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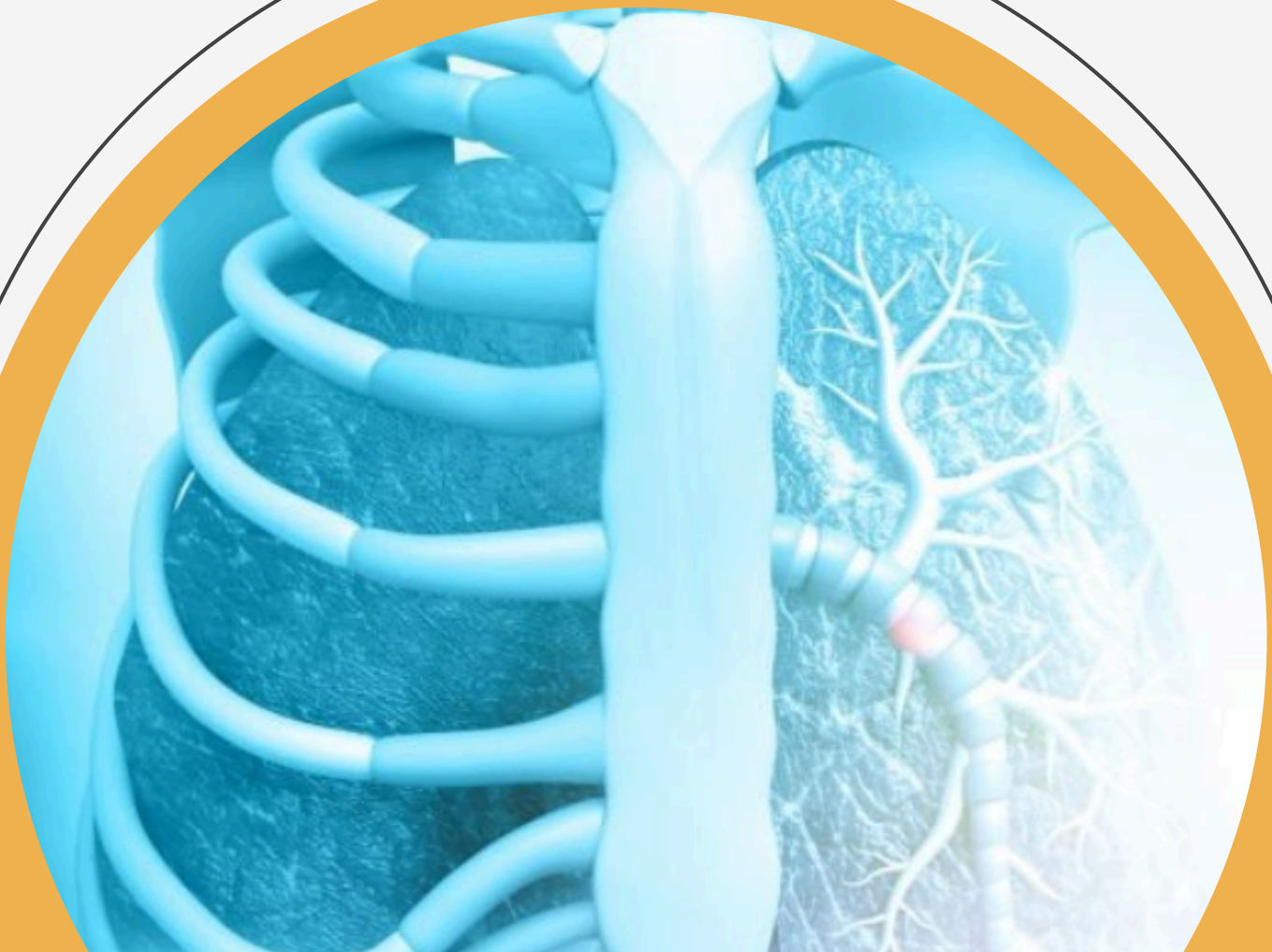
GUIDELINE FOR MANAGEMENT OF BRONCHIAL ASTHMA IN ADULTS

2024



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Abbreviations

ACO -Asthma COPD Overlap

COPD -chronic obstructive pulmonary disease

CVD -cardiovascular disease

GERD -Gastro-esophageal reflux disease

FEV1 -forced expiratory volume in 1 second

FVC -forced vital capacity

ICS -Inhaled corticosteroids

LABA -long-acting beta 2 agonists

LAMA -long-acting muscarinic antagonists

LTRA -leukotriene receptor antagonist

MART -Maintenance and reliever therapy

OCS -oral corticosteroids

PEF -Peak expiratory flow

SABA -Short acting beta 2 agonists

SAMA -short acting muscarinic antagonists

TB -Tuberculosis

MANAGEMENT OF ASTHMA IN ADULTS

1.0 Introduction

1.1 What is asthma?

Asthma is a common chronic respiratory disease that can affect people of all ages. It is one of the most common chronic respiratory conditions that manifests in childhood with a high probability to continue into adulthood. Asthma may also present for the first-time during adulthood which is called adult-onset or late-onset asthma.

Asthma is characterized by variable air flow limitation manifesting with symptoms of wheeze, shortness of breath, chest tightness and cough that vary over time and intensity. Symptoms of asthma are often triggered by respiratory infections, allergens, exposure to tobacco smoke and exercise. These symptoms are reversible and may resolve spontaneously or in response to medication.
Some who have childhood symptoms seem to recover completely while some have long remissions with occasional mild relapses, while some get worse and develop irreversible airway obstruction.
Asthma envelops a range of recognizable clusters of clinical and/ or pathophysiological characteristics often called Asthma phenotypes. Several clinical phenotypes have been identified, of which the common types include allergic asthma, intrinsic asthma, adult-onset asthma, neutrophilic asthma, aspirin-intolerant asthma, and asthma with persistent airflow limitation.
More research is needed to understand the clinical utility of phenotypic classification in asthma.
Although asthma cannot be 'cured' but clinical episodes can largely be prevented and controlled by proper management of the condition.

Atopy, allergies and eczema are common presentations in Maldives and these conditions may contribute to number of asthma patients. Data regarding asthma diagnosis from outpatient and in-patient records needs to be collated to better understand the prevalence of Asthma in Maldives. Maldives Health Statistics 2020 show 250 hospitalizations during the year due to asthma. Many remain undiagnosed and among those who gets diagnosed, many remain poorly and inadequately treated. Many are reluctant to use inhalers and from those taking, many do not use the inhaler correctly or may only be on a SABA prn despite uncontrolled symptoms. Hence there is a need to have a guidance document to assist health care professionals to diagnose and appropriately manage asthma in Maldives.

