Chronic Obstructive Pulmonary Disease Pathway

Background

- COPD is the number 2 cause of mortality in India
- Obstructive lung diseases are the 2nd most common reason for presentation to primary care practitioners in India
- Up to 70% of COPD worldwide may be un-diagnosed
- Smoking and environmental exposures (e.g. indoor fuel burning) are major risk factors for COPD

India specific challenges to overcome

- Diagnostic challenges
    - Spirometry access + training of providers
        - Adequate technique required to generate meaningful flow curves for diagnosis
    - Diagnostic entities unique to India
        - Non-smoker COPD (e.g. biomass fuels)
        - TB-associated COPD/ Post TB
        - Occupation associated
    - In the absence of spirometry, how do we diagnose?
        - Current standard practice in India dx based on symptom complex
- Cost barriers
    - Inhalers are costly
- Cultural barriers
    - Stigma associated with inhaler use
    - Compliance issues with increasing number of inhalers (not necessarily India-specific)
- Existing practice
    - Broad use of theophylline

Diagnosis

- Consider COPD if history of shortness of breath/dyspnoea or chronic cough, and risk factors for COPD – consider duration of symptoms
- Consider and rule out differentials, including:
    - Respiratory: Asthma, bronchiectasis, TB, obliterative bronchiolitis, diffuse bronchiolitis (sputum and CXR)
    - Cardiac: heart failure (see CSA HF pathway)
- **Spirometry** is required for diagnosis: post-bronchodilation FEV1/FVC < 0.70
    - See spirometry instructions in Appendix
    - Training staff in adequate spirometry technique will be a challenge
- CXR: not diagnostic but can rule out other causes. COPD may present with lung hyperinflation
- IF spirometry unavailable (all CSA sites to be given spiro)

- In the absence of spirometry, diagnosis of COPD in India is often made based on symptom complex
- Symptoms suggestive of COPD include:
- There is significant overlap between COPD symptoms and other lung pathologies, including asthma, bronchiectasis, interstitial lung disease, etc.
- If COPD is diagnosed based on symptoms alone, trial therapy with careful follow up. If no clinical improvement, diagnosis **must** be revisited

Severity Assessment

- COPD severity can be categorised based on symptoms (mMRC scale; see appendix)
- Frequency of exacerbations/hospitalisations for COPD

Management of comorbidities

- COPD specific: sarcopenia/fragility, weight loss – Promote nutrition
- Others: cardiovascular diseases, metabolic syndrome, osteoporosis, lung cancer, mental health
- See CSA pathways for appropriate management

