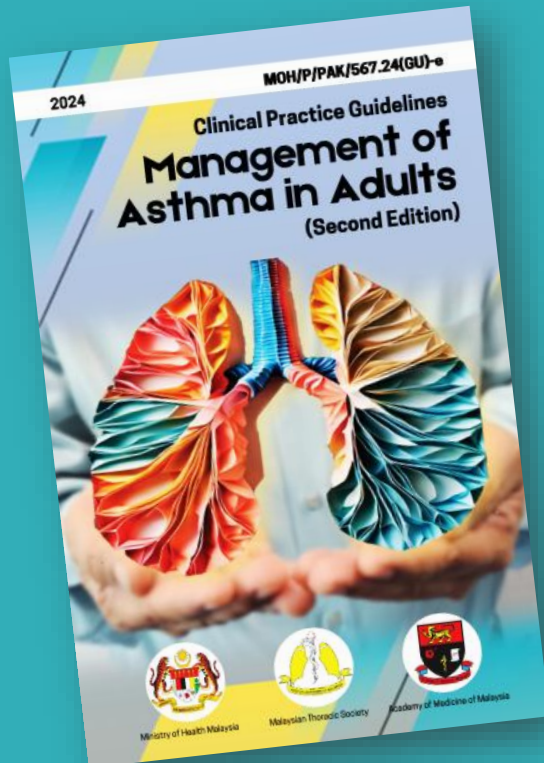


TRAINING OF CORE TRAINERS ON CPG

MANAGEMENT OF ASTHMA IN ADULTS (SECOND EDITION)



LECTURE 3

Stable Asthma – Assessment and Treatment

Dr. Aisya Natasya Musa
Respiratory Physician
Universiti Teknologi MARA (UiTM)



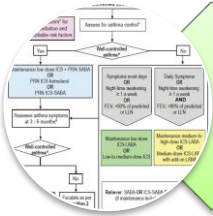
Learning Objectives



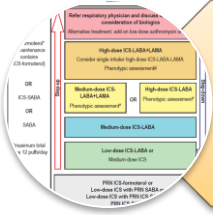
Pharmacological treatment in stable asthma



Non-pharmacological treatment in stable asthma



Initiating treatment in asthma



Stepping-up and stepping-down of treatment

Treatment of Stable Asthma



Reliever therapy = taken as needed for QUICK RELIEF of asthma symptoms

Maintenance targets asthma symptom control and prevents exacerbation.

It is used on a regular basis, even when asthma symptoms are absent.

Pharmacological

- Reliever therapy
 - i. SABA
 - ii. AIR
 - iii. LABA
- Maintenance therapy
 - i. ICS
 - ii. ICS/LABA
 - iii. MART
 - iv. LTRA
 - v. Methylxanthine
 - vi. LAMA
 - vii. Macrolides
 - viii. OCS
 - ix. SLIT

Non-pharmacological

- Smoking cessation
- Supplements - Vitamin D
- Physical activity & exercises
- Pulmonary Rehabilitation
- Dietary modification
- Weight reduction
- Allergen avoidance
- Vaccination
- Medication to use with caution



Pharmacological Therapy

Reliever Therapy



Short Acting
 β 2-agonist
(SABA)

Anti-
inflammatory
Reliever (AIR)

Long Acting
 β 2-agonist
(LABA)

Reliever Therapy - SABA



- **EXCESSIVE SABA (≥ 3 200-dose canisters a year) = RISK OF ASTHMA EXACERBATION AND MORTALITY**
- **Inhaled SABA should NOT BE USE AS MONOTHERAPY.**
- Monotherapy use is associated with:
 - Decreased bronchodilator response
 - Increased airway hyperresponsiveness
- Inhaled SABA may be use as a reliever with regular inhaled corticosteroids.
- No additional advantage of combination with short-acting muscarinic antagonists
- **ORAL SABA NOT RECOMMENDED DUE TO HIGHER SIDE EFFECTS**



Reliever Therapy – Anti-inflammatory Reliever



- Anti-inflammatory reliever (AIR) contains both low-dose inhaled corticosteroids (ICS) and short or fast-acting bronchodilator
- **AIR therapy (either ICS with formoterol or ICS with SABA) may be used as reliever therapy**
- Cochrane systematic review in mild asthma AIR (budesonide-formoterol inhaler) vs regular ICS (budesonide + SABA PRN)²⁴
 - No significant differences in exacerbation
 - Asthma control better in regular ICS group (but did not reach MCID 0.5)
 - FENO higher in budesonide-formoterol group

Reliever Therapy – Long Acting β 2-Agonists



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- **LABA USE WITHOUT ICS IS STRONGLY DISCOURAGED** due to risk of fatal and non-fatal adverse events.^{3,26}

3. MoH, Malaysia. Clinical Practice Guidelines Management of Asthma in Adults. Putrajaya: MoH; 2017

26. SIGN & BTS. British guideline on the management of asthma. UK: SIGN-BTS; 2019

Maintenance Therapy



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Inhaled
Corticosteroids
(ICS)

ICS-LABA
combination

Maintenance and
reliever therapy
(MART)

Leukotriene
Receptor
Antagonist
(LTRA)

Methyl-
xanthines

Long-Acting Anti-
Muscarinic
(LAMA)

Macrolides

Oral
Corticosteroids

Sublingual
Immunotherapy
(SLIT)

Maintenance Therapy – Inhaled Corticosteroids



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- Significantly reduces asthma symptoms, risk of asthma-related exacerbations, hospitalisation and death.
- ICS dosage can be categorised into low-, medium-, or high-dose
- Switching ICS within a category may change asthma control as different ICS may differ in potency
- Systemic side effects may occur with high doses and long-term use of ICS. E.g. osteoporosis, cataracts, glaucoma and adrenal suppression

Maintenance Therapy – Inhaled Corticosteroids



Inhaled corticosteroids (alone or in combination with LABA)	Total daily ICS dose (µg)		
	Low	Medium	High
Beclometasone dipropionate (pMDI, standard particle, HFA)	200 - 500	>500 - 1000	>1000
Beclometasone dipropionate (DPI or pMDI, extrafine particle, HFA)	100 - 200	>200 - 400	>400
Budesonide (DPI, or pMDI, standard particle, HFA)	200 - 400	>400 - 800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80 - 160	>160 - 320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100 - 250	>250 - 500	>500
Fluticasone propionate (pMDI, standard particle, HFA)	100 - 250	>250 - 500	>500
Mometasone furoate (DPI)	Depends on DPI device - refer to product information		
Mometasone furoate (pMDI, standard particle, HFA)	200 - 400		>400

Examples :

Salmeterol/fluticasone propionate

25/125 µg 1 puff BD

= 125 µg x 1 puff x 2

= 250 µg total daily fluticasone propionate

= Low dose ICS

Budesonide/formoterol 160/4.5µg 2 puff BD

= 160 µg x 2 puffs x 2

= 640 µg total daily budesonide

= Medium dose ICS

Maintenance Therapy – ICS and LABA Combination



- Indication : Asthma patients who remain **symptomatic** despite good adherence & inhaler technique to **regular daily low-dose ICS or as-needed ICS-formoterol**
- **Combination of ICS-LABA is preferred to high dose ICS during stepping-up of treatment** - More effective in reducing exacerbation than high dose ICS alone³
- Proactive regular dosing (PRD) = medication taken at scheduled consistent interval.
- PRD compared to PRN budesonide-formoterol or ICS & SABA PRN significantly²⁷:
 - improve symptom control
 - reduced hospitalisation & systemic corticosteroids use

3. MoH, Malaysia. Clinical Practice Guidelines Management of Asthma in Adults. Putrajaya: MoH; 2017

27. Ismail AI, et al. Pulm Ther. 2025;11(1):25-40.

Maintenance Therapy – ICS and LABA Combination



- No safety concerns between choice of salmeterol-ICS and formoterol-ICS combination²⁸
- No significant difference between extra-fine beclomethasone-formoterol and non-extrafine ICS-LABA in²⁹:
 - pulmonary function
 - ACT scores
 - Exacerbation rates

28. O'Shea O et al. Cochrane Database Syst Rev. 2021;4(4):CD007694.

29. Liu T, et al. PloS one. 2021;16(9):e0257075.

Maintenance Therapy – Maintenance and Reliever Therapy (MART)