2.0 Scope of this guideline

Although National Guidelines for management of Asthma in children is available, there is no local guidance to manage Asthma in Adults except for adapted WHO PEN package for primary care, which also needs revision and updating based on new research and developments in asthma management. Hence it is important to have a guidance document for standardized and effective quality care to manage Asthma.

This Guideline is based on published clinical evidence and is intended to provide guidance on best evidence-based practices on the diagnosis, evaluation and management of Bronchial Asthma and is intended for use by health care providers in diagnosing, evaluation and management of asthma in adults.
It is intended for use by health care providers, including general medical practitioners, physicians, respiratory physicians, nurses, and community health workers involved in the health care team providing care to Asthma patients.

3.0 Definition of Asthma

- Asthma is a heterogenous disease usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and intensity, together with variable expiratory airflow limitation.

3.1 Risk factors

- Although the exact cause of asthma is unknown; it could be partly genetic or environmental in origin. There are some major factors that either cause and/or produce the clinical manifestations of asthma and these include:
    - Personal or family history of asthma or Atopy
    - Air pollution
    - Tobacco smoke (active, passive and tertiary)
    - Occupational exposure
    - Biomass exposure (combustion of solid fuels)
    - Respiratory syncytial and para influenza virus infections

3.2 Asthma triggers

- A trigger is defined as a factor which when exposed to it, elicits an exacerbation in a stable or previously asymptomatic patient of asthma. Several major factors have been known to precipitate asthma and these include:
    - Gastro-esophageal reflux disease
    - Post nasal drip (due to allergies)
    - Down feathered comforters
    - Pollens, mold, house dust mite and pets
    - Cotton dust/wood dust
    - Viral infections
    - Tobacco smoke and Air pollution
    - Psychological and extreme emotional states
    - Cold exposure

4.0 Diagnosis of Asthma

- Diagnosis of Asthma is based on clinical assessment to assess the probability of asthma which is further supported by variable expiratory air flow limitation demonstrated by spirometry or peak expiratory flow meter.

- The presence of characteristic respiratory symptoms and their pattern that is typical of asthma, if present, increases the probability of a clinical diagnosis of asthma.
  It is important that while taking the history, to enquire regarding the presence of other symptoms that would be helpful in ruling out other diseases that may cause similar symptoms. The presence of fever, weight loss, hemoptysis, chronic sputum production or chest pain should alert of an alternative or a coexisting disease.

4.1 Symptoms and Signs that favor a clinical diagnosis of asthma.

History of variable respiratory symptoms suggestive of asthma include:

- Symptoms of cough, wheeze, shortness of breath and/or chest tightness
- Symptoms vary over time and in intensity.
- Symptoms often worsen at night or on waking in the morning.
- Symptoms are often triggered by allergens, viral infections, changes in weather, smoke or strong smells and laughter.

History that increases the probability that the symptoms may be due to asthma include:

- Onset of respiratory symptoms in childhood
- Family history of asthma or allergy
- Personal history of atopic dermatitis, eczema and rhinitis

Physical examination

Presence of diffuse expiratory polyphonic wheeze is present in asthma but note that even if examination results are normal at the time of examination, the person may still have asthma. Wheeze may also be absent during severe asthmatic exacerbations. Examination may reveal signs that may be indicative of alternative respiratory conditions.

Symptoms that make diagnosis of asthma more likely	Asthma less likely or suspect a coexisting disease
Variable, intermittent and recurrent symptoms	Clinical feature suggestive of alternative diagnosis
Nocturnal/early morning worsening	Purulent expectoration, hemoptysis, fever and significant constitutional symptom
Worsening after exposure to nonspecific triggers: Seasonal/ temperature changes, exercise, noxious fumes, drugs or infections Personal history of atopy	Clubbing
Family history of atopy and asthma	Focal chest signs (bronchial breathing, crackles, monophonic wheeze)
Diffuse bilateral wheeze on auscultation and/or hyperinflation	No response to adequate trial of asthma therapy
Response to therapy with bronchodilators, corticosteroids	

4.2 Role of Chest X-RAY

A chest X-ray has no role in diagnosis of stable asthma but is required when patient has a complication of asthma like exacerbation or when other alternative conditions like tuberculosis, bronchiectasis, lung cancer, or parenchymal lung disease needs to be ruled out. Similarly, an electrocardiogram aids in diagnosis of a cardiac disorder.

4.3 Spirometry

Wherever available, spirometry should be done for all patients suspected to have asthma for confirmed variable expiratory air flow limitation and for monitoring asthma control. A normal spirometry does not rule out asthma.

A forced expiratory volume in 1 second /forced vital capacity (FEV1/FVC) ratio of less than <0.7 documents airflow limitation.

If spirometry is not available:

- Where spirometry is not available, peak expiratory flow (PEF) should be done using a PEF meter. It is a good indicator for asthma diagnosis as bronchodilator reversibility can be assessed with PEF meters. Bronchodilator reversibility is defined as an increase in PEF of ≥ 20% after bronchodilator administration with at least 60 L/min absolute increment.

- **For PEF recording**:
    - First measure the patient's peak expiratory flow rate
    - Then give two puffs of salbutamol and
    - measure PEFR again in 15 minutes
    - If the PEF improves by 20%, a diagnosis of asthma is very probable.

- Peak expiratory flow (PEF) should be recorded as the best of three forced expiratory blows from total lung capacity with a maximum pause of two seconds before blowing. The patient can be standing or sitting. Further blows should be made if the largest two PEF are not within 40 L/min.

- If there is any doubt on diagnosis, refer the patient to a specialist for spirometry and further evaluation.

4.4 Peak expiratory flow variability

- Variable expiratory airflow limitation is one characteristic feature of untreated asthma and refers to improvement and/ or deterioration in symptoms and lung function and may be identified by diurnal variation, from visit to visit or seasonally or by a reversibility test.

- Reversibility or responsiveness refers to rapid improvement in FEV1 measured within minutes after inhalation of a rapid acting bronchodilator such as 200-400mcg of salbutamol or more sustained improvement over days or weeks after effective controller treatment as ICS.

- Generally, in a patient with a history suggestive of asthma, the diagnosis of asthma is supported by an increase or decrease in FEV_1 by more>12% or increase in volume >200 mL from baseline. If using a PEF meter, a change in PEF of at least 20% is consistent with asthma.
- Diurnal PEF variability is calculated as each day's highest minus the day's lowest reading, divided by the mean of the day's highest and lowest, then these results are averaged over one week.
  Excessive diurnal PEF variability is defined as a mean variability of >10% in PEFs in adults or >13% variability in children. When measuring PEF, the same meter should be used for all readings.

