

Stable COPD Treatment Guidelines

Diagnosing COPD

Think of diagnosis of COPD for patients who are:

- over 35 years old
- cigarette, cannabis or shisha smokers or ex-smokers (>10 pack years)
- have any of these symptoms:
 - exertional breathlessness
 - chronic cough
 - regular sputum production
 - frequent winter 'bronchitis'
 - wheeze
- and have no clinical features of asthma (see table below)

Exclude other potential diagnoses

- **Physical examination** (possible cardiac causes, TB, obstructive sleep apnoea, localised wheeze – ?lung cancer, clubbing)
- **Chest X-Ray** – TB / lung cancer
- **Serial peak flow diary** – 20% or more variation suggests asthma (see below)
- **Bloods** i.e. FBC, ESR, TFT (i.e. anaemia, polycythaemia, Hypothyroidism, TB)

Consider bronchiectasis if producing large amounts of sputum daily, frequent infections or basal crackles (may also indicate pulmonary fibrosis). (Refer to local bronchiectasis treatment guidelines)

Perform spirometry post bronchodilator (see below):

Spirometry should be carried out by a healthcare professional competent in its performance.

Airflow obstruction is defined as:

- FEV₁/FVC ratio is <0.7 and FEV₁ <80% predicted **OR**
- FEV₁/FVC ratio is <0.7 and FEV₁ ≥80% predicted **and** symptoms present

Perform oximetry

Diagnose asthma when:

- serial peak flow measurements show ≥ 20% diurnal or day-to-day variability or
- spirometry returns back to normal after steroid trial or bronchodilator
- there is a > 400ml response to bronchodilators (see below) or
- there is a > 400ml response to a steroid trial (see below)

READ CODE as ASTHMA H33

Diagnose COPD when:

- Patient has proven airways obstruction **and**
- serial peak flow measurements show no significant diurnal or day-to-day variability and
- there is a < 400ml response to bronchodilators (see below) or
- there is a < 400ml response to a steroid trial (see below)

READ CODE as COPD H3

Diagnose asthma & COPD (ACOS*) when:

- At new assessment, the patient responds to bronchodilator / steroid reversibility trial but evidence of obstruction remains on spirometry after treatment optimisation.
 - In patients who have been diagnosed with COPD, spirometry then found to improve or show variability over time
 - In patients who have been diagnosed with asthma, spirometry then found to show fixed airway obstruction over time
- READ CODE as ASTHMA H33 AND COPD H3 (ACOS*) Treat as asthma & COPD

Consider an alternative diagnosis in:

- younger people with symptoms of COPD where the FEV₁/FVC ratio is ≥ 0.7
- older people without typical symptoms of COPD where the FEV₁/FVC ratio is < 0.7

Symptomatic patients under age 50:

- COPD rare
- measure alpha-1 anti-trypsin
- ask about cigarette, cannabis and shisha and passive smoking

*ACOS = Asthma COPD Overlap Syndrome

Reversibility testing is used to exclude asthma, not diagnose COPD

Determine and EMIS Read code disease severity (see table below)

Start appropriate treatment (see flowchart overleaf)

Reassess diagnosis in view of response to treatment

Bronchodilator reversibility

Spirometry should be measured before and after an adequate dose of inhaled bronchodilator. Use nebulised bronchodilator 2.5mg – 5mg salbutamol. Alternatively, use inhaled bronchodilator (using high doses via a disposable spacer) 4 puffs x 100 micrograms salbutamol. Measure lung function 15 minutes after β₂-agonist.

Steroid trial to exclude asthma

Spirometry must be measured before and within 24 hours of completing an adequate course of steroid. Use oral prednisolone 30mg (non-enteric coated) every morning for 2 weeks.

Spirometry

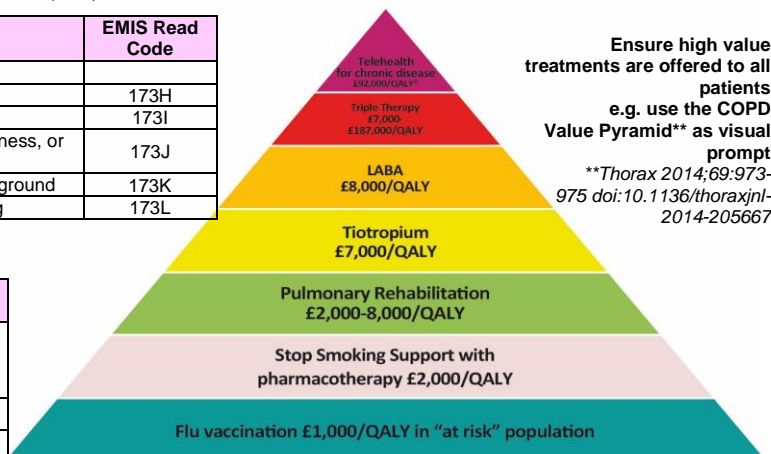
Obstructive spirometry is required to make a diagnosis of COPD. NB FEV₁/FVC ratio is a net result and obstruction may be masked by obesity. Spirometry is a near patient test and therefore should be performed in the community. Support is available from the Integrated Respiratory Team regarding spirometry services, provision and training. (Refer to local service)