- MART = daily use of ICS-formoterol inhaler for asthma maintenance and as-needed for symptom relief
- **In moderate to severe asthma, either low-to-medium dose MART or high-dose ICS/LABA plus as-needed SABA may be used**
- Evidence of MART in preventing risk of severe asthma exacerbation³⁰:
 - In mild to moderate asthma : low-dose MART was more effective than ICS-LABA and ICS with as-needed SABA
 - In moderate to severe asthma : low-to-medium dose MART is :
 - Equally effective compared to high-dose ICS-LABA + PRN SABA
 - More effective compared to low-to-medium dose ICS-LABA + PRN SABA and ICS + PRN SABA

MAINTENANCE THERAPY –

Leukotriene receptor antagonists (LTRA)



- LTRA as monotherapy is less effective than ICS for symptoms control, long function improvement and exacerbations^{2,3}
- LTRA may be added to ICS-containing therapy in patients with allergic asthma
- Evidence³¹:
 - Addition of LTRAs compared to same dose ICS alone – reduce exacerbation risk requiring rescue OCS, improved lung function and asthma control
 - Combination therapy of LTRA and ICS vs. higher dose ICS alone – no significant difference in exacerbation
- CAUTION: neuropsychiatric adverse effects – new-onset nightmares, behavioural changes & suicidal ideation³²

2. GINA. Global Strategy for Asthma Management and Prevention (2024 update). 2024

3. MoH, Malaysia. Clinical Practice Guidelines Management of Asthma in Adults. Putrajaya: MoH; 2017

31. Chauhan BF, et al. Cochrane Database Syst Rev. 2017;3(3):CD010347.

32. US FDA. Drug Safety Communications

MAINTENANCE THERAPY – Methylxanthine



- **Theophylline should not be used for treatment of asthma** – limited effectiveness and potentially life-threatening side effects at higher doses^{2,33}
- Doxofylline, a newer immediate-released methylxanthine, has been shown to have better effectiveness and fewer side-effects
- Doxofylline compared to theophylline and placebo³⁴:
 - reduce daily asthma events
 - Safer with lower risk of AEs
- Doxofylline in pre-post study improve FEV1 from baseline and reduce asthma events³⁵

2. GINA. Global Strategy for Asthma Management and Prevention (2024 update). 2024

33. Plaza Moral V, et al. Spanish Guideline on the Management of Asthma. Open Respir Arch. 2023;5(4):100277.

34. Rogliani P, et al. Multidiscip Respir Med. 2019;14:25.

35. Calzetta L, et al. PulmcPharmacol Ther. 2020;60:101883.

Maintenance Therapy – Long-Acting Muscarinic Antagonists (LAMA)



- LAMAs may be considered as add-on therapy to medium or high-dose ICS-LABA
- **Triple therapy (ICS/LABA/LAMA) should be used** (separate inhaler or combination) **in patients with uncontrolled asthma despite treatment with medium-to-high dose ICS/LABA**
- In moderate to severe asthma, medium-dose or high-dose triple therapies vs. medium-high dose ICS-LABA³⁸:
 - reduced risk if severe exacerbation
 - Improved asthma control

Maintenance Therapy – Macrolides



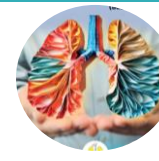
- Macrolides is an antibacterial with immunomodulatory properties which can reduce airway hyperactivity and eosinophilic inflammation
- Comparing macrolides with placebo – reduced symptoms and exacerbations requiring ED visits or systemic corticosteroids³⁹
- Long-term macrolides should be part of a comprehensive personalised asthma management plan and should only be started after consultation with a specialist

Maintenance Therapy – Oral Corticosteroids (OCS)



- Last resort for patients with severe asthma – use minimum necessary dose and for the shortest time
- OCS stewardship – minimise use of OCS and mitigate harm associated with use⁴⁰

Maintenance Therapy – Sublingual Immunotherapy (SLIT)



- SLIT involves administering allergen extracts to desensitise and decrease sensitivity to specific allergen trigger in patients with allergy
- Allergen immunotherapy in allergic asthma is advised to be administered by experienced specialists, when there is clinical evidence of IgE-mediated sensitisation to common airborne allergens³³



Non-Pharmacological Therapy

Non-Pharmacological Treatment



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Smoking
cessation

Vitamin D

Physical Activity

Breathing
exercise & Yoga

Pulmonary
rehabilitation

Dietary
Modification

Weight
Reduction

Vaccination

Medication to
use with caution

Non-pharmacological Treatment – Smoking cessation



- Asthma patients who smoke are at^{2,3,42} :
 - Higher risk of adult-onset asthma
 - Affects airway inflammation
 - Reduces response to corticosteroids therapy
 - Poorer disease control
- **Asthma patients who smoke or vape should be strongly encouraged to quit** at every clinic visit and be provided access to counselling and smoking cessation programmes

2. GINA. Global Strategy for Asthma Management and Prevention (2024 update). 2024

3. MoH, Malaysia. Clinical Practice Guidelines Management of Asthma in Adults. Putrajaya: MoH; 2017

42. Thomson NC, et al. J Allergy Clin Immunol Pract. 2022;10(11):2783-97.

Non-Pharmacological Treatment – Vitamin D



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- Improve asthma control in patients with vitamin D deficiency^{2,43,44}
- Cochrane review – did not reduce asthma exacerbation or improve asthma control in mild to moderate asthma⁴⁵

43. Andújar-Espinosa R, et al. Thorax. 2021;76(2):126-33.

44. Camargo CA, et al. Nutrients. 2021;13(2).

45. Williamson A, et al. Cochrane Database Syst Rev. 2023;2(2):CD011511.

Non-Pharmacological Treatment – Physical activity



- **Physical activities should be encouraged in asthma patients**
- Improve cardiopulmonary effectiveness and should be promoted as part of general approach to improving lifestyle and rehabilitation
- No specific recommendation for type of exercise²
- Regular physical activity enhance cardiopulmonary fitness leading to improved asthma and QoL
- Careful consideration of potential EIB² – patient can exercise with triggering asthma symptoms with proper treatment

Non-Pharmacological Treatment – Breathing exercise



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- Involve techniques taught by physiotherapists complementary to medication
- No impact on lung function or asthma exacerbation²
- Improve QoL^{2,47}, alleviate dyspnoea and reduce emotional stress⁴⁷

Non-Pharmacological Treatment – Yoga



- Yoga includes physical postures, breathing exercises, meditation and relaxation techniques
- Offer improvement in⁴⁹:
 - Pulmonary function test (PEFR, FEV₁, FVC)
 - Health related QoL
- Yoga may be considered as supplementary therapy or an alternative to other types of breathing exercises²

Non-Pharmacological Treatment – Pulmonary Rehabilitation (PR)



- PR is a comprehensive multifaceted patient assessment and personalised therapy includes supervised exercise training, education sessions and behaviour modification strategies
- PR goal is to improve both physical and psychological conditions
- PR in asthma results in improvement on exercise performance, asthma control⁵⁰ and QoL²
- **Refer asthma patient to a pulmonary rehabilitation programme if available²**

Non-Pharmacological Treatment – Dietary Modification



- Consumption of a diet high in fruits and vegetables can significantly reduce lung function decline hence improve asthma control and reduce risk of exacerbations²
- High sodium intake is associated with increased bronchial hyper-responsiveness²⁶
- Omega-3 (fish oils) may reduce inflammation and lessen severity of exacerbation²⁶

Non-Pharmacological Treatment – Weight Reduction



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- Weight loss interventions including dietary and exercise programmes should be recommended for overweight and obese adults with asthma to enhance asthma control²⁶

Non-Pharmacological Treatment – Vaccination



- Influenza vaccination reduces influenza infection and exacerbations resulting in hospitalisation or ED visit
- Pneumococcal vaccination recommended for patients who require maintenance corticosteroids or frequently repeated systemic corticosteroids⁵²
- Vaccination in adults with asthma should follow local immunisation schedule²

