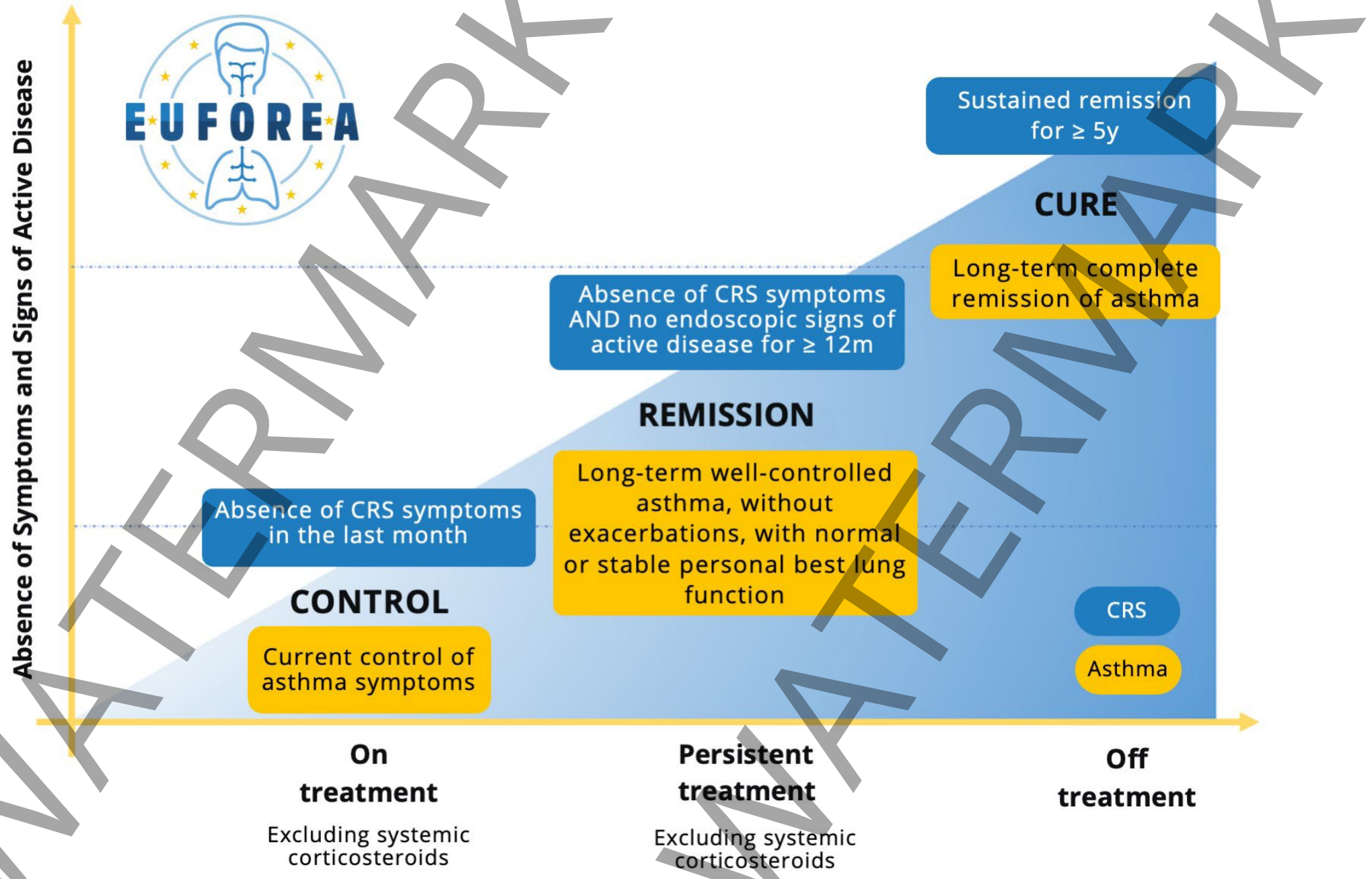
Click here for CRS Pocket Guide OR scan above QR code

Click here for Asthma Pocket Guide OR scan above QR code

Biologics in airway diseases

	Chronic Rhinosinusitis with nasal polyps (CRSwNP)	Asthma	CRSwNP & Asthma
	Educate patient about chronicity and severity of disease, need for optimal adherence and avoidance of infectious, occupational, and environmental triggers e.g. by wearing a mask		
	For all diseases give basic maintenance therapy		
Indication for biologic	**Patients with CRSwNP and a history of sinus surgery, with ≥ 3 of 5 criteria:** • Evidence of type 2 inflammation • Need for systemic corticosteroids or contraindication to systemic corticosteroids • Significantly impaired quality of life • Significant loss of smell • Co-morbid asthma	**Patients with poor asthma control** • Asthma symptoms despite ICS/LABA • Interference with daily activity and/or sleep • Chronic OCS use • At least 2 exacerbations in prior year	**Patients with CRSwNP & asthma** • Most patients with CRSwNP and asthma have type 2 disease • Indication based on CRSwNP and/or asthma
Choice of biologics Based on network meta-analysis and/or expert opinion	• Dupilumab, mepolizumab, omalizumab and tezepelumab have demonstrated efficacy • Dupilumab shows the most pronounced benefit in the available real-world data • Mepolizumab: consider in patients with co-morbid hypereosinophilic disease • Pregnancy: omalizumab has the most safety experience	• Type 2-high asthma: dupilumab, tezepelumab, benralizumab, mepolizumab, reslizumab and depemokimab • Allergy-driven asthma: omalizumab, consider dupilumab and tezepelumab • Hypereosinophilic disease: mepolizumab, reslizumab, benralizumab, tezepelumab or depemokimab • Type 2 –low asthma: tezepelumab • Pregnancy: omalizumab has the most safety experience	• Type 2 disease: dupilumab, mepolizumab, omalizumab and tezepelumab have demonstrated efficacy • Hypereosinophilic disease: mepolizumab, tezepelumab • Pregnancy: omalizumab has the most safety experience
Real life experience	• Excellent effect on QOL and relevant signs and symptoms • Rescue OCS or surgery seldom needed • Significant percentage achieve control and clinical remission	• Excellent effect on QOL and relevant signs and symptoms including exacerbations, variable effect on lung-function • Significantly reduced OCS need • Significant percentage achieves control and a third clinical remission	• Excellent effect on QOL and relevant signs and symptoms including exacerbations, lung-function • Rescue OCS or surgery seldom needed
Comorbidities	**Consider evaluating (type-2) comorbidities such as allergies/ eosinophilic otitis media/AERD, atopic dermatitis /eosinophilic oesophagitis/eosinophilic COPD**		