Pulse oximetry

Measure in any patient with acute or worsening breathlessness to identify new or worsening respiratory failure, the need for admission and to assess the need for referral for Long Term O₂ therapy (SaO₂ < 92% on air) in stable patients with severe disease (FEV₁ < 50%) or new ankle swelling. During acute exacerbations, aim for saturation of 88-92% pending arterial blood gases or range documented on Patient Specific Protocol (PSP).

MRC Breathlessness Scale	EMIS Read Code
0 No breathlessness	
1 Not troubled by breathlessness except on strenuous exertion	173H
2 Short of breath when hurrying or walking up a slight hill	173I
3 Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace	173J
4 Stops for breath after walking about 100m or after a few minutes on level ground	173K
5 Too breathless to leave house, or breathless when dressing or undressing	173L

Grading of airflow obstruction			
Post-bronchodilator FEV ₁ /FVC ratio	FEV ₁ % predicted	Post-bronchodilator	EMIS Read Code
<0.7	≥ 80%	Stage 1 - Mild***	H36
<0.7	50-79%	Stage 2 - Moderate	H37
<0.7	30-49%	Stage 3 - Severe	H38
<0.7	≤ 29%	Stage 4 – Very Severe	H39



Ensure high value treatments are offered to all patients e.g. use the COPD Value Pyramid** as visual prompt

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***Symptoms should be present to diagnose COPD in people with mild airflow obstruction

Stable COPD Treatment Guidelines

IDENTIFY & TREAT TOBACCO DEPENDENCE AT EVERY REVIEW. TREAT & CODE AS ANY OTHER RELAPSING, REMITTING LONG-TERM CONDITION.

Ask about current and past tobacco, cannabis, shisha & passive smoking.

Provide brief quit smoking advice yourself - http://www.ncsct.co.uk/publication_very-brief-advice.php

- Measure CO routinely at every review of a current or recently quit smoker. Assess patient motivation to quit
- Offer full range of COMBINATION nicotine replacement therapies (NRT) and / or varenicline by trained HCP in line with local guidance and referral to quit smoking services for behavioural and psychological support. Ensure follow-up of tobacco dependence treatment arranged. Useful resources are available at: <http://www.londonsebate.nhs.uk/helping-smokers-quit/>

Refer to local **Stop Smoking Services** by phone or email

EXPLAIN, OFFER AND REFER TO PULMONARY REHABILITATION (PR) EVERY PATIENT WITH BREATHLESSNESS MRC≥3 (or hospital admission for COPD or frequent exacerbations irrespective of MRC score, provided COPD diagnosis confirmed). If MRC score 1 or 2 offer EXERCISE ON REFERRAL and local LIFESTYLE EDUCATION program.

- Perform Spirometry – NB obstructive spirometry can indicate COPD, asthma or both.
- Calculate BMI – NB Raised BMI may mask obstructive spirometry but obesity is also a common contributing cause of breathlessness.
- Where BMI > 30, excessive sleepiness and/or low O₂ sat consider referral for respiratory assessment, sleep studies, measure venous bicarbonate.
- Offer pneumococcal and annual influenza vaccination and promote influenza vaccination for health care providers and carers to protect patients.
- Ask whether breathlessness has ever been frightening and identify and address anxiety / depression if present.
- Assess for co-existing ischaemic heart disease, heart failure, diabetes and osteoporosis risk and treat as appropriate.
- Offer personalised information on COPD e.g. First steps to living with COPD, BLF website - <http://www.blf.org.uk/support-for-you/copd>
- Signpost to local patient support group e.g. Breathe Easy - <https://www.blf.org.uk/support-for-you/breathe-easy>
- Explore inhaler use and beliefs – do not step up if not using inhalers appropriately and / or tobacco dependence not already being addressed.
- Check inspiratory flow. Check and optimise inhaler technique (MDI always with spacer device).
- Explore and develop patient confidence in self-management, including appropriateness of exacerbation pack. Offer appropriate diet and physical activity advice to all patients. Consider dietitian involvement.