4.5 Other tests

Bronchial provocation tests

- In people with suspected asthma who have normal expiratory airflow and no significant reversibility with diagnostic uncertainty, a bronchoprovocation test using challenge agents such as methacholine, histamine or inhaled mannitol can reveal airway hyperresponsiveness.
- These tests have moderate sensitivity but limited specificity for diagnosing asthma as airway responsiveness to inhaled methacholine has also been described in other conditions like allergic rhinitis and COPD as well.
- Hence for a patient not on ICS, if the test is negative asthma can be excluded but a positive test does not always mean that the patient has asthma.

Allergy tests

- Atopic status can be identified by allergy tests or by measuring the level of specific immunoglobulin E in serum. The presence of atopy increases the probability that a patient with respiratory symptoms has allergic asthma, but this is not specific for asthma.
- A positive sIgE and skin test doesn't mean that the allergen is causing the asthma symptoms and the relevance of allergen exposure and its relation to symptoms must be verified from history.
- Measurement of sIgE is no more reliable than skin tests but may be opted for uncooperative patients and those with a risk of anaphylaxis.

Fractional concentration of Exhaled Nitric Oxide (FeNO)

- FeNO is modestly associated with eosinophilia but has not been established to diagnose or rule out asthma as it is also elevated in non- asthma conditions while not elevated in some asthma phenotypes like neutrophilic asthma.

4.6 Confirming the diagnosis of Asthma in patients already on controller treatment.

- For patients already on controller treatment, this may include a trial of either a lower or a higher dose of controller or for some it may be necessary to step down the controller treatment. If the patient has risk factors for exacerbations, do not step down without close supervision.

If the spirometry does not depict variable air flow limitation:

- Consider repeating spirometry after withholding the bronchodilator, 4 hours for SABA, 24hours for twice daily ICS/LABA, 36 hours for once daily ICS-LABA. Check between visits variability of FEV1 and bronchodilator responsiveness. If still normal consider other diagnosis.
- If FEV1>70% predicted, consider stepping down controller treatment and reassess in 2-4 weeks, then consider bronchial provocation test or repeating bronchodilator responsiveness.
- If FEV<70% predicted: consider stepping up controller treatment for 3 months, then reassess symptoms and lung function. If no response, resume previous treatment and refer the patient to pulmonology for further evaluation.

For few respiratory symptoms and normal lung function, and no variable air flow limitation:

- Consider repeating bronchodilator responsiveness test again after withholding bronchodilator as above or during symptoms. If normal consider alternate diagnosis.
- Consider stepping down controller treatment and if symptoms emerge and lung function falls, asthma is confirmed. Step up controller treatment to previous lowest effective dose. If no change in symptoms or lung function at lowest controller step, then consider ceasing controller and monitor patient closely for at least 12 months.

Persistent shortness of breath and persistent airflow limitation:

- Consider stepping up controller treatment for 3 months then reassess symptoms and lung function. If no response, resume previous treatment and refer patient for diagnosis and investigation. Consider asthma-COPD overlap

4.7 Diagnosis of Asthma in other contexts

- **Cough variant asthma**: Patients present with persistent non- productive cough as the only respiratory symptom associated with airway responsiveness. It worsens at night.
  Lung function may be normal and documentation of variability in lung function is important. This also has to be differentiated from eosinophilic bronchitis in which eosinophilia is present but spirometry and air way responsiveness is normal
- **Occupational asthma and work exacerbated asthma:** Asthma may be induced or aggravated by allergens or sensitizing agents at work and rhinitis may precede asthma by up to a year. Persistent exposure is associated with worse outcomes. 5-20% of new cases of adult-onset asthma can be due to occupational exposure. Improvement of symptoms when away from work and PEF monitoring at and away from work often helps to establish the diagnosis.
  Specialist referral is needed in these cases, as it is important to diagnose objectively as the diagnosis can lead to change in occupation.

5.0 Differential Diagnosis

Many conditions may present with symptoms similar to asthma. These must be excluded with a careful history and examination and particularly if the criteria for a diagnosis of asthma are not fulfilled.
Many people with asthma who smoke develop COPD, and patients with COPD may also have concomitant asthma. This overlap of both asthma and COPD frequently makes the control of symptoms more difficult and are labelled as ACO if and to default to an asthma-led treatment approach.

- **Cough as an isolated symptom** is a common symptom of asthma and is also seen in upper respiratory tract infections, usually caused by viruses, ACE inhibitor use and Gastro-esophageal reflux disease.

- **Chronic rhinitis and sinusitis** with a postnasal drip may also present with a chronic cough and may be the first manifestation of atopy with asthma developing later.

- **Upper airway obstruction** may present with stridor that is often mistaken for a wheeze unless one auscultates carefully and times the ‘wheeze’ which occurs during inspiration.

- **Endobronchial obstruction:** Has presence of localized wheeze

- **Acute and chronic bronchitis**: can present with diffuse wheeze
- **COPD**
- **Left ventricular failure**
- **Bronchiolitis.**

6.0 Asthma Control

6.1 level of Asthma Symptom control

- The level of asthma control is the extent to which the features of asthma can be observed in the patient or have been reduced by treatment and is assessed by symptom control and risk of adverse outcomes.
  Lung function is an important part of future risk and if available, should be assessed at start, after 3-6 months of treatment and periodically, at least once every 1-2 years.

Asthma symptom control - In the past 4 weeks	**YES/NO**
Are Daytime asthma symptoms more than twice/ week	
Any night time symptoms or waking due to asthma	
Any limitation of daily activities	
Uses a reliever more than two times per week	

- If None of the above is present: asthma is well controlled.
- If 1 - 2 of the above is present: asthma is partly controlled
- If 3 - 4 of the above is present: asthma is uncontrolled

6.2 Assessing asthma severity

Mild asthma	Asthma that is well controlled with (Step1 or Step 2 treatment) as needed ICS-formoterol or with low dose ICS
Moderate Asthma	Asthma that is well controlled with (Step 3 treatment) low or medium dose ICS-LABA
Severe Asthma	Asthma that remains uncontrolled despite optimized treatment with high dose ICS-LABA (Requires Step4 or 5 treatment) Severe asthma should be diagnosed after excluding: ▪ poor inhaler technique ▪ poor medication adherence ▪ incorrect diagnosis ▪ other comorbidity such as rhinosinusitis, GERD ▪ Ongoing exposure to triggers or risk factors at home or work

6.3 Risk factors for exacerbations and poor asthma outcomes

- Having uncontrolled asthma symptoms
- Ever intubated or in intensive care unit
- ≥ 1 severe exacerbation in last 12 months
- Potentially modifiable risk factors for exacerbation
- Comorbidities such as obesity, pregnancy, chronic rhinosinusitis, GERD
- Medications: poor adherence, improper inhaler technique, not receiving ICS, high SABA use (>3x200-dose canister /year)
- Continuous exposures: smoke, allergens, air pollution
- Lung function: Low FEV1 especially <60% predicted
- Major psychological or socioeconomic problems

