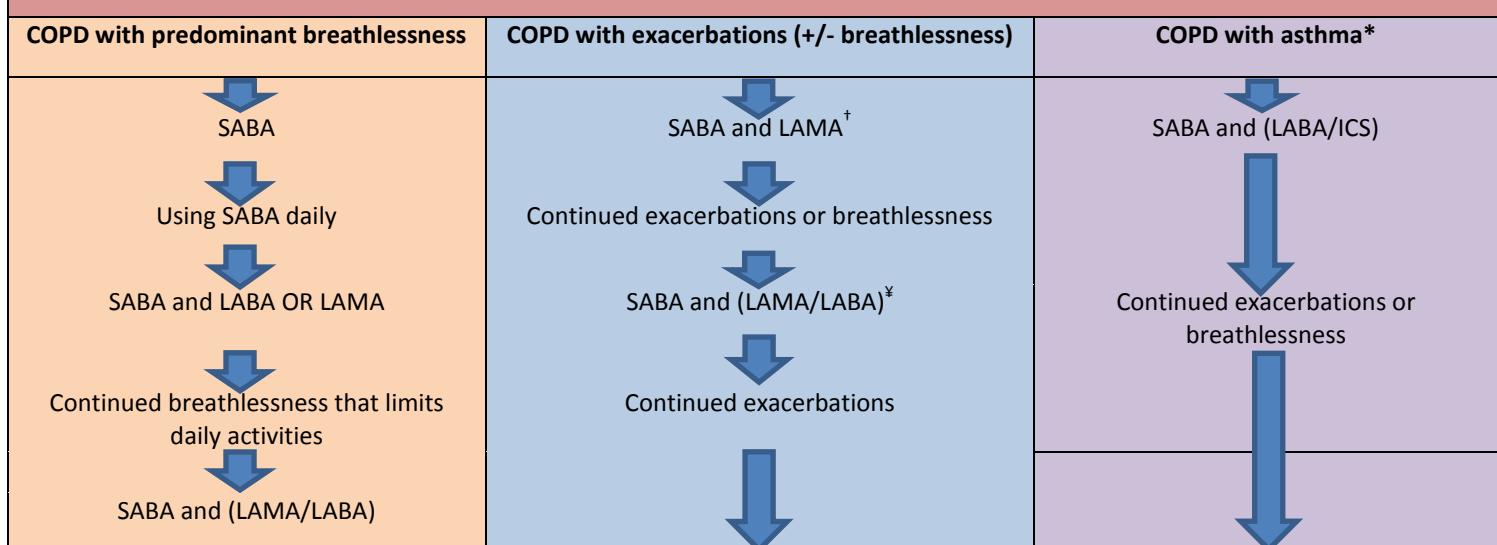


Guidelines for the Pharmacological Management of Chronic Obstructive Pulmonary Disease (COPD) in Primary Care May 2018

COPD is diagnosed in the presence of characteristic symptoms (cough, shortness of breath) and confirmed by post bronchodilator spirometry (absolute AND % predicted). Do CXR, FBC, BMI. Then start treatment:

Treat tobacco dependency, offer flu vaccination, optimise BMI, promote exercise and offer pulmonary rehabilitation (if MRC ≥3)



Still poorly controlled? STOP, THINK, TAKE STOCK. Consider referring to specialist

BEFORE CHANGING MEDICATION AT ANY STEP:

Check inhaler technique & compliance. Recheck diagnosis. Consider smoking status, co-morbidities. Is patient suitable for pulmonary rehabilitation or oxygen?

NOTES: *Assess for COPD/asthma overlap by reviewing history/examination/FBC for eosinophilia/evidence of symptomatic or lung function response to short trial of inhaled corticosteroids.

† Those with exacerbations & a greater burden of symptoms should proceed straight to SABA and LAMA/LABA. ‡ Whilst the use of a LAMA/LABA is recommended as an option by both GOLD and NICE for patients with exacerbations of COPD. Such use is not within license.