Guide to Inhaled therapy: For use with patients with spirometry confirmed diagnosis of COPD

FEV₁ guides disease severity / prognosis but assess symptoms and exacerbation rate to determine inhaled therapy

Start at step appropriate to symptoms (including MRC score, page 1) and exacerbation rate

Review patients with mild - moderate COPD (FEV₁ < 80%) once a year and severe COPD (FEV₁ < 50% twice a year)

PRESCRIBE INHALERS BY BRAND NAME except non-breath actuated salbutamol pMDI

The inhaler choices suggested below are for newly diagnosed patients, those that cannot use their current inhaler device correctly or are undergoing review of treatment. Patients should not be switched between inhaler devices unnecessarily and without appropriate counselling.

Step 1 MILD <ul style="list-style-type: none"> • Few Symptoms ≤ 1 exacerbation / year 	PRN SABA / SAMA <ul style="list-style-type: none"> • Salbutamol MDI 100 mcg, 2 puffs QDS / PRN and/or • Ipratropium bromide MDI (Atrovent® MDI) 20 mcg, 2 puffs QDS / PRN 	Treat tobacco dependence
Step 2 MODERATE <ul style="list-style-type: none"> • Breathless on exertion, MRC 2 ≤ 1 exacerbation / year 	Regular LAMA (and continue SABA, stop SAMA) <ul style="list-style-type: none"> • Tiotropium 10 mcg OD (Braltus® Zonda®) OR • Tiotropium 18 mcg OD (Spiriva® Handihaler®) OR • Umeclidinium 55 mcg OD (Incruse® Ellipta®) 	Check inhaler technique and inspiratory flow No MDI without spacer
Before adjusting inhaled therapy:	Treat tobacco dependence. Measure Oxygen saturations. Arrange GP review. Refer to pulmonary rehabilitation. Consider indication for referral to respiratory physician (see page 4)	
Step 3 SEVERE <ul style="list-style-type: none"> • Choose A OR B (B if also asthma) • Breathless on minimal exertion, MRC 3 and / or • ≥ 2 exacerbations / year • Re-confirm diagnosis (review spirometry) 	A. Regular LAMA & LABA or LABA/LAMA combination <ul style="list-style-type: none"> • Tiotropium 10 mcg OD (Braltus® Zonda®) OR • Tiotropium 18 mcg OD (Spiriva® Handihaler®) AND • Salmeterol MDI 25mcg, 2 puffs BD via spacer OR • Umeclidinium 55 mcg with Vilanterol 22 mcg OD (Anoro® Ellipta®) (Continue PRN salbutamol) 	B. Regular ICS/LABA combination If concomitant asthma must be on: <ul style="list-style-type: none"> • Beclometasone with formoterol (Fostair® MDI) 100/6 2 puffs BD via spacer device OR • Fluticasone Furoate 92 mcg with Vilanterol 22 mcg (Relvar® Ellipta®) OD OR • Budesonide with formoterol (DuoResp® Spiromax®) 160/4.5mcg 2 inhalations BD or 320/9mcg 1 inhalation BD (Continue PRN salbutamol)
Step 4 VERY SEVERE <ul style="list-style-type: none"> • Progressive breathlessness or ongoing exacerbations despite step 3 and non-pharmacological management 	“Triple therapy” ICS/LABA and LAMA <ul style="list-style-type: none"> • If already on ICS/LABA combination, continue, and add Tiotropium 10mcg OD (Braltus® Zonda®) or Tiotropium 18mcg OD (Spiriva® Handihaler®) • If on single agent LAMA and LABA, continue LAMA, and replace salmeterol with Fostair® MDI 100/6 2 puffs BD with spacer device or DuoResp® Spiromax® 160/4.5mcg 2 inhalations BD or 320/9mcg 1 inhalation BD • If on LABA/LAMA combination inhaler (Umeclidinium with vilanterol (Anoro® Ellipta®)) change to Fluticasone Furoate with vilanterol 92/22mcg (Relvar® Ellipta®) OD with Umeclidinium 55mcg OD (Incruse® Ellipta®) Refer for respiratory physician input if worsening breathlessness / exacerbations or other indications (see page 4)	
		Treat tobacco Dependence <ul style="list-style-type: none"> Check inhaler technique and inspiratory flow Refer for Pulmonary Rehab Measure oxygen Saturations Consider indications for respiratory referral Minimise device changes where possible Prescribe by BRAND NAME rather than generically Discuss risk of pneumonia with ICS