Non-pharmacological management

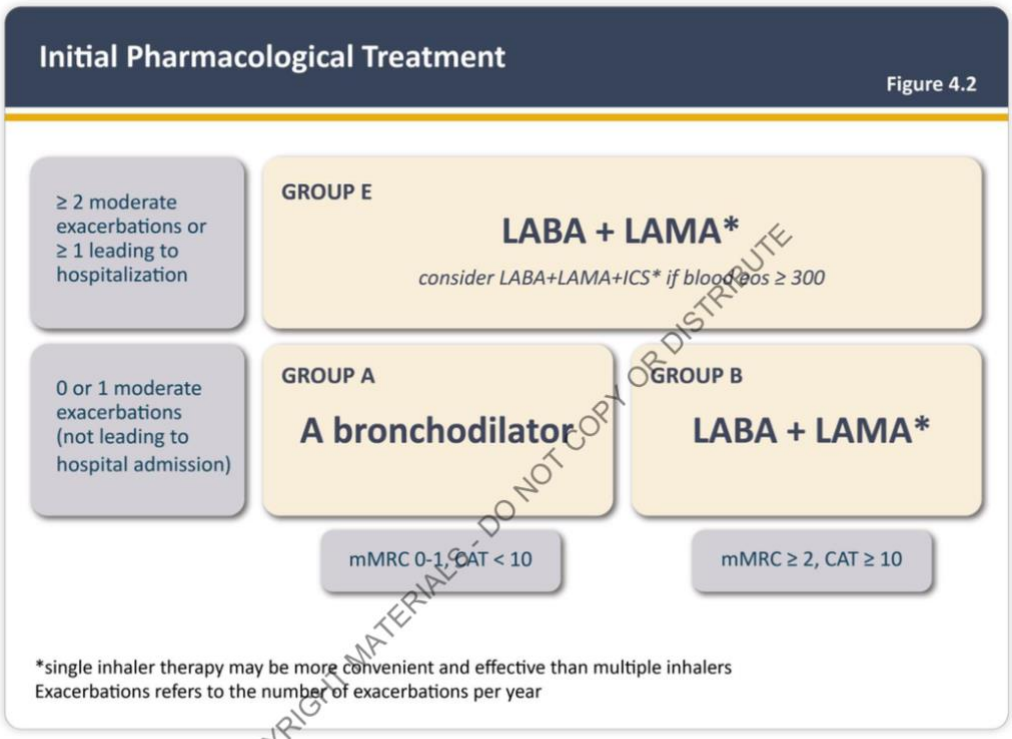
- **Smoking cessation**
  - Do we need a CSA pathway for this?
- Reduce exposure to indoor smoke/biomass fuels
  - Use of biomass fuels may be more prevalent in rural settings (i.e. places where CSA partner sites are)
  - How do we make this practical for people? This is a big structural issue
- Pulmonary rehab
  - Rehab/physiotherapy pathway TBD
  - Offer alternate occupation
  - Treat comorbidity

Maintenance medical therapy

- WHO basic minimum package:
  - Maintenance: Salbutamol PRN +/- PO theophylline, +/- theophylline if available
  - Exacerbation: abx, pred, salbumtamol, O2
- Need costings for all the below:
- SABA
  - Salbutamol
- LABA
  - Salmeterol or Formeterol
- SAMA
  - Ipratropium
- LAMA
  - Tiotropium
- ICS

Assess disease severity and initiate maintenance therapy

- mMRC system (appendix)
- A – less symptomatic and low risk of exacerbation
    - PRN bronchodilator – SABA or SAMA (see formulary for options) **OR**
    - Combination SABA/SAMA
- B – more symptomatic and low risk of exacerbation
    - Regular long-acting bronchodilator (LABA or LAMA) **AND**
    - PRN SABA
- E – high risk of exacerbation (>2 moderate exacerbations or >= 1 leading to hospitalization)
- ICS: Can consider if 2 or more exacerbations annually and if blood eosinophils greater than 300



Definition of abbreviations: eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