FORMULARY INHALER OPTIONS (ALWAYS PRESCRIBE INHALERS BY BRAND NAME)

Steroid card required for those on high dose inhaled steroids (>=1000mcg BDP or equiv/day)

	DPI (breathing technique: hard fast & deep)	pMDI (breathing technique: slow, gentle & long)
SABA (All pts)	Salbutamol EASYHALER 100mcg 2 puffs PRN Terbutaline (BRICANYL) TURBOHALER 0.5mg 1 puff PRN	Salbutamol (VENTOLIN) EVOHALER 100mcg 2 puffs PRN VIA AEROCHAMBER
LAMA	Tiotropium (BRALTUS) ZONDA INHALER 13mcg od (delivers same dose as 18mcg Spiriva handihaler, but is cheaper).	Tiotropium (SPIRIVA) RESPIMAT 2.5mcg 2 puffs od
	Glycopyrronium ▼ (SEEBRI) BREEZHALER 50mcg 1 capsule inhaled OD	
	Aclidinium bromide ▼ (EKLIRA) GENUAIR 322mg 1 puff bd (use if eGFR <30ml/min. Useful for pts with manual dexterity problems)	
	Umeclidinium ▼ (INCRUSE) ELLIPTA 55mcg 1 puff od	
LABA	Formoterol EASYHALER 12mcg bd	Olodaterol▼ (STRIVERDI) RESPIMAT 2.5mcg 2 puffs od
	Formoterol (OXIS) TURBOHALER 12mcg bd	
	Salmeterol (SEREVENT) ACCUHALER 50mcg bd	
LAMA/LABA	Glycopyrronium/Indacaterol▼ (ULTIBRO) BREEZHALER 50/110	Tiotropium/olodaterol (SPIOLOTO) RESPIMAT 2.5/2.5 2 puffs od
	Umeclidinium/Vilanterol ▼ (ANORO) ELLIPTA 55/22 od	
	Aclidinium/Formoterol▼ (DUAKLIR) GENUAIR 340/12 bd	
ICS/LABA	Budesonide/Formoterol (DUORESP) SPIROMAX 320/9 1 puff bd or 160/4.5 2 puffs bd.	Beclomethasone/Formoterol (FOSTAIR) MDI 100/6 2 puffs bd VIA AEROCHAMBER.
	Budesonide/Formoterol (SYMBICORT) TURBOHALER 400/12 bd or 200/6 2 puffs bd.	
	Fluticasone Furoate/Vilanterol ▼ (RELVAR) ELLIPTA 92/22 od	
LAMA/LABA/ICS	Fluticasone Furoate/Vilanterol/Umeclidinium▼ (TRELEGY) ELLIPTA 92/55/22 1 puff OD	Beclomethasone/Formoterol/Glycopyrronium (TRIMBOW) MDI 87/5/9 2 puffs BD

TRIPLE THERAPY (ICS/LABA/LAMA) is delivered via a triple inhaler device such as Trelegy® or Trimbow® or an ICS/LABA device plus a LAMA device (preferably using the same type of inhaler devices) which is a more expensive option. There are no single agent ICS devices licensed for COPD.

SABA = Short acting β_2 agonist
SAMA = Short acting muscarinic antagonist
LABA = Long acting β_2 agonist
LAMA = Long acting muscarinic antagonist
ICS = Inhaled corticosteroid

ROFLUMILAST: NICE TA461 (July 2017) recommends Roflumilast, as an add-on to bronchodilator therapy for pts with severe exacerbating disease. Specialist initiation. See guidance on p5-6.

Treatment flowchart above reproduced with permission from PCRS: see further information p4

Be aware of the potential risk of developing side-effects including non-fatal pneumonia in people treated with ICS. Use only in frequent exacerbators (i.e. ≥ 2 exacerbations/yr) or in patients with significant asthma overlap. Discuss risks with patient. Also consider their effect on bone health and the glaucoma risk.

If there is diagnostic uncertainty at any stage **REFER**

- If in spite of dual therapy or triple therapy a patient still exacerbates consider referral
- Meanwhile, consider increasing short-acting bronchodilators &/or palliative treatment with low dose oral morphine 5mg/2.5ml up to 4 hrly (ask for specialist advice if necessary)
- Consider pulmonary rehabilitation
- Consider referral for oxygen assessment in non-exacerbating hypoxic patients (saturation ≤92% on air)
- Consider palliative care issues, is a community DNAR order needed?
- Fan therapy

Acute exacerbations

- Increase frequency of short acting bronchodilator MDI e.g. Salbutamol (or Ipratropium if not on a LAMA) via a spacer
- SABAs can be as effectively delivered via an inhaler and a spacer as by a nebuliser. Given this, patients rarely require nebuliser equipment at home.
- Aim to keep oral steroid courses for exacerbations to just 7 days. COPD patients do not benefit from a 'slow wean' from a respiratory perspective. Maintenance use of oral prednisolone is not recommended in COPD.