Additional Prescribing Information (see <http://www.evidence.nhs.uk/formulary/bnf/current> for full prescribing info)

Inhaled Therapy Prescribing Tips

- The choice of inhaler device needs to take account of patient preference and an individual's willingness and ability to use the selected device. Refer to [UKIG Inhaler standards and competency document](#).
- The inhaler choices suggested above are for newly diagnosed patients or those that cannot use their current inhaler correctly. Patients should not be switched between inhaler devices unnecessarily and without appropriate counselling.
- MDI and spacer device remains the first choice of device.
- MDIs (apart from salbutamol) should always be used with a spacer. Spacers should be replaced every 6 – 12 months.
- Dry Powder Inhalers (DPI) require adequate inspiratory flow rates: see information below for individual devices.
- Ensure adequate inhaler technique with device(s) chosen including inspiratory flow above minimum needed and review regularly.
- The optimum dose and place in therapy of ICS in COPD without asthma continues to be debated. ICS adverse drug reactions are dose dependent and prescribers should consider the risks vs benefits of ICS in discussion with their patient when selecting an appropriate product.
- Withdrawal of ICS can be difficult, but may be indicated for some patients with COPD (See [NICE evidence commentary](#) and [Derbyshire guidance](#) for more information).
- Some patients admitted to hospital with community acquired pneumonia may have their ICS stopped and this should not be restarted unless there is an overriding indication for further ICS.
- Any patient on long-term high dose ICS (≥ 1000 micrograms of standard beclometasone daily or equivalent) should be provided with a High Dose Inhaled Steroid card (Contact Medicines Management for supplies or available via [London Respiratory Network](#)).
- For information on standard beclometasone equivalents, refer to document from [London Respiratory Network](#).
- Inhaled therapy prescriptions should only be changed after (re)addressing tobacco dependence and after review and optimisation of current technique and pattern of inhaler use.
- Patients who might benefit from further support to optimise inhaler use and technique can be referred to their community pharmacy for a [medicines use review](#) or a [new medicines review](#)

Emphysema

Inhaled therapy may be less helpful for symptom control in individuals where emphysema, as opposed to airway obstruction is the predominate cause of their breathlessness.

Beta Blockers (for treatment of co-existing heart failure)

β_2 blockers (predominantly cardio-selective) may confer reductions in mortality, exacerbations, and hospital admissions in patients with COPD, in addition to the benefits attributable to addressing cardiovascular risk. COPD is not a contraindication to β_2 blockers and β_2 blockers should be prescribed in COPD as for any patient according to cardiac or other (e.g. glaucoma) indications. (See <http://www.bmj.com/content/342/bmj.d2549>).

Mucolytics

- Consider only when chronic productive cough is identified as a key symptom by a patient, once bronchiectasis has been excluded.
- Review after 4 weeks and discontinue if no improvement in symptom.

'Nebulisers'

Some people with disabling breathlessness, despite treatment of tobacco dependence, completing PR and maximal inhaled drug treatment describe symptomatic benefit from nebulised bronchodilators driven by a compressor at home. Patients should not be asked to buy compressors themselves. Nebules should only be prescribed following assessment for and compressor provision by a respiratory team which includes ongoing compressor servicing.

Inhaler Device Types - The inhaler colour will vary depending on drug content

Aerosol and Spacer devices "Slow and Steady" inspiration			Dry Powder devices "Quick and Deep" inspiration			
Metered Dose Inhaler 	Volumatic® 	AeroChamber® Plus 	HandiHaler® 	Zonda® 	Ellipta® 	Spiromax® 
			Inspiratory flow required 30-60L/min	Inspiratory flow required 30-60L/min	Inspiratory flow required 30-90L/min NB: Anoro® Ellipta® shown above. Relvar Ellipta® has yellow cap. Incruse Ellipta has green cap	Inspiratory flow required 30-90L/min

Pulmonary Rehabilitation

Pulmonary Rehabilitation (PR) should be offered and explained to anyone with breathlessness due to COPD, including those who have had a recent hospitalisation for an acute exacerbation and those who consider themselves functionally disabled by COPD (usually MRC grade 3 or above). PR is highly cost effective in the management of COPD. PR also reduces admissions to hospital and is one of three interventions that prolong life in COPD; the other two are treatment of tobacco dependence and long term oxygen therapy in hypoxic patients.