Non-Pharmacological Treatment – Medication to be Used with Caution

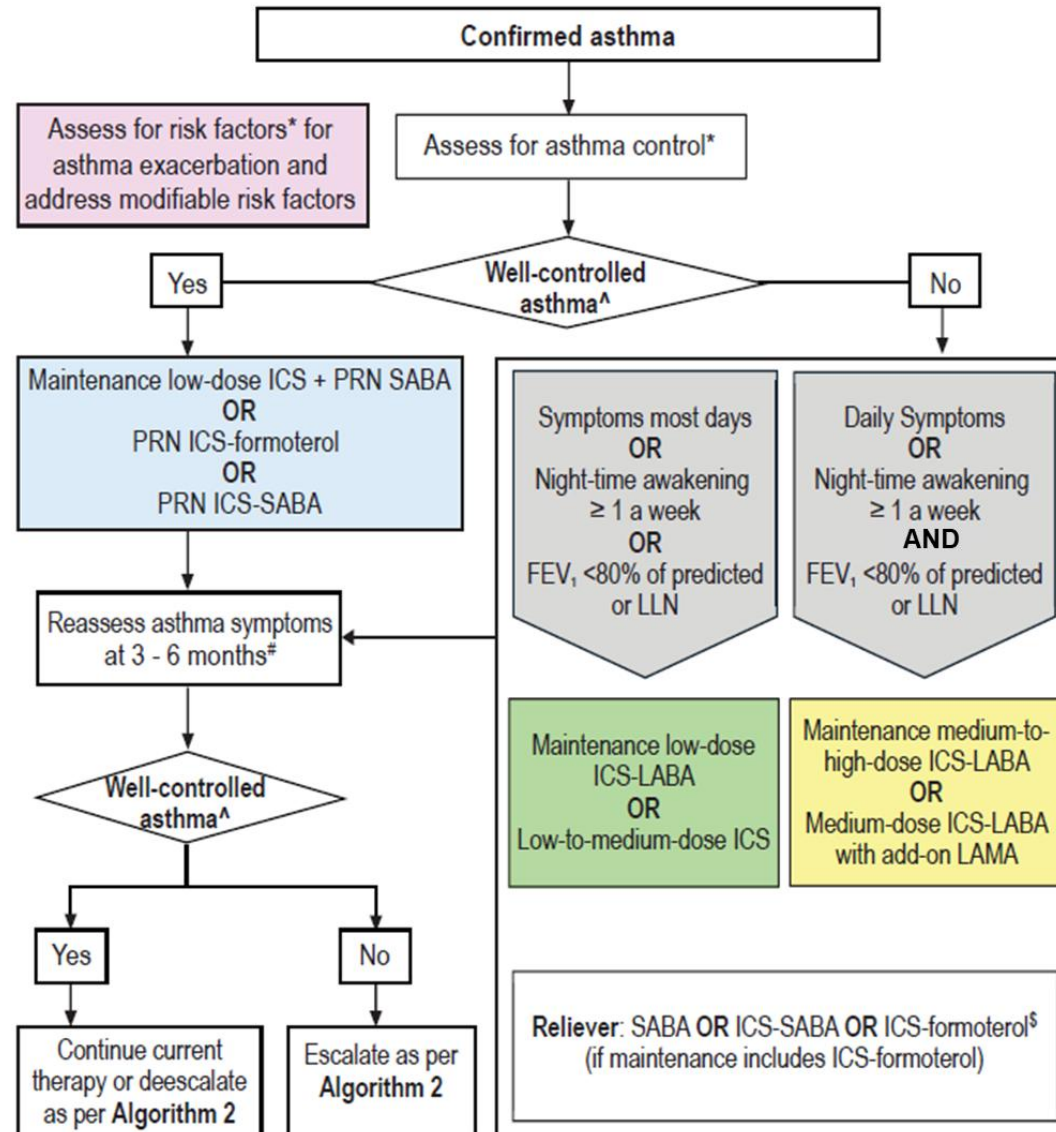


- Aspirin & Non-steroidal anti-inflammatory drugs
 - Not contraindicated unless there is a history of adverse reactions
 - If NSAIDs is indicated – selected COX2 inhibitors (e.g. celecoxib) and paracetamol may be used as alternative
- β -blockers
 - Non-selective β -blockers including eyedrops can induce bronchospasm
 - Should be initiated with caution
 - Cardio-selective- β -blockers are NOT absolutely contraindicated and have not shown to affect FEV₁ or asthma exacerbation in mild to moderate asthma^{2,3,26}



Treating Stable Asthma

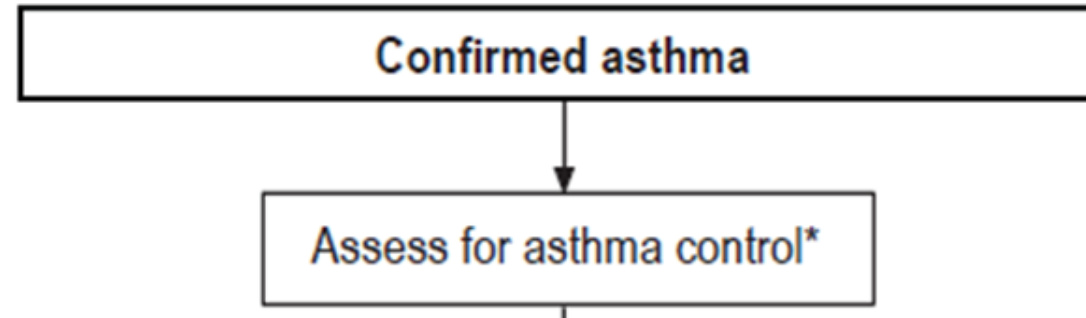
Treatment of Stable Asthma - Initiation



Treatment of Stable Asthma - Initiation



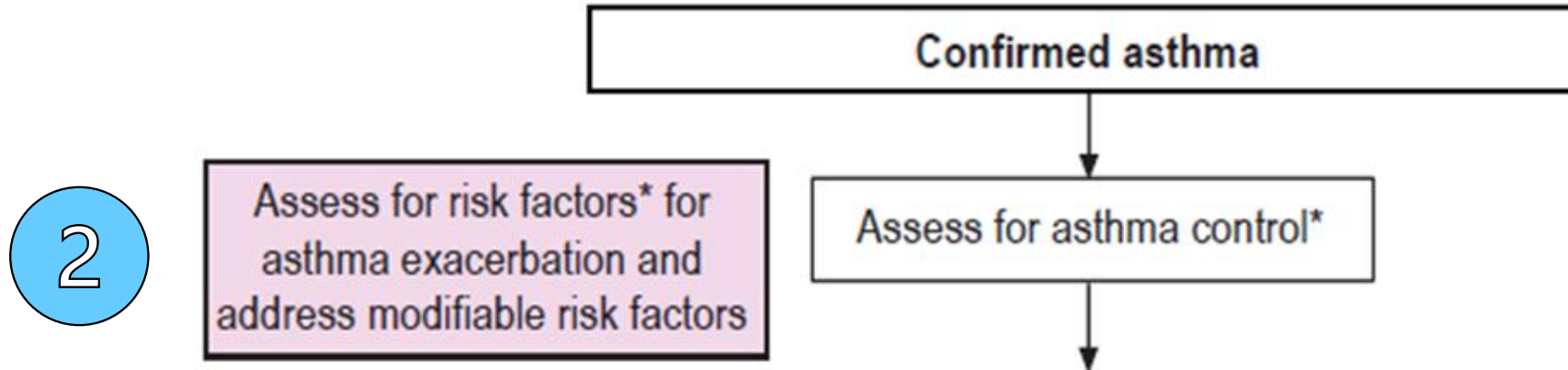
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- Start with assessing asthma control
- Use validated tools e.g. GINA assessment or ACT