6.4 investigating a patient with poor symptom control despite treatment

Investigating a patient with poor symptom control despite treatment	
Observe the patient using the inhaler	Teach the correct technique to use inhaler and recheck the patient using it. Recheck at each visit
Discuss adherence	Discuss to find out about adherence, whether using medication as prescribed. Address factors that may affect adherence such as: ▪ Not understanding instructions ▪ Forgetfulness ▪ Difficulties using inhaler device, ▪ Multiple inhalers and multiple dosing ▪ Denial of asthma diagnosis ▪ Concerns about side effects ▪ Stigmatization
Address potential risk factors	Check for triggers such as smoking, allergen exposure at home or work and if possible, to remove them.
Assess and manage comorbidities	Manage comorbidities that may contribute to symptoms or make it difficult to control asthma such as GERD, rhinitis, anxiety. obstructive sleep apnea
Step up treatment	Consider stepping up treatment to the next level or alternate option on present level
Refer to specialist	If asthma is not controlled after 3-6 months of high dose ICS-LABA. Refer earlier if asthma very severe and difficult to manage or if doubts about diagnosis

7.0 Management of Asthma

7.1 Asthma Management Goals

- Achieve and maintain control of symptoms
- Maintain normal activity levels, including exercise
- Maintain pulmonary function as close to normal levels as possible
- Prevent asthma exacerbations
- Avoid adverse effects from asthma medications
- Prevent asthma mortality
- Educate the patient and develop an asthma Action Plan for self-management

7.2 Pharmacological therapy

- The choice of medication, device and dose should be based on symptom control, risk factors, patient preference, adherence, and ability use of the device. Inhalation therapy is the first line of choice for delivery of drugs to treat asthma than oral medications.
- Advantages of inhaled route include:
    - Rapid onset of action: Directly delivers medicine to the lung, hence rapid delivery of high pulmonary drug concentrations increasing efficacy.
    - Less severe and less frequent systemic adverse effects
    - Small, inhaled doses required, which is therapeutically equivalent or even superior to higher doses of systemically administered therapy
    - Convenient & patient friendly: painless and relatively comfortable

- Using the inhaler must be learnt by the patient and maintained, for it to be effective. Poor inhaler technique is associated with poor asthma control and most patients are unable to use their inhaler correctly.

- For MDI, use of a spacer improves delivery of the medicine, hand- to-mouth coordination, reduce oropharyngeal deposition and achieve desired clinical outcomes and decrease side-effects.

- The drugs available for management of asthma are divided into two broad categories, i.e. controller medications and reliever medications.
    - **Controller medications**: These contain ICS and are primarily meant to prevent and control symptoms, reduce airway inflammation, and decrease the risk of exacerbations.

    - **Reliever medications**: These are also known as rescue medications and are taken as and when needed, to relieve the acute symptoms. They provide as-needed breakthrough symptomatic relief during exacerbations. They are also used for short-term prevention of exercise-induced bronchoconstriction.
    - **Add-on therapies in severe asthma**: They are ideally considered for persistent symptoms and/or exacerbations despite optimized treatment with high dose controller medications. Add-on therapies can also be considered as a treatment of modifiable risk factors.

7.2.1 Common Medications, route, action and use of Controller Medications in asthma

Medication Class	Route	Action and use
Inhaled corticosteroids (ICS) Beclomethasone Budesonide Fluticasone propionate, Fluticasone furoate Mometasone Triamcinolone	MDIs or DPIs (Inhaled once or twice daily)	▪ Most effective anti - inflammatory medications for asthma ▪ Reduce symptoms, increase lung function, reduce risk or exacerbations and asthma related hospitalizations and death
ICS and long-acting beta2-agonist bronchodilator combinations (ICS-LABA) Beclomethasone- formoterol Budesonide- formoterol Fluticasone propionate-formoterol Fluticasone propionate-salmeterol Mometasone-formoterol Fluticasone furoate-vilanterol	MDIs or DPIs (Inhaled once or twice daily)	▪ When low dose of ICS alone fails to achieve good control, addition of LABA to ICS improves symptoms, lung function, reduces exacerbations than doubling ICS dose
Leukotriene modifiers Montelukast, zafirlukast,zileuton	Oral	▪ Used as an option for controller therapy, particularly in children ▪ When used alone: Less effective than low dose ICS ▪ When added to ICS: Less effective than ICS-LABA
Chromones Sodium cromoglycate and nedocromil sodium	MDIs or DPIs	▪ Very limited role in long-term treatment of asthma ▪ Weak anti -inflammatory effect, less effective than low-dose ICS ▪ Requires meticulous inhaler maintenance

7.2.2 Medication class, route, action and use of Reliever Medications in asthma

Medication Class	Route	Action and use
Short-acting inhaled beta2-agonist bronchodilators) Salbutamol (albuterol) terbutaline	MDIs, DPIs and solution for nebulization or injection	▪ Quick relief of symptoms and bronchoconstriction, acute exacerbations and for pretreatment of exercise-induced bronchoconstriction
Low-dose ICS-formoterol Beclomethasone-formoterol Budesonide-formoterol	MDIs or DPIs	▪ Reliever prescribed as-needed controller therapy for mild asthma compared with SABA only treatment ▪ Reliever for those with moderate to severe asthma, both as maintenance and reliever treatment where It reduces the risk of exacerbations compared with as needed SABA,
Short- acting anti cholinergic Ipratropium bromide, Oxitropium bromide	MDIs or DPIs	▪ Ipratropium has a short-term use in acute asthma and is a less effective reliever medication than SABAs for long term use.

7.2.3 Medication class, drug molecules, route, action and use of Add on therapies in asthma

Medication Class	Route	Effects
Long-Acting anticholinergic Tiotropium, ≥ 6 years of age	MDIs /DPIs	• Add-on option at Step 4 or 5 for patients with a history of exacerbations despite ICS ± LABA
Anti Immunoglobulin E (Anti - IgE) Omalizumab, SC, ≥ 6 years	SC,Inj once every 2-4 weeks	▪ Add-on option for patients with severe allergic asthma uncontrolled on high dose ICS-LABA
Anti -Interleukin 5 (Anti -IL5) and Anti - interleukin-5 receptor Anti -IL5 mepolizumab [SC, ≥ 12 years] or reslizumab [IV, ≥ 18 years], or Anti -IL-5 receptor benralizumab [SC, ≥ 12 years]	SC, IV	▪ Add-on options for those with severe eosinophilic asthma uncontrolled on high dose ICS-LABA
Anti -Interleukin-4 receptor Dupilumab, SC, ≥ 12 years	SC	▪ In severe eosinophilic or type 2 asthma uncontrolled on high dose ICS-LABA, or requiring maintenance OCS
Systemic corticosteroids Prednisone, prednisolone, methylprednisolone, hydrocortisone	Oral, IV, IM	▪ Use in severe acute exacerbations ▪ oral preferred to IM/IV therapy for preventing relapse ▪ Tapering required if treatment given for > 2 weeks

7.2.4 Starting controller treatment in Asthma

- ICS containing treatment should be started after diagnosis. Managing stable asthma with SABA -only treatment without ICS is not recommended. Before starting treatment, it is crucial to:
    - record evidence for asthma diagnosis
    - document symptom control and risk factors and assess lung function.
    - Consider factors influencing choice between available treatment options.
    - Ensure the patient can use the inhaler correctly.