Ask patients: **"Do you want to breathe better? Do you want to feel good? Do you want to be able to do more?"**

Information from BLF - <http://www.blf.org.uk/support-for-you/exercise/pulmonary-rehabilitation>

Refer to local Pulmonary rehabilitation services

USEFUL PULMONARY REHABILITATION RESOURCES

- 2 minute film: <http://www.nhs.uk/video/pages/pulmonaryrehabilitation.aspx>
- 7 minute film: http://www.oxleas.nhs.uk/video/pdescription-herrep-1/?clip=site-media/videos/Pulmonary_Rehab.flv
- 4 minute film: Living Well with COPD from British Lung Foundation: http://www.youtube.com/watch?v=KkQ2ii_UUF0
- King's PR educational YouTube video Part 1: <http://youtu.be/3goKl9Vr8iw> Part 2: <http://youtu.be/cthKnGK6Gzs>

CPD Exacerbations Treatment Guidelines

EXACERBATION ACTION PLAN

Educate patients regarding symptoms of exacerbation, how to distinguish from 'bad days' and what action to take early for proactive treatment.

Exacerbations can be associated with:

- ↑ breathlessness
- ↑ sputum purulence
- ↑ sputum volume
- ↑ cough

Every patient with COPD should have a jointly agreed personalised action plan ([access London Respiratory Network resources](#)) on how to respond quickly to symptoms of exacerbations (NB not every deterioration in symptoms is an exacerbation requiring antibiotics and steroids) by:

- **Increasing frequency of bronchodilator use**
- **Oral prednisolone (non-EC) 5mg tablets. Prescribe 40mg OM for 5 days** unless contraindicated (refer to [London Respiratory Network guidance](#) and GOLD guidance)
- **If purulent sputum – consider oral antibiotics (amoxicillin 500mg TDS for 5 days or doxycycline 200mg on day 1 then 100mg OD for 4 further days** (as per Public Health England [Managing Common Infections: guidance for primary care](#) – May 2017)
- **Letting a healthcare professional know if they are unwell and being seen as soon as possible**

Exacerbation Prescriber Tips:

- Establish understanding of and confidence in managing exacerbations before prescribing an 'exacerbation pack'.
- An 'exacerbation pack' is a course of corticosteroid tablets and antibiotics for a patient to keep at home. Instructions for use include contacting a healthcare professional if a pack is used or if their symptoms do not improve within 24 hours of starting the treatment.
- All patients should be reviewed in the practice after an exacerbation so as to log and read code the episode and discuss next steps e.g. association with tobacco smoking, PR referral, review of oxygen saturation and medication and need for respiratory review.
- Review the need for and use of this exacerbation medication regularly. Do not issue 'exacerbation packs' as a repeat prescription.
- An exacerbation pack is not always appropriate e.g. where a patient has cognitive impairment; communication is made more difficult by language barriers and any other situation where you do not feel confident that instructions have been understood.
- If a second exacerbation pack is used within 8 weeks consider:
 - sending sputum sample for MC & S **and**
 - whether a different exacerbation antibiotic should be prescribed e.g. clarithromycin 500mg BD for 5 days or co-amoxiclav 625mg TDS (co-amoxiclav if resistance) for 5 days
- All patients needing frequent courses of steroids should be kept under close review to minimise cumulative dose, risk of adrenal insufficiency and other side effects of oral steroids.
- Consider prescribing a bisphosphonate for patients receiving more than or equivalent to prednisolone 7.5 mg daily for 3 months or longer.
- **Weaning Dose of Prednisolone:** Consider prescribing a weaning course of oral prednisolone if the patient has received > 15mg prednisolone for more than 21 days, more than 3 x 5 day courses of prednisolone per 4-6 weeks, is on long term prednisolone for another indication or is within a year of being on long-term corticosteroids in order to reduce the risk of adrenal insufficiency.