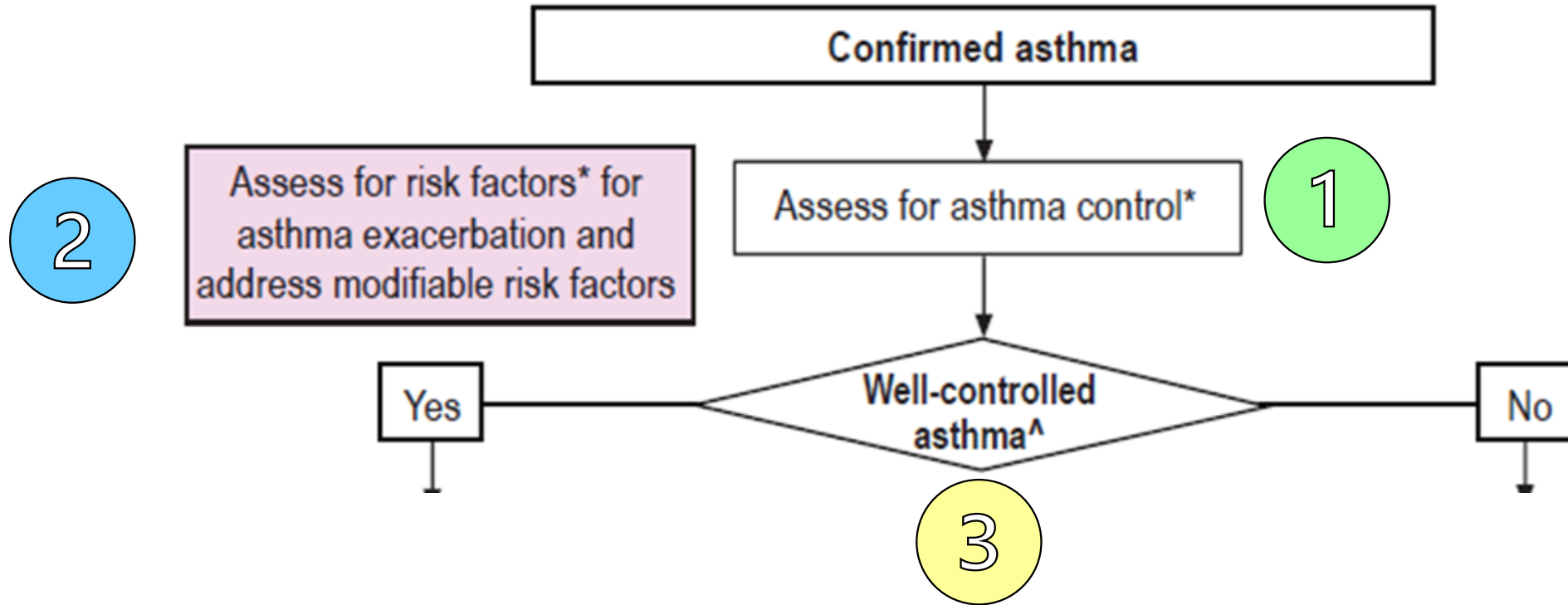
Treatment of Stable Asthma - Initiation



- Assess risk factors for asthma exacerbation
- Address and rectify modifiable risk factors for asthma exacerbation including poor adherence and incorrect inhaler techniques



Treatment of Stable Asthma - Initiation

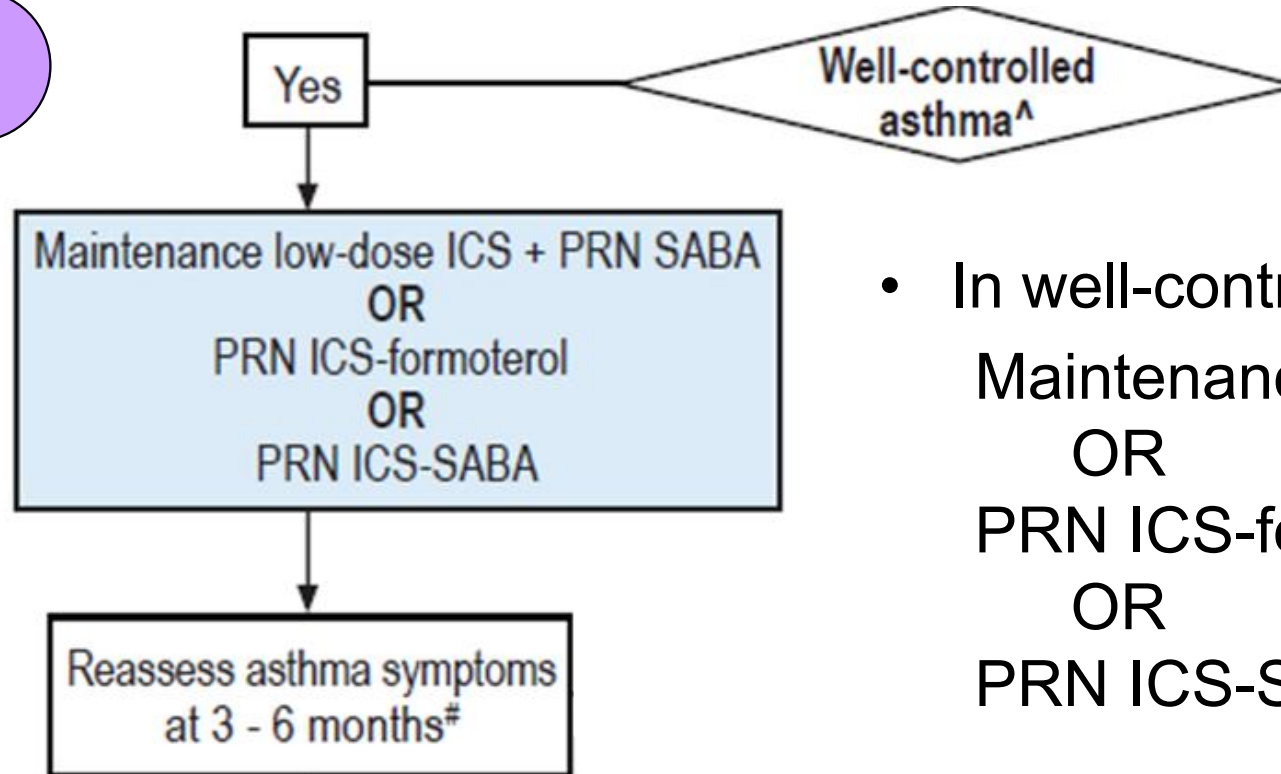


- If the asthma control is well-controlled – go to the left of the algorithm
- If the asthma control is NOT well-controlled – go to the right of the algorithm



Treatment of Stable Asthma - Initiation

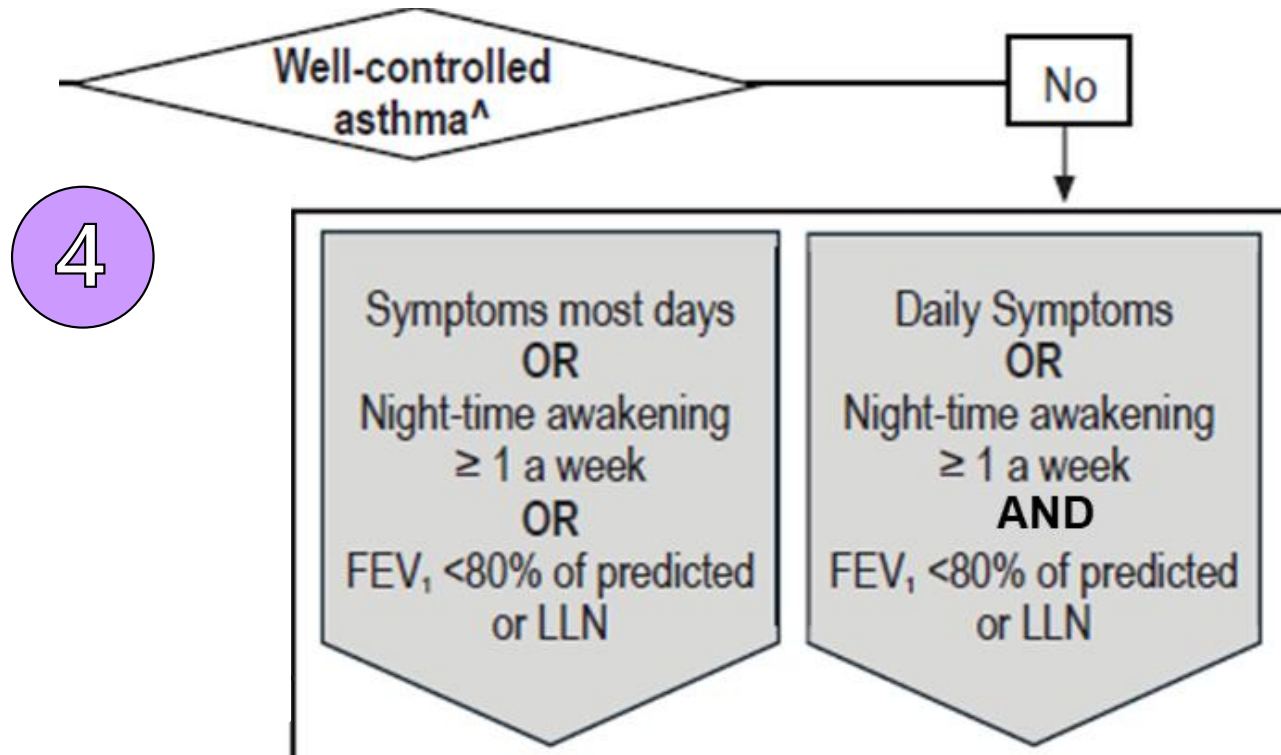
4



- In well-controlled asthma start on either:
Maintenance low-dose ICS + PRN SABA
OR
PRN ICS-formoterol
OR
PRN ICS-SABA
- Symptoms should be reassess at 3-6 months after initiation of treatment