- Once asthma treatment is started, ongoing treatment decisions are based on patient response and controller can be adjusted up or down in a stepwise approach to achieve symptom control and minimize risk of exacerbation, and side effects of medication.

    - **Step 1** is for patients with mild asthma and symptoms less than twice a month and no exacerbation risk factor.
    - **Step 2** is for patients with mild asthma with risk of exacerbations and symptoms twice a month or more but less than 4-5 days a week.
    - **Step 3** is for patients with daily symptoms or waking with asthma once a week or more.
    - **Step 4** is for patients with daily symptoms or waking with asthma once a week or more and low lung function.
    - **Step 5** is for patients with severe asthma with uncontrolled symptoms and/or exacerbations despite being on step 4 treatment.

Starting controller treatment - PREFERRED PATHWAY (ICS-formoterol - as needed reliever)

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
RELIEVER:	**As needed Low dose ICS-Formoterol**				
CONTROLLER	As needed low dose ICS - formoterol AND not to give SABA only as a treatment	As needed low dose ICS - formoterol	low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Consider high dose maintenance ICS-formoterol +/- tiotropium OR Low dose oral corticosteroids

ALTERNATIVE RELIEVER Pathway Using as needed SABA as reliever

(If as needed ICS-formoterol is not available or the patient is unlikely to take regular ICS)

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
RELIEVER:	**As needed SABA**				
CONTROLLER	Take ICS whenever SABA taken	Low dose maintenance ICS OR LTRA (less effective than ICS)	low dose maintenance ICS- LABA OR Medium dose ICS OR Low dose ICS +LTRA	Medium /high dose maintenance ICS-LABA IF not controlled Add on LAMA/add on LTRA	Consider high dose maintenance ICS-LABA Add on LAMA OR Low dose OCS

ICS doses and their pharmacological strengths vary across different formulations. For adults, ≤400mcg budesonide or equivalent would be considered a low dose and a dose >400mcg to 800mcg budesonide would be considered a moderate dose and >800mcg budesonide would be considered a high dose.

STEP 1: Preferred treatment option

- Low dose combination ICS-Formoterol taken as needed and if needed before exercise
- Usual dose of as needed ICS_formoterol in mild asthma is a single inhalation 200/6 mcg taken whenever needed for symptom relief
- Rinsing the mouth is not generally needed after as needed-use of low dose ICS-formoterol
- ICS formoterol formulations other than budesonide- formoterol have not been studied for as – needed only use, but beclomethasone- formoterol may also be suitable.

Alternative treatment Options-

- If ICS -formoterol not available or cannot be taken, take SABA as needed. Low dose ICS to be taken whenever SABA is used

STEP 2: Preferred treatment

- low dose combination ICS-Formoterol taken as needed and if needed before exercise

Alternative options

- Daily Low dose ICS taken whenever SABA is used (in combination or separate inhalers) is another option
- Leukotriene receptor antagonists (LTRA) - they are less effective than ICS, particularly for exacerbations and patients should be counselled about neuropsychiatric events.

STEP 3: Preferred treatment:

- Low dose ICS-formoterol maintenance and reliever therapy

Alternative options:

- Low dose maintenance ICS-LABA with as needed SABA

Other Step 3 options:

- For adults with allergic rhinitis with sub optimally controlled asthma despite low to high dose ICS, consider adding sublingual allergen immunotherapy
- Another option is to increase ICS to medium dose
- Another option is low dose ICS plus LTRA or low dose sustained release theophylline

STEP 4: Preferred Option

- Medium dose ICS-formoterol maintenance and reliever therapy

Alternate options:

- Medium or high dose ICS-LABA with as needed SABA (If MART is not possible or asthma is stable)

Other options:

- LAMA may be considered as add on therapy if asthma is uncontrolled despite medium or high dose ICS_LABA
- Consider adding sublingual allergen immunotherapy for adult patients with sub optimally controlled asthma despite high dose ICS for those with allergic rhinitis and sensitization to house dust mite
- Other options that can be added to high dose ICS but less efficacious than adding LABA include LTRA or low dose sustained theophylline

STEP 5: Should be referred to a specialist with expertise in the management of severe asthma

Treatment options that may be considered:

- Combination high dose ICS -LABA when control is not achieved with medium dose ICS plus LABA and a third controller (LTRA or SR theophylline).
- Add on LAMA (tiotropium)
- Add on azithromycin (three times a week) for at least 6 months after checking sputum for atypical mycobacteria. ECG should be checked for long QTc and the risk of increasing microbial resistance should also be considered.
- Add on biologic therapy, if available and affordable and review response by symptom control, exacerbations, lung function and side effects as there is no well-defined criteria at present to monitor response.
  If response unclear, consider extending for 6-12 months. If no response, stop biologic therapy and review. Consider switching to a different type 2 targeted therapy if available.
  - Anti-IgE for severe allergic asthma: Omalizumab given SC every 2 to 4 weeks for at least 4 months
  - Anti-interleukin-5/5R in severe eosinophilic asthma: SC Mepolizumab, 100 mg every 4 weeks or Benralizumab, 30mg by SC every 4 weeks for 3 doses then every 8 weeks or Iv Reslizumab, 3mg/kg iv infusion every 4 weeks.
  - Anti-interleukin-4R for severe eosinophyllic asthma or patients requiring maintenance OCS: SC dupilumab 200 or 300mg every 2 weeks
- Add on low dose maintenance oral corticosteroids (≤ 7.5mg/day prednisone equivalent) as a last resort.

7.3 Review; follow-up and adjustment of treatment

- Patients should be monitored and reviewed for symptom control, adherence to treatment and inhaler technique at each visit.
- It is important to monitor response to treatment and any side effects and to adjust the dose accordingly. Periodic adjustments in treatment may be required to attain control.
- Once good control is maintained over 2-3 months, the ICS dose should be carefully titrated to minimum dose that will maintain good symptom control, minimize exacerbation risk while reducing potential side effects.
- The patient should be trained to use the inhaler correctly, check their technique and finally schedule a patient follow up visit. Likewise, after starting initial controller treatment it is vital to review response after 2 -3 months, or according to clinical urgency

- Frequency of follow up visits depends on the patients' level of symptom control and response to treatment. Patients should be seen at 1-3 months after starting treatment and every 3-12 months thereafter.