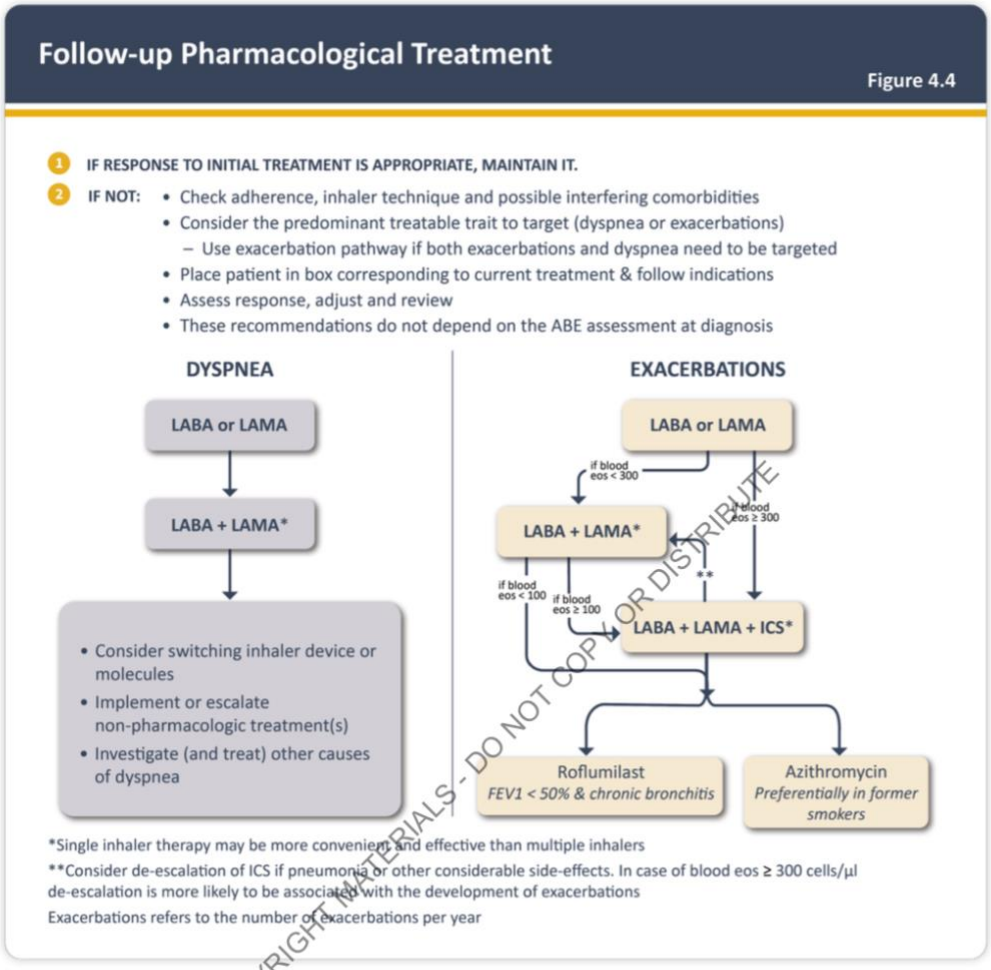


Figure 4.4 presents suggested escalation and de-escalation strategies based on available efficacy and safety data. The response to treatment escalation should always be reviewed. Patients, in whom treatment modification is considered, in particular de-escalation, should be undertaken under close medical supervision. We are fully aware that treatment escalation has not been systematically tested; trials of de-escalation are also limited and only include ICS.

Ongoing management

- COPD is a chronic disease and requires follow-up and medication titration
- A constant COPD cycle of care is required
- If patient is not improving or remains symptomatic despite initiation of medical therapy, consider and address:
    - Inhaler technique/non-compliance
    - COPD diagnosis – is there are more compelling differential diagnosis?
    - Exacerbation of COPD
    - Concomitant pathology
    - Need for additional inhaler
- If inappropriate response to treatment AND if inhaler technique adequate AND if diagnosis is still COPD, can consider additional agent:
    - If on LABA or LAMA □ LAMA + LAMA

    - If on LABA + LAMA and if eosinophils > 300 □ LABA + LAMA + ICS
    - If on LABA + LAMA and if eosinophils > 100 and if 2+ exacerbations a year □ LABA + LAMA + ICS
    - If on ICS and inadequate response to treatment, consider de-escalation of ICS
- How do we want to address roflumilast? Any role for azithro?

Preventative care
- Preventative vaccination
    - COVID (all), flu (all), pneumococcal (65+ and high risk), pertussis

Interventions to avoid
- Do not use methylxanthines (theophylline) routinely for the management of COPD
    - Inhalers are first line therapy – they are safer and more effective
- Do not use inhaled steroids as monotherapy in COPD
- Mucolytic agents are not effective for the treatment of COPD
- Do not use long term oral steroids for the treatment of COPD

Management of advanced COPD (referral to specialist)
- Supplemental O2
- Procedural interventions
- Palliative care

Indications for home oxygen therapy (given now possible after COVID)
- From UpToDate
- PaO2 ≤55 mmHg (7.32 kPa) or SaO2 ≤88 percent
- If cor pulmonale AND
    - PaO2 ≤59 mmHg (7.85 kPa) or SaO2 ≤89 percent
    - EKG evidence of P pulmonale
    - Hematocrit >55 percent
    - Clinical evidence of right heart failure