Treatment of Stable Asthma - Initiation



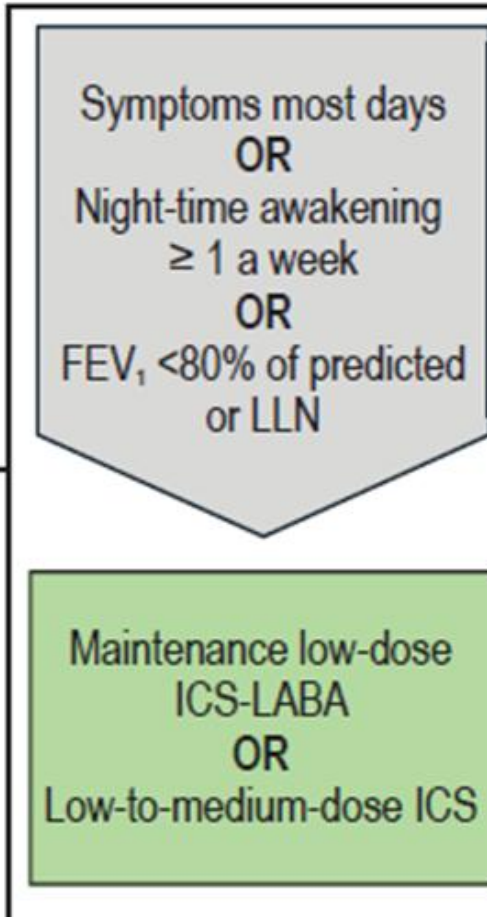
In uncontrolled asthma assess the:

- frequency of symptoms
- Frequency of night-time awakening due to asthma
- FEV₁ percentage predicted



Treatment of Stable Asthma - Initiation

4



Reliever: SABA OR ICS-SABA OR ICS-formoterol[§]
(if maintenance includes ICS-formoterol)

- If the symptoms are present on most days OR there is night-time awakening due to asthma ≥ 1 a week OR FEV₁ <80% of predicted or LLN, start on either:
 - Maintenance low-dose ICS-LABA
 - OR**
 - Low-to-medium dose ICS
- Reliever used can be either SABA or ICS-SABA or ICS-formoterol (if maintenance using ICS-formoterol)



Treatment of Stable Asthma - Initiation

4

Daily Symptoms
OR
Night-time awakening
≥ 1 a week
AND
FEV₁ <80% of predicted
or LLN

Maintenance medium-to-high-dose ICS-LABA
OR
Medium-dose ICS-LABA
with add-on LAMA

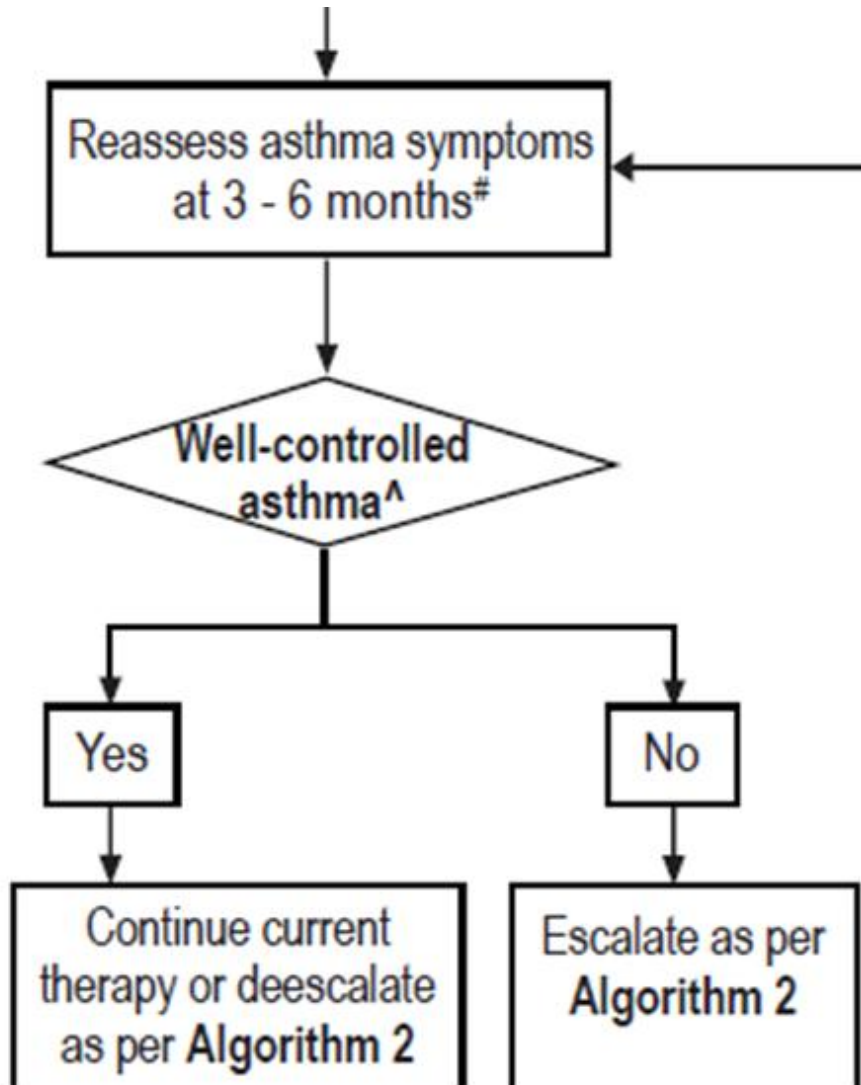
Reliever: SABA OR ICS-SABA OR ICS-formoterol[§]
(if maintenance includes ICS-formoterol)

- If the symptoms are present DAILY or there is night-time awakening due to asthma ≥ 1 a week AND FEV₁ <80% of predicted or LLN, start on either:
 - Maintenance medium-to-high-dose ICS-LABA
OR
 - Medium-dose ICS-LABA with add-on LAMA
- Reliever used can be either SABA or ICS-SABA or ICS-formoterol (if maintenance using ICS-formoterol)



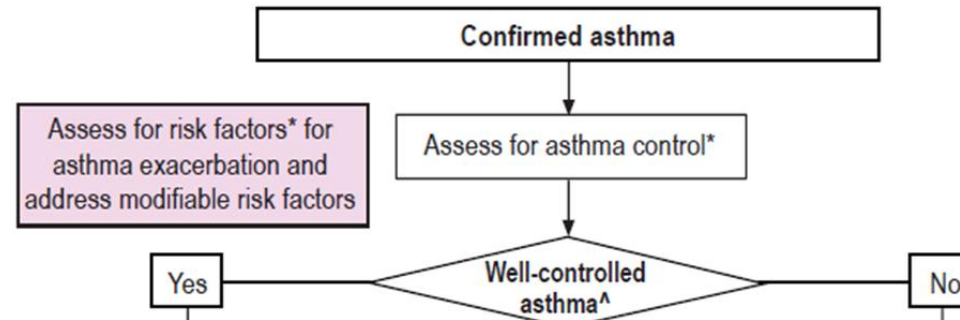
Treatment of Stable Asthma - Initiation

5



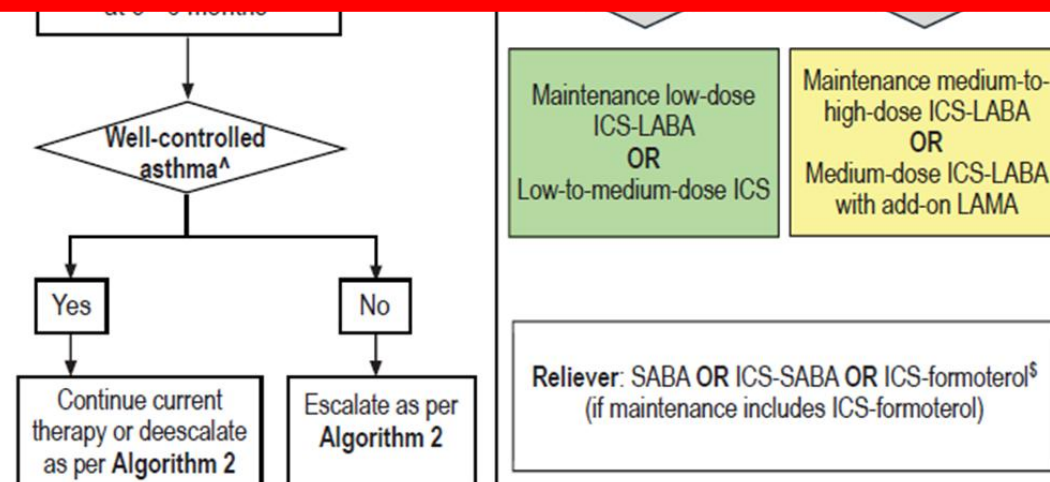
- After treatment is initiated, asthma control is reassessed at 3-6 months
- If the asthma is WELL-CONTROLLED either continue current therapy or step-down (deescalate) therapy
- If the asthma is NOT well-controlled, therapy may be step-up (escalate)