- After an exacerbation a review visit should be scheduled within early on 1 week

7.3.1 Issues to be assessed and addressed before considering a step-up in treatment

- Are symptoms due to asthma or other co morbid conditions
- Incorrect inhaler technique
- poor adherence
- continuous exposure to allergens and environmental triggers
- Modifiable risk factors, e.g., smoking
- Regular or overuse of SABA
- Anxiety, depression
- Medication side effects

7.3.2 Stepping up treatment

- If asthma remains uncontrolled despite good adherence and inhaler technique, the treatment may need to be stepped up for at least 2-3 months.

- Short-term step up of maintenance ICS for 1-2 weeks may be necessary, during viral infections or seasonal allergen exposure.

7.3.3 Stepping down treatment

- Consider stepping down once good asthma control has been achieved and maintained for 2-3 months on their current maintenance therapy, to find the lowest treatment that controls both symptoms and exacerbations, and minimizes side-effects.

- Choose an appropriate time for step-down (no respiratory infection, patient not travelling, not pregnant)

- Document baseline status and provide the patient with a written asthma action plan

- Do not completely withdraw ICS unless it is needed temporarily to confirm the diagnosis of asthma. Step down through available formulations to reduce the ICS dose by 25–50% at 2–3-month intervals

- Review asthma control every 3-6 months and more frequently when treatment has been changed or asthma is not well controlled.

7.4 Managing Asthma in specific conditions

7.4.1 Exercise Induced bronchoconstriction

- Exercise induced bronchospasm may indicate poorly controlled asthma, so assess symptoms, inhaler technique, adherence to medication and step up controller treatment.

- Regular controller treatment with ICS significantly reduces exercise induced bronchoconstriction. Though SABA and LABA are also effective but tolerance develops with regular (more than once daily use).

- Those taking ICS -formoterol on as needed basis in mild asthma can use the same prior to exercise and do not need to prescribed a SABA

- Training and Warm up before exercise also reduces the incidence and intensity of Exercise induced bronchospasm

7.4.2 Pregnancy

- Exacerbations and poor asthma control in pregnancy occur due to hormonal changes or due to stopping of medications by mother that it may affect the baby or it may be due to inadequate treatment by the practitioner.

- Advantages of actively treating asthma in pregnancy markedly outweighs any potential risks of usual medications. Poor control and exacerbations are associated with worse outcomes for both baby and the mother.

- Monthly monitoring of asthma to be done during pregnancy. Usual controller medicines with reliever if needed, should be taken during labour and delivery. **Avoid LTRA and theophylline during pregnancy.**

- Hyperventilation during labour may induce bronchoconstriction and should be managed with SABA. Watch out for neonatal hypoglycemia especially in preterm babies if high doses of SABA have been given within 48 hours prior to delivery

7.4.3 Occupational asthma

- Asthma may be induced or aggravated by allergens or sensitizing agents at work. Rhinitis may precede asthma by up to a year. Persistent exposure is associated with worse outcomes.

- Improvement of symptoms when away from work and PEF monitoring, at and away from work often helps to establish the diagnosis.

- Early identification and elimination of sensitizers and removal of patient from any further exposure are important steps. Specialist referral is needed as it is important to diagnose objectively as the diagnosis can lead to change in occupation.

7.4.4 Aspirin exacerbated respiratory disease (AERD)

- AERD is prevalent in 7% in general adult asthma. In those with AERD, rhinosinusitis occurs before onset of asthma and there is hypersensitivity to aspirin and NSAIDS.

- A History of asthma exacerbation after taking aspirin or NSAIDs is highly suggestive AERD. Acute asthma attack can occur within minutes to 1-2 hours after ingestion of aspirin or NSAIDs accompanied usually by rhinorrhea, conjunctival irritation, flushing of head and neck and may sometimes progress to severe bronchospasm, shock and respiratory arrest.

- Patients with AERD should avoid aspirin or NSAIDs. ICS are the mainstay of asthma treatment in AERD but OCS may sometimes be needed. LTRA may also be useful.

- An additional option is in hospital aspirin desensitization which should be done only by a specialist. This can be associated by GI adverse effects such as gastritis and GI bleeding.

7.4.5 Allergic bronchopulmonary aspergillosis (ABPA)

- ABPA is characterized by repeated episodes of wheezing, fleeting pulmonary opacities and development of bronchiectasis sometimes with malaise, weight loss and hemoptysis and occurs due to a hypersensitivity response to a common mold, Aspergillus Fumigatus

- Diagnosis is based on serum IgE, Specific IgG to A. fumigatus, blood eosinophilia and radiological findings

- First line therapy is oral corticosteroids, eg: 4 month tapering course with itraconazole reserved for those with exacerbations or requiring long term corticosteroids

7.5 Referral for specialist consultation

- When asthma remains poorly controlled
- When the diagnosis of asthma is uncertain
- When you suspect occupational asthma – refer for confirmation and specific advice about eliminating exposure and treatment
- Severely uncontrolled asthma or near fatal asthma attack such as requiring ICU admission and mechanical ventilation
- Need for long term oral prednisolone or frequent courses of oral steroids
- Recommendation to do Pulmonary function test which are not available
- Refer earlier if diagnosis is uncertain and symptoms are severe

8.0. Non-Pharmacological interventions

Vaccination

- Influenza vaccination yearly for patients with moderate to severe asthma as Influenza infections can cause asthma exacerbations. The risk of influenza infection is reduced by annual vaccination

Smoking cessation

- Patients should be advised on the dangers of smoking and second-hand smoke exposure and be offered appropriate help to stop smoking
- Cessation counselling at each visit and offer pharmacological therapy if needed or refer to smoke cessation clinic if available
- Advise parents of asthmatic children to quit smoking and make their living environment smoke free
-

Avoidance of occupational exposures

- Identify and try to eliminate occupational sensitizers or remove sensitized patients from further exposure to these agents
- Use of nonpolluting heating and cooking sources and for sources of pollutants to be vented outside

Physical Activity

- Advise patients to engage in regular physical activity
- Provide advice on prevention of exercise induced breakthrough symptoms such as low dose ICS formoterol before exercise and warm up before exercise

Avoidance of medicines that may worsen asthma

- Ask about concomitant medicines.
- Aspirin and NSAIDS are not generally contraindicated unless there is a history of previous reactions
- Decide about prescription of beta blockers on case-by-case basis

Avoidance of indoor allergens and pollution

- Eliminating mould and moist conditions
- Reducing Exposure to House Dust Mites
  - Use bedding encasements
  - Wash bed linens weekly/ Avoid down fillings
  - Limit stuffed animals to those that can be washed
  - Reduce humidity level
- Reducing Exposure to Pets

Weight reduction

- Weight loss interventions should be considered for those overweight and obese to improve asthma control

9.0 Management of asthma exacerbations

Exacerbations are sub-acute or acute progressive worsening of symptoms and lung functions from the patient's usual status. A brief focused history and relevant physical examination should be done concurrently with the prompt initiation of treatment. Severity of the exacerbation and factors that increase the risk of death should be taken into account.