Contact local specialist team for advice on managing exacerbations. See also [London Respiratory Network guidance](#)

Referral indications for Respiratory Physician review include:

- Disease onset at < 40 years old
- Family history of alpha 1 antitrypsin deficiency
- Diagnostic uncertainty
- 'Milder' patients with declining FEV1 despite optimised treatment
- Frequent exacerbations
- Breathlessness disproportionate to airway obstruction
- Rapidly progressive course of disease (decline in FEV1, worsening breathlessness, decreased exercise tolerance, unintentional weight loss)
- New symptoms not explained by COPD e.g. Haemoptysis
- At risk of hospital admission e.g. lives alone, multiple co-morbidities, co-existing mental illness, learning disabilities, high tobacco dependence, drug and alcohol dependence, experiencing homelessness
- One or more hospital admissions and not known to a supporting respiratory team
- Possible indication for surgery e.g. LVRS, bullectomy for emphysema
- Nebuliser trial
- Disabling breathlessness
- Concern about prolonged steroid use or adrenal insufficiency
- Review for severe COPD
- New respiratory failure
- Onset of cor pulmonale
- Ankle oedema
- Need for O₂ therapy (SpO₂ < 92%) Chronic respiratory failure & advanced care planning

GOLD COPD Classification (2017)

The Global initiative for Chronic Obstructive Lung Disease (GOLD) classification is being increasingly used by respiratory clinicians to phenotype patients with COPD and to guide management. It may be a helpful tool in deciding who and when to refer ([www.goldcopd.org](#)). Patients in GOLD category B, C or D may be considered for referral to a respiratory physician

COPD Patient Staging Assessment Tool				RISK Exacerbation History	
RISK GOLD Classification	3-4	C High risk, less symptoms	D High risk, more symptoms		≥2
	1-2	A Low risk, less symptoms	B Low risk, more symptoms		0-1
		MRC 1-2 CAT < 10	MRC ≥ 3 CAT ≥ 10		
CAT: COPD Assessment Test MRC: Medical Research Council Breathlessness Scale Adapted from GOLD guideline 2017					

- The 2017 GOLD guidance includes risk classification based on symptom and exacerbation history, not spirometry.
- Exacerbation History is over the course of 12 months.
- Severity of symptoms is assessed using a validated questionnaire e.g. CAT GOLD refers to mMRC for assessment of breathlessness. NB: MRC used in practice in the UK and hence MRC score is used in the patient staging too
- Suggested inhaled therapy for each GOLD phenotype:
 - A = SABA or SAMA
 - B = LAMA or LABA (if no asthma overlap)
 - C = LAMA + LABA
 - D = ICS + LABA +/- LAMA

Patient Specific Protocols (PSPs)

PSPs are documents held electronically by the London Ambulance Service (LAS) following a request from a health professional.

They are person and address specific and advise on the following:

- Treatment that is outside standard pre hospital clinical practice guidelines
 - Specific treatment of patients with high risk medical conditions.
- Patients also have a copy which they know to make available to the ambulance crew immediately upon their arrival.
- PSPs are used by respiratory teams to protect patients with COPD (and others) at risk of oxygen toxicity from being given too much oxygen.

London Ambulance Service NHS Trust
Patient Specific Protocol
This document MUST be checked on the ambulance crew immediately upon arrival and the treatment to be given in specified circumstances.

Emergency Number: 999 (In England) 112 (In Wales)

Name of Patient: _____ Date of Birth: _____

Address: _____

Reason for request: ONCE RESPONDERS HAVE ARRIVED AT THE SCENE, THE PATIENT SHOULD BE ASSESSED FOR OXYGEN THERAPY. IF OXYGEN IS TO BE GIVEN, THE PATIENT SHOULD BE MONITORED FOR OXYGEN SATURATION. IF OXYGEN SATURATION IS MAINTAINED AT 92% OR ABOVE, THE PATIENT SHOULD BE MONITORED FOR OXYGEN TOXICITY. IF OXYGEN SATURATION IS MAINTAINED AT 92% OR ABOVE, THE PATIENT SHOULD BE MONITORED FOR OXYGEN TOXICITY. IF OXYGEN SATURATION IS MAINTAINED AT 92% OR ABOVE, THE PATIENT SHOULD BE MONITORED FOR OXYGEN TOXICITY.

If essential contact the Clinical Risk for advice.

Name of Responsible Clinician: _____ Date of Issue: _____

Signature (Printed Name): _____

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Glossary

- SABA – short acting β₂ agonist
- SAMA – short acting muscarinic antagonist
- LABA – long acting β₂ agonist
- LAMA – long acting muscarinic antagonist
- ICS – inhaled corticosteroid
- MDI – Metered dose inhaler
- DPI – Dry powder inhaler
- BDP – Beclometasone dipropionate equivalent
- Low dose ICS – BDP equivalent 200 – 400 mcg/day
- Medium dose ICS – BDP equivalent > 400 – 1000 mcg/day
- High dose ICS – BDP equivalent > 1000 mcg/day
- ADR – Adverse Drug Reaction