Treatment of Stable Asthma - Initiation



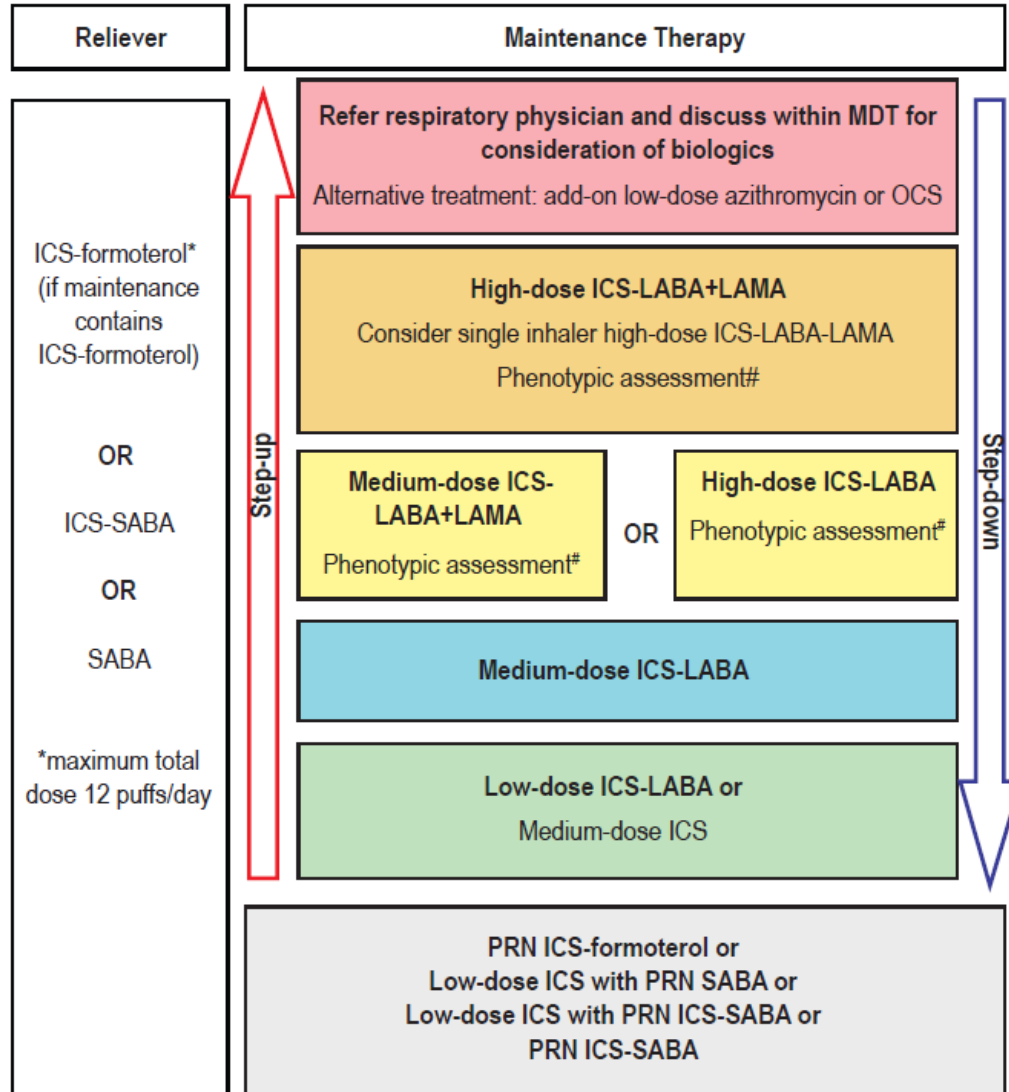
NO MORE SABA MONOTHERAPY!

ALL SHOULD BE ON ICS-CONTAINING THERAPY!





Treatment of Stable Asthma: Step-Up

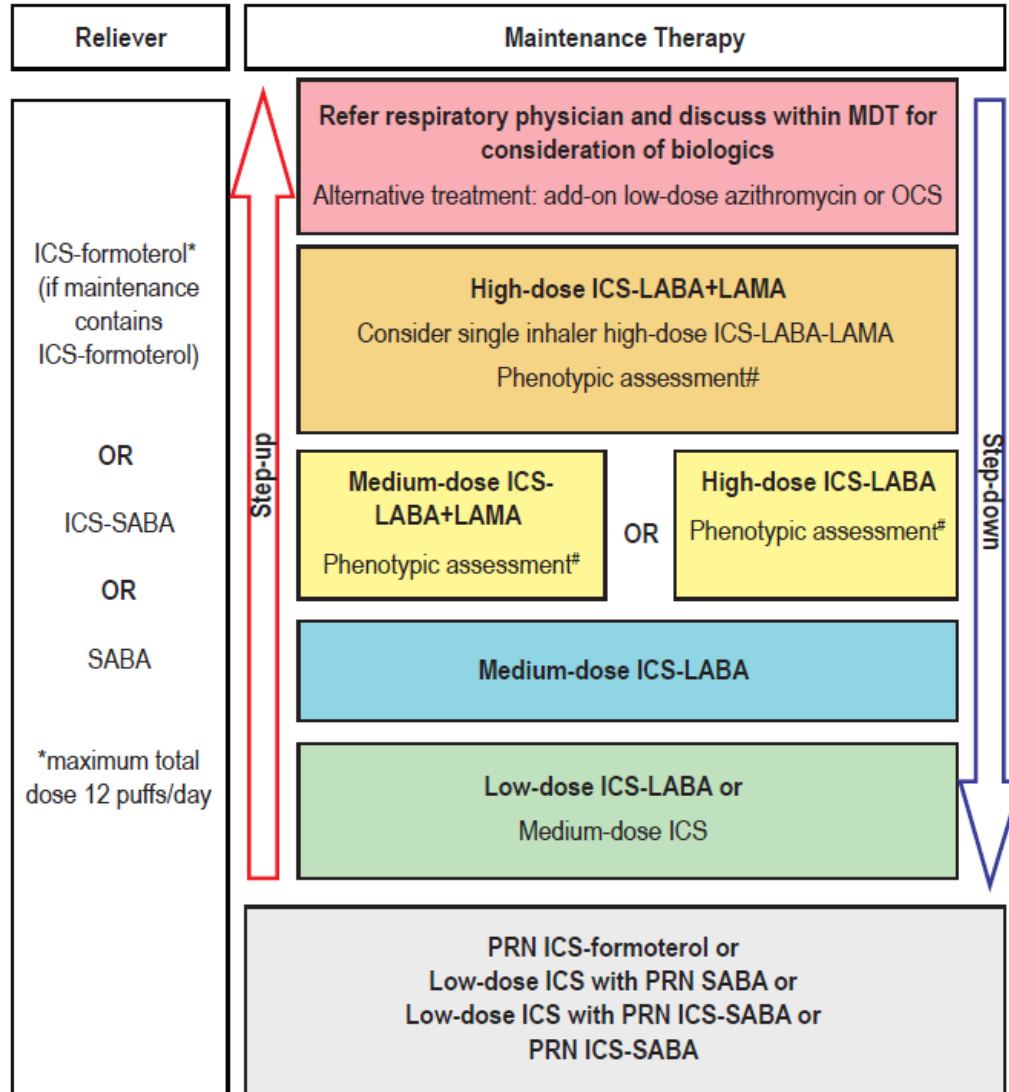


- Why step-up? – to ensure asthma is well-control
- STEP 1: Identify the box with your CURRENT treatment
- STEP 2: Identify the box that is above your current treatment box
- STEP 3: Change treatment to the selected box