- History should include timing of onset, cause of exacerbation if known, severity of symptoms, exercise limitation, effect on sleep along with all current medication with doses, adherence and response to them

- Assess vital signs, level of consciousness, use of accessory muscles, presence of wheeze, ability to complete sentences, oxygen saturation and for complicating factors like pneumonia and anaphylaxis
  Also assess for signs of alternative conditions that could be the cause of acute breathlessness such as cardiac failure and pulmonary embolism

- Oxygen saturation should be closely monitored by Pulse oximetry and oxygen saturation <90% signals, the need for aggressive therapy
  ABG should be considered for patients who do not respond to initial treatment or are deteriorating. PaO2<60mmHg and either normal or increased PaCO2, especially >45mmHg indicate respiratory failure

- Chest Xray should be done, if the patient is not responding to treatment or there are signs of parenchymal involvement, pneumothorax, or an alternative cardiopulmonary condition is suspected.

Signs of Mild or moderate Exacerbation	**Severe Exacerbation**	**Very severe/ life threatening**
Talks in phrases, prefers sitting to lying	Breathless at rest/ Hunched forward	Exhaustion
Respiratory rate increased, no use of accessory muscles	Inability to complete sentences in one breath/ use of accessory muscles	cyanosis, silent chest,
Pulse rate 100-120/min	Heart rate ≥ 120 beats/min	Hypotension
Not agitated	Agitated	altered conscious level
SPO2 -90-95%	Respiratory rate>30/minute	
PEF >50 % predicted	PEF 33-50% of best or predicted	

9.1 Factors that increase the risk of asthma related death

- Hospitalization or emergency care visit in the past year
- Currently using or having recently stopped using OCS
- Not currently using inhaled corticosteroids or poor adherence
- Over use of SABA, especially use of more than a canister monthly
- Food allergy in a patient with asthma
- Several comorbidities including pneumonia, diabetes and arrhythmia show an increased risk after hospitalization for asthma exacerbation.
- A history of near fatal asthma requiring intubation and mechanical ventilation

9.2 Treatment

- If there are signs of severe exacerbation or life-threatening signs, arrange immediate transfer to an acute care area facility where monitoring and expertise are available. Mild and moderate exacerbations can be managed at primary care setting depending on available resources.

- Give inhaled SABA i.e. Salbutamol in repeated doses by MDI and spacer - 4-10 puffs of 100 mcg salbutamol repeated every 20 minutes for 1 hour or using a nebulizer

- Administer controlled flow Oxygen via nasal cannula or mask to maintain SPO2 levels of 93-95%

- Systemic corticosteroids should be administered within the first hour. Intravenous steroid when patient is too dyspnoeic to swallow or when patient requires ventilatory support, otherwise, can administer oral prednisolone or equivalent to 1mg /kg/day up to a maximum of 50mg/day and it should be continued for 5 to 7 days

- For patients already on controller medicine, increase the dose for next 2-4 weeks and those not taking controller medication should be started on regular ICS containing therapy.

- For patients presenting with anaphylaxis, in addition to standard asthma treatment, intra muscular epinephrine is indicated

- **Reassess in 1 hour: Assess clinical status and oxygen saturation**

- **If the patient is not responding to treatment**:
  - Increase frequency of SABA dosing via MDI and spacer or by nebulizer
  - Add ipratropium to nebulized salbutamol
  - Decide on admission based on clinical status, response to treatment, history of exacerbations, and ability to manage at home
  - Consider magnesium sulphate IV (2g infusion over 20 minutes) for those not responding for initial treatment with persistent hypoxemia
  - Arrange immediate referral to a higher level if there are signs of severe exacerbation, hypoxia and cannot be managed at that level
  - Antibiotics only if evidence of infection

- **If the patient is responding to treatment:**
  - prescribe regular controller therapy or increase current dose. Before discharge, arrange ongoing treatment.
  - Continue increased controller doses for 2–4 weeks, and reduce reliever to as-needed.
  - Arrange early follow up
  - Provide the patient with a written asthma action plan and Check inhaler technique before discharge

10.0 Individual self-management plan

Patients with asthma should be provided with education and skills to manage their asthma. Health care worker should:

- Educate the patient on asthma, asthma triggers and on self-monitoring of symptoms

- Educate to use inhalers effectively by physical demonstration and check patient technique again

- Educate regarding medications (controller and quick-relief) and importance of adherence

- Ask the patient to keep an asthma diary that can help patients to monitor their asthma.

- Provide a written asthma action plan so that the patient knows to recognize and how to respond for worsening asthma, when and how to change the controller and reliever medicines