PATIENT PARTICIPATION IN TREATMENT PLAN



Recommendation for follow-up of patients on biologics

Timepoint	CRSwNP	Asthma
Baseline	- History (symptoms, severity, SNOT-22/VAS) - Disease control - Nasal endoscopy - Blood/tissue eosinophils - Smell test - Allergy test if indicated	- History (symptoms, severity, exacerbations) - Disease control - Lung function - Blood/sputum eosinophils + FeNO - Allergy test if indicated
3 months	- History (symptoms, severity, SNOT-22/VAS, AE) - Disease control - Nasal endoscopy - Monitor blood eosinophilia (only with dupilumab)	- History (symptoms, exacerbations, AE) - Disease control - Lung function + FeNO - Monitor blood eosinophilia (only with dupilumab)
6 months	- History (symptoms, severity, SNOT-22/VAS, AE) - Disease control - Nasal endoscopy - Monitor eosinophilia (only with dupilumab in case of persistent high value) - Assess therapeutic response	- History (symptoms, exacerbations, AE) - Disease control - Lung function + FeNO - Monitor eosinophilia (only with dupilumab in case of persistent high value) - Assess therapeutic response
12 months - 18 months *(based on clinical severity)*	- History (symptoms, severity, SNOT-22/VAS, AE) - Nasal endoscopy - Assess disease control/remission criteria - Assess therapeutic response	- History (symptoms, exacerbations, AE) - Lung function + FeNO - Assess disease control/remission criteria - Assess therapeutic response
24 months – annual follow-up	- History (symptoms, severity, SNOT-22/VAS, AE) - Nasal endoscopy - Disease control/remission criteria	- History (symptoms, exacerbations, AE) - Lung function + FeNO - Disease control/remission criteria

Personalized follow-up	- Assess therapy adherence, spray technique, comorbidities
	- In case of uncontrolled CRSwNP or AEs:
	  - Reconsider diagnosis and treatable traits
	  - CT-scan
	  - Switching biologic or salvage/revision surgery
	  - Discontinue biologic if indicated
		- Assess therapy adherence, inhaler technique, comorbidities
		- In case of uncontrolled asthma or AEs:
		  - Reconsider diagnosis and treatable traits
		  - CT-scan
		  - Consider switching biologic
		  - Discontinue biologic if indicated

Additional Resources:

CRS pocket guide

Asthma pocket guide

Biologics: How to inject a pre-filled pen?

Biologics: How to inject a pre-filled syringe?

EUFOREA patient portal

EUFOREA E-Academy

Abbreviations

ACQ:	Asthma control questionnaire
ACT:	Asthma Control Test
AD:	Atopic dermatitis
AE:	Adverse event
AERD:	Aspirin-exacerbated respiratory disease
ATAD:	Aspirin treatment after desensitisation
COPD:	Chronic obstructive pulmonary disease
CRS:	Chronic rhinosinusitis
CRSwNP:	Chronic rhinosinusitis with nasal polyps
CT:	Computed tomography scan
EPOS:	European Position Paper on Rhinosinusitis and Nasal Polyps
ESS:	Endoscopic sinus surgery
FeNO:	Fraction of exhaled nitric oxide
FEV1:	Forced expiratory volume in one second
FVC:	Forced vital capacity
HPF:	High power field
ICS:	Inhaled corticosteroids
LABA:	Long-acting beta-agonist
LFT:	Lung function test
LTRA:	Leukotriene antagonists
NE:	Nasal endoscopy
NP:	Nasal polyps
NSAID:	Non-steroidal anti-inflammatory drugs
PEF:	Peak expiratory flow
OCS:	Oral corticosteroids
QOL:	Quality of life
SABA:	Short-Acting Beta Agonist
SC:	Subcutaneously
SNOT-22:	Sinonasal outcome test

The nature of pocket guides by reason of their brevity, should not be considered completely inclusive or exclusive. Further information can be sought in the appropriate guidelines/statements.

Vision

The vision of EUFOREA is that chronic respiratory diseases are preventable through multidisciplinary collaboration on optimal care strategies, involving all stakeholders in the respiratory field.

Mission

The mission of EUFOREA is to reduce the prevalence and burden of chronic respiratory diseases via innovative care strategies including prevention.

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