E.g. salmeterol/fluticasone 25/125 µg 1 puff BD
(low dose) step up to 2 puffs BD (medium dose)



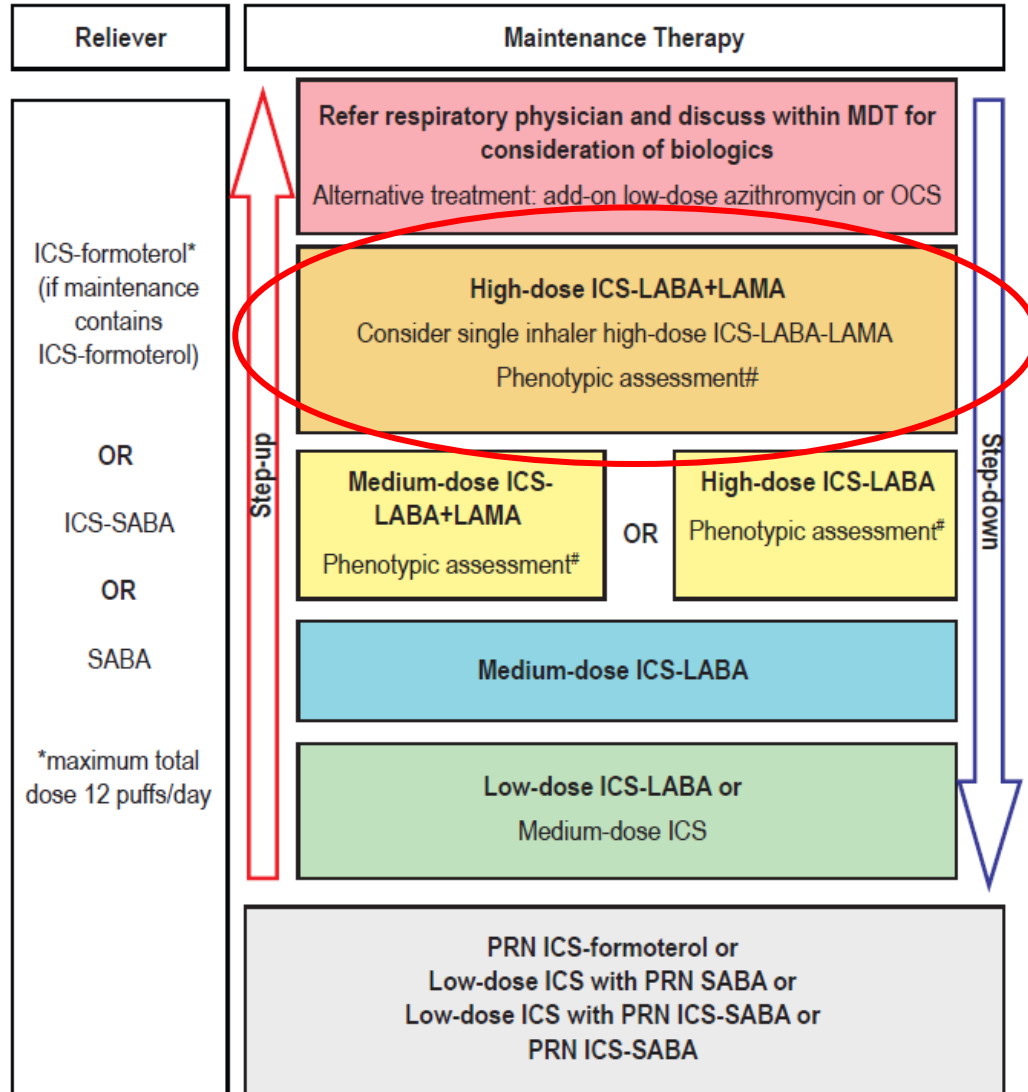
Treatment of Stable Asthma: Step-Up



- Reliever choice depends on maintenance therapy:
 - ICS-LABA or ICS monotherapy – either SABA or ICS-SABA
 - ICS-formoterol PRN if on it (max 12 puffs/day)
- LTRA may be added in patients with allergic rhinitis



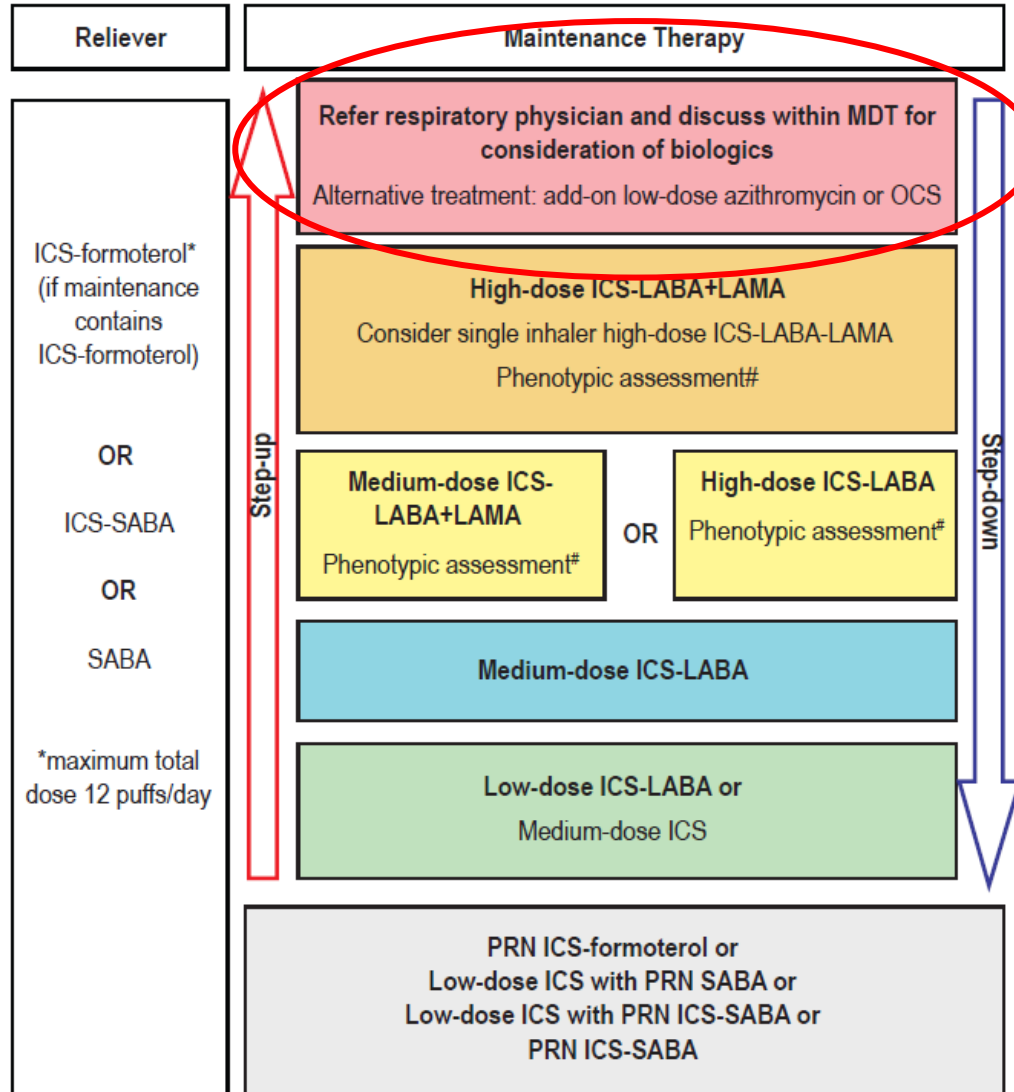
Treatment of Stable Asthma: Step-Up



- Once reached high-dose ICS-LABA+LAMA or single inhaler high-dose ICS-LABA-LAMA:
 - do phenotypic assessment
 - consider early referral to respiratory physicians