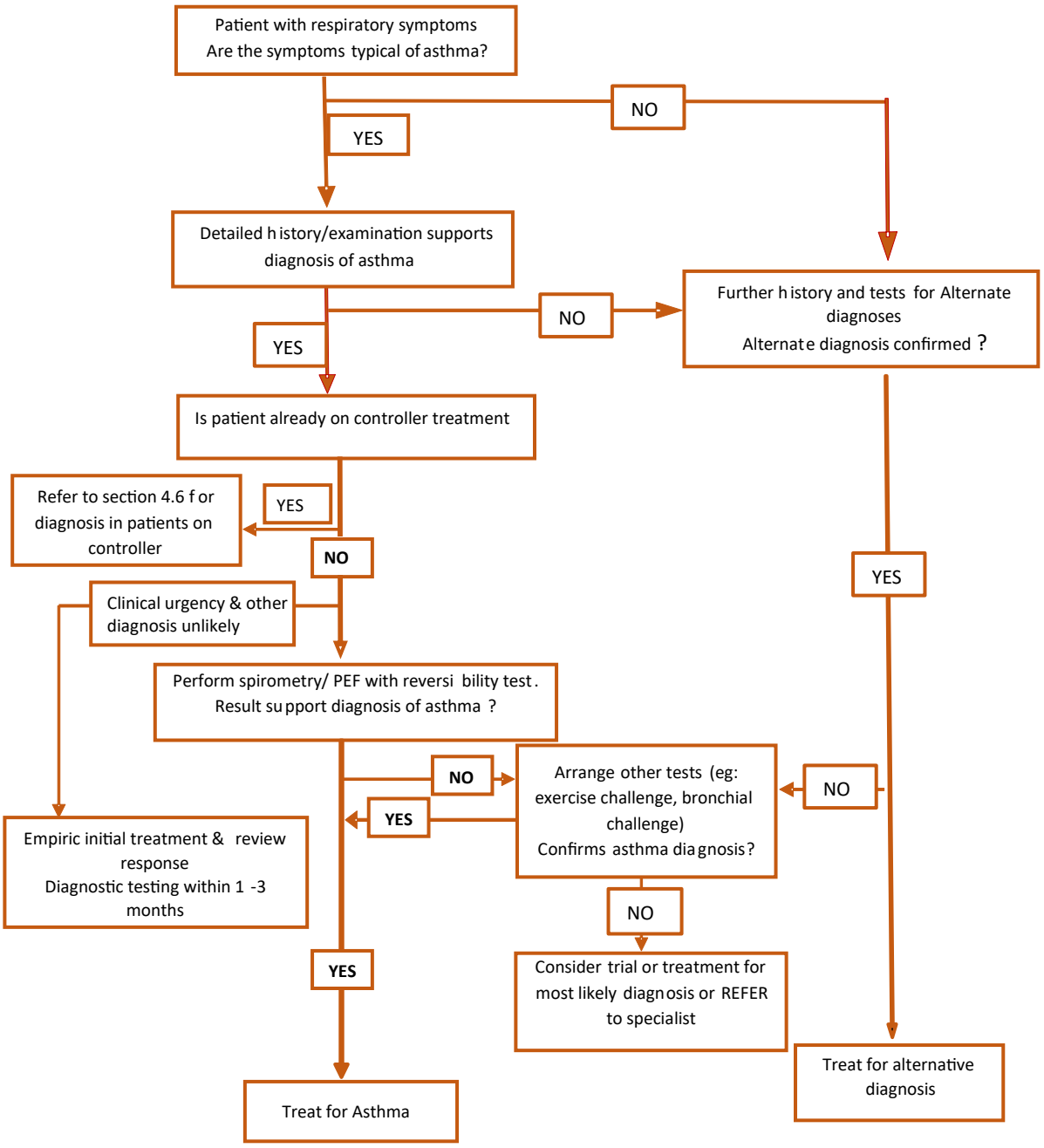
- Base the action plan on symptoms or PEF such as asthma symptoms interfering with normal activities or PEF has fallen >20% for more than 2 days.

- Instructions should be given in the plan, how and when to use OCS that includes those patients who show no response to increased controller and reliever for 2-3 days and those who deteriorate rapidly or those with PEF <60% of their baseline.
  Typically, a short course of OCS, 40-50 mg/day for 5 to 7 days is given.

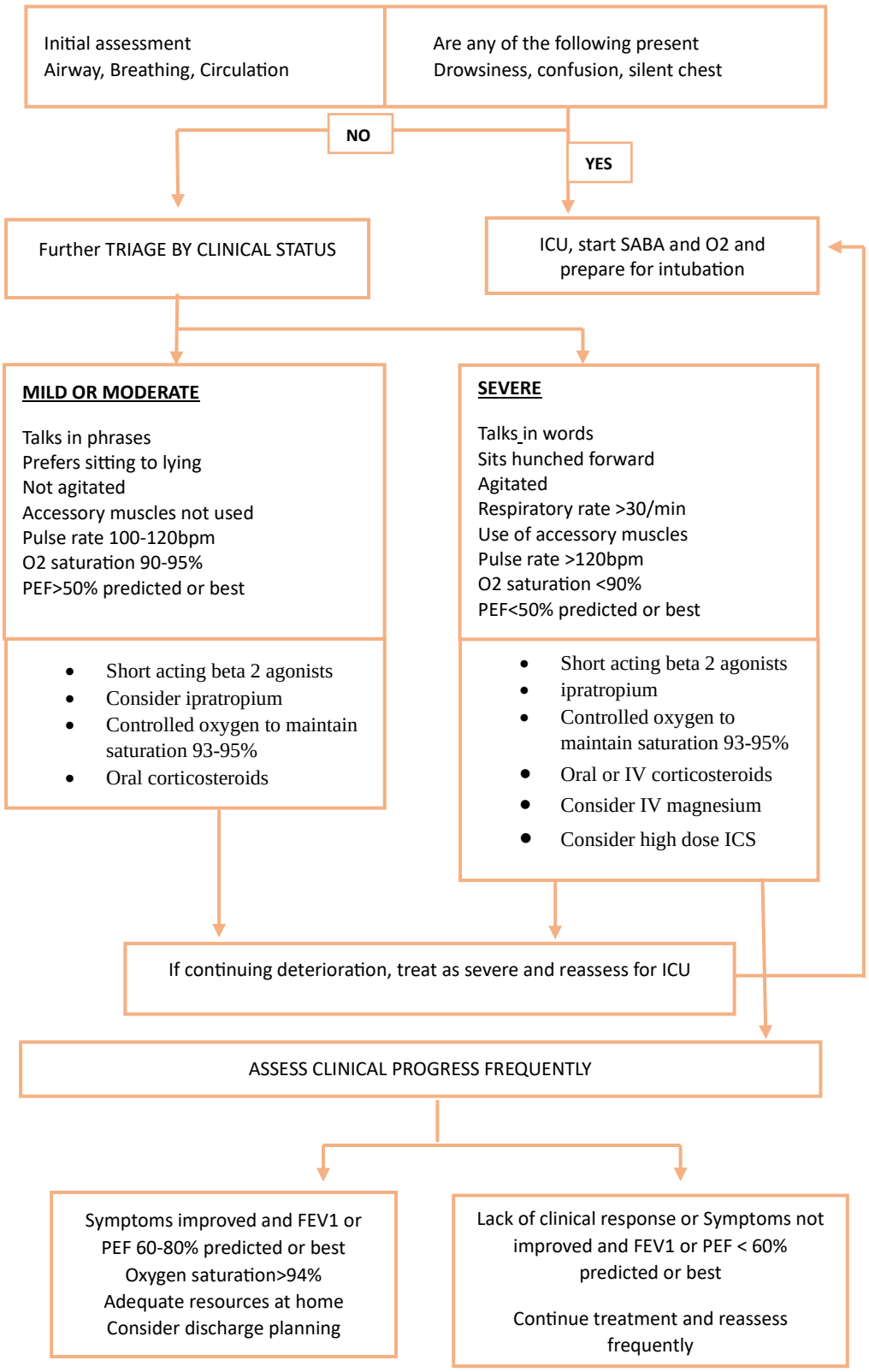
- Plan should also include how to access medical care if symptoms fail to respond

11.0 Algorithms

11.1 Diagnostic Flowchart



11.2 Management of asthma exacerbation



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