Management of exacerbations
- Assess stability
    - Transfer patient if unstable, or if signs of airway compromise
- Cardinal symptoms of COPD exacerbation
    - Increased frequency/severity of cough
    - Increase/change in sputum
    - Increased dyspnoea
- Consider differentials (see relevant CSA pathways for management)
    - Respiratory: CAP, COVID, pulmonary embolism, pneumothorax, ptld
    - Cardiac: HF, ACS
    - Other: sepsis
- Airway management
    - All patients: Supplemental O2 if hypoxic, titrate to SpO2 88-92%
    - NIV or intubation according to patient status and operator availability

- Relevant investigations (not required if outpatient management)
    - ABG – not often available or understood for management
    - CXR
    - ECG
    - Electrolytes
    - Covid swab (CXR and CBC – infection)
- Determining outpatient vs inpatient management
    - Potential indications for inpatient management
        -
- Initial therapy
    - Regular SABA +/- SAMA via spacer
    - Prednisone 40mg for 5 days
- Threshold for antibiotic administration
    - 2 or more of:
        - Increased dyspnoea
        - Increased sputum volume
        - Increase sputum purulence
    - Abx option
        - Azithromycin
        - 2nd or 3rd generation cephalosporin
        - Amox/Clav
        - Potentially cipro for pseudomonal cover (though use in India given TB) – Duration (avoid Levi in view of its anti-tubercular action)
        - only Amox (BHS)

(Elderly + diabetics)

Appendices

mMRC system

mMRC Grade	Description
Grade 0	I only get breathless with strenuous exercise
Grade 1	I get short of breath when hurrying on the level or walking up a slight hill
Grade 2	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level
Grade 3	I stop for breath after walking about 100 metres or a few minutes on the level
Grade 4	I am too breathless to leave the house or I am too breathless when dressing or undressing

APPENDIX A

List of available drugs along with cost information

Drug Class	Drug name	Type	Brand	Pricing
SABA	Salbutamol	Rotacaps	Cipla - Asthalin	200 mcg - 60 capsules in 1 bottle- Rs 98/pack
		Metered dose inhaler	Cipla - Asthalin	Rs 110/ box
		Respules	Cipla - Asthalin	2.5mg/2.5 ml pack of 5 - Rs 28
	Levisalbutamol	Rotacaps	Cipla- Levolin	100 mcg- 30 capsules in 1 bottle - Rs 30/pack
		Metered dose inhaler	Cipla- Levolin	50 mcg inhaler / Rs 200 per pack
		Respules	Cipla - Levolin , Lupin- Salbair	0.63 Mg/ 1 respule- Rs 5 per respule, 0.63mg/2.5 mL respule - Rs 7 per respule
Combination - SABA and SAMA	Ipravent and Levosalbutamol	Rotacaps	Cipla - Duolin	60 capsules - 100 + 40 mcg/ Rs 144 per bottle
		Metered dose inhaler	Cipla - Duolin Forte	200 mdi inhaler - Rs 393
		Respules	Cipla - Duolin	3 ml respules - pack of 5- Rs 104
ICS	Fluticasone	Rotacaps		
		Metered dose inhaler	Cipla - Flohale	125 mcg/dose, Rs 267/ inhaler

		Respules	Cipla-Flohale	0.5 mg respules - Rs 240
	Budesonide	Rotacaps	Cipla - Budecort	200 mcg , 30 capsules in 1 bottle - Rs 92
		Metered dose inhaler	Cipla-Budesonide inhaler	100, 200 mg- Rs 400
		Respules	Cipla - Budecort respules	0.5 mg respules, Rs 115 - pack of 5
	Ciclesonide	Rotacaps	Cipla - Ciclohale	400 mcg -30 capsules , Rs 195
		Metered dose inhaler	Cipla-Ciclohale, Ranbaxy - Osonide	Ciclohale- 160 mcg- Rs 350, Osonide- 160 mcg- Rs 300
		Respules	NA	
Triple therapy, combination drug ICS+LABA+LAMA	beclometasone dipropionate/formoterol fumarate/glycopyrronium bromide (BDP/FF/G)	pressurized metered-dose inhaler	TRIMBOW®, Chiesi Farmaceutici SpA	Single dosage- 87/5/9 µg (two inhalations twice daily)
	Fluticasone Furoate/Umeclidinium/Vilanterol FF/UMEC/VI	Multidose dry-powder inhaler (MDDPI) formulation to be delivered through the ELLIPTA inhaler device (Single-Inhaler Triple Therapy (SITT))	TRELEGY ELLIPTA®, GlaxoSmithKline	Single dosage- 92/22/55 µg (one inhalation per day) - Maintenance treatment of both asthma and COPD