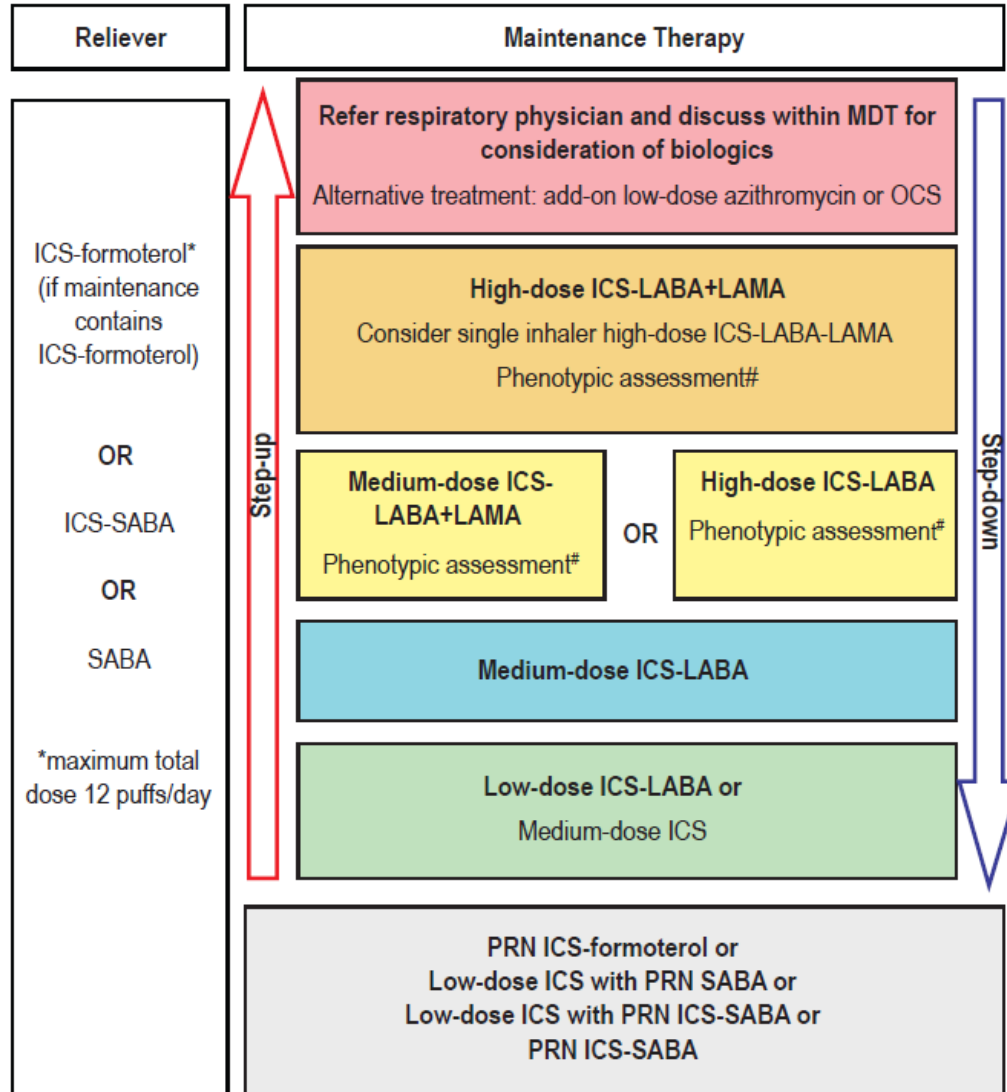
Treatment of Stable Asthma: Step-Up



- Despite high-dose ICS-LABA-LAMA and still uncontrolled:
 - refer to respiratory physicians
 - Discuss in MDT to optimize treatment & for consideration of biologics
 - Low-dose azithromycin or oral corticosteroids may be offered

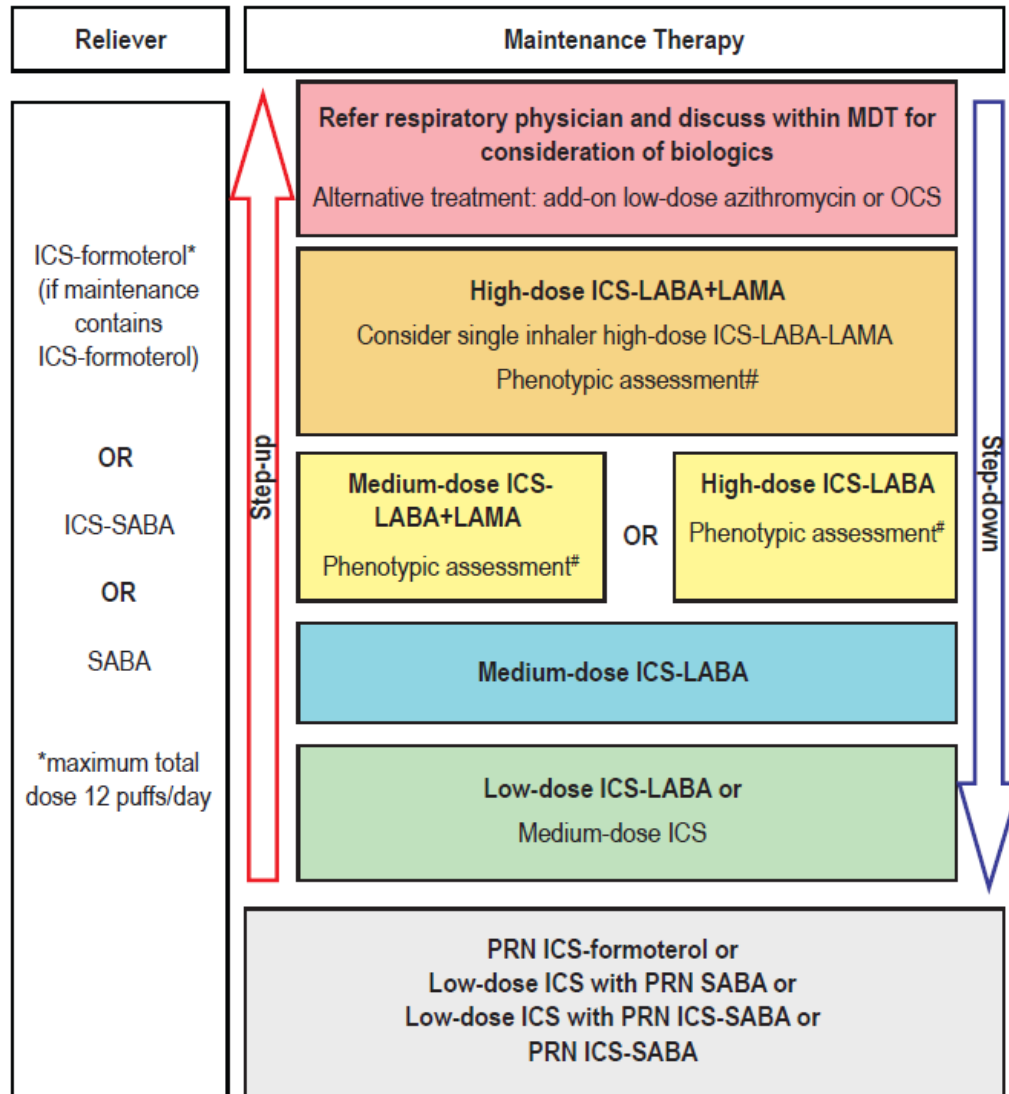


Treatment of Stable Asthma: Step-Up



- Once STEP-UP:
 - reassess at 3-6 months
- Consider short-term step up (for 1-2 weeks) in situations with identifiable triggers (e.g. viral infection or allergen exposure)
- Utilize Asthma Action Plan (AAP)

Treatment of Stable Asthma: Step-Down



- Why step-down? – to find the lowest effective dose and minimize side effects
- STEP 1: Choose an appropriate time
 - e.g. no respiratory infection, not pregnant
 - Caution if history of severe exacerbations
- STEP 2: Identify the box with your CURRENT treatment
- STEP 3: Identify the box that is below your current treatment box
- STEP 4: Change treatment to the selected box
- Reassess at 3-6 months and utilize AAP

TAKE HOME MESSAGES



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- Initiation of treatment will depend on asthma control and symptoms frequency
- Treat to achieve asthma control & find the lowest effective dose to minimise side effects
- Non-pharmacological management such as smoking cessation, regular physical activity and weight reduction should be initiated

NO MORE SABA MONOTHERAPY!
ALL SHOULD BE ON ICS-CONTAINING THERAPY!

Thank You!!



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