	GlaxoSmithKline FF/UMEC/VI	Dry powder inhaler	Trelegy Ellipta	Once daily - Maintenance treatment of COPD; ₹2822/box
	AstraZeneca BDP/FOR/GP Beclomethasone/Formoterol/Glycopyrronium	pressurized metered-dose inhaler	BREZTRI	Twice daily (CJ: can't find this drug online; probably not sold in India yet)
	Novartis IND/GLY/MF Indacaterol/Glycopyrronium/Mometasone furoate	Dry powder inhaler	Enerzair Breezhaler	Once daily (CJ: can't find this drug online; probably not sold in India yet)
	Glenmark GLY/FOR/FP Glycopyrronium/Formoterol/Fluticasone propionate	Dry powder inhaler	Airz-FF	Twice daily ; ₹535/box of 30 capsules
	Cipla GLY/FOR/BUD Glycopyrronium/Formoterol/Budesonide	Dry powder inhaler	Glycohale-FB	Twice daily; ₹184.7/box of 10 rotacaps
	Tiotropium/Formoterol/Ciclesonide (TFC)	Dry powder inhaler (DPI)/ Pressured metered dose inhaler (pMDI)	Triohale®, Cipla	18 mcg/12 mcg/400 mcg - once-daily; ₹1132/ inhaler with 200 metered doses

ICS and LABA-combination	Fluticasone and Salmeterol	Rotacaps	Macleods Pharma-Flutrol, Zydus Cadila-Forair R cap, Seroflo-500 rotacaps	Flutrol rota capsule- 50/100 mcg- Rs 155, Forair R cap-100/50 mcg- Rs 361- for 30 capsules, Seroflo500 rotacaps -500/50 mcg- Rs 472
		Respules	Lupin Labs-Esiflo,	Esiflo- 100/50 mcg- 30 capsules Rs 108
		Metered dose inhaler	Glenmark - Airtec SF, Sun pharma-Combitide	Airtec SF- 50 mcg/100 mcg- Rs 330, Combitide - 25/125 mcg - Rs 292
(rapid onset)	Budesonide and Formoterol	Rotacaps	Zydus cadila - Formonide Resicaps ,	Formonide resicaps- 200/6 mcg- Rs 147- for a bottle of 30
		Respules		
		Metered dose inhaler	Kopran Pharma-VentFB inhaler	Vent FB inhaler - 100/6 mcg- Rs 134
	Fluticasone and Vilanterol	Rotacaps		
ICS and SABA combo	Budesonide (0.5 Mg) + Salbutamol / Albuterol(1.25 Mg)			Budesal 0.5mg 2ml Packet Of 5 Respules for ~ Rs 240
				Derisal 0.5mg 2ml Packet Of 7 Respules for ~ RS 340

	Levosalbutamol (50mcg) + Beclometasone (50mcg)		Cipla	Aerocort Inhaler for ~Rs 270 / 1 Packet 200 MDI Inhaler
		Respules		
		Metered dose inhaler		
LABA+LAMA	Formoterol Fum.	single inhaler device disposable	Tioform	Dosage- 6 or 12 µg (18/12 mcg; 9/6 mcg); ₹677
Prednisolone		(40-50mg)	various brands	40mg oral - avg Rs 25/ strip of 10 tablets
			Depomax S 40mg Injection, Mpss 40mg Injection	Rs 100-150