Purulent sputum production

- If antibiotics are being considered in an acute exacerbation, please refer to the primary care antibiotic guidance: <https://prescribing.wiltshireccg.nhs.uk/prescribing-guidance-by-bnf-chapter/infections>
- Prophylactic antibiotics should not be prescribed unless advised by a respiratory consultant. Such patients should be reviewed regularly

Follow up

- Lower risk patients (no/few exacerbations in the past year, few symptoms and FEV-1 >50%), review annually. For patients at higher risk (2 or more exacerbations in the past year, FEV-1 <30%, MRC>=3), review every 6 months.
- Reviews to include spirometry
- Ensure recall date is highlighted to patient and coded on system
- Review compliance and assess inhaler technique

General Information

Lifestyle Advice

Smoking Cessation:

- The most important and cost-effective intervention is smoking cessation
- Ensure smoking cessation advice or referral to smoking cessation service is offered at every opportunity
- Stopping smoking at any age decreases the rate of FEV-1 decline in patients with COPD
- If the patient is on aminophylline/theophylline the dose may need reducing by about $\frac{1}{4}$ to $\frac{1}{3}$ one week after stopping smoking
- Ensure levels monitored regularly until stable
- See <http://www.wiltshirestopsmoking.co.uk/> for further information for Wiltshire patients
- See <http://www.sirona-cic.org.uk/services/stop-smoking-support/> for BaNES patients
- The Swindon Stop Smoking Service is free and helps thousands of people to quit for good. Find out more by calling the Live Well Swindon hub on 01793 465513 or email: livewell@swindon.gov.uk or livewellswindon@nhs.net

Diet:

- Ensure dietary advice is offered to patients if BMI is less than 20 as low BMIs are a predictor of poor outcome
- Pay attention to weight changes in older patients (especially >3kg)
- Screen for risk of malnutrition using the MUST tool and consider nutritional support if appropriate. See Food First patient leaflet and [A guide to managing requests for oral nutrition supplements](#)

Exercise: Promote gentle exercise

Immunisation

- Influenza annually
- Pneumococcal as per Green Book schedule (DoH)

Co-morbidities

- Remember the common co-morbidities associated with COPD e.g. cardiac, lung cancer, muscle wasting, osteoporosis, anaemia, anxiety & depression as well as the differential diagnosis.
- Screen for anxiety and depression and offer treatment
- Consider the patient's bone health if they are on high-strength inhaled corticosteroids. If the patient has been on systemic corticosteroid therapy lasting longer than 3 months, consider a bisphosphonate (Alendronate first-line) with calcium and vitamin D

Pulmonary Rehabilitation

- May be of benefit to patients who find themselves disabled by COPD if MRC Dyspnoea scale is 3 or above (though some patients who score lower than this may be suitable)
- Is not suitable for patients who are unable to walk, have unstable angina or have had a recent MI or have impaired cognition
- Tailored to individual needs and include physical training, disease education, nutritional, psychological and behavioural intervention
- For South Wiltshire patients, see: <http://www.icid.salisbury.nhs.uk/ClinicalManagement/Respiratory/Pages/IndexPage.aspx> (LEEP service)
- For West & North Wiltshire patients, use NEW & WWYKD COPD referral form on the medicines management website: <https://prescribing.wiltshireccg.nhs.uk/prescribing-guidance-by-bnf-chapter/respiratory>
- Swindon Lead is Nick Lowe N.Lowe@swindon.gov.uk 07824 081208. Find out more by calling the Live Well Swindon hub on 01793 465513 or email: livewell@swindon.gov.uk or livewellswindon@nhs.net

Oxygen Therapy

• Referral for Long Term Oxygen Treatment (LTOT)

- The need for oxygen therapy should be assessed in:

- Patients with oxygen saturation \leq 92% breathing air, in a stable state and all patients with severe airflow obstruction ($FEV_1 < 30\%$ predicted)
- Patients presenting with cyanosis or peripheral oedema or polycythaemia or raised JVP
- Note that most community services would be very reluctant to offer home oxygen to a current smoker nowadays due to the fire and burns risks.

• LTOT is indicated in patients who:

- Have $PaO_2 < 7.3\text{kPa}$ when stable or a PaO_2 between 7.3kPa and 8.0kPa and one of the following: secondary polycythaemia, nocturnal hypoxaemia (oxygen saturation of arterial blood (SaO_2) $< 90\%$ for more than 30% of the time), peripheral oedema or pulmonary hypertension
- To gain maximum clinical benefits from LTOT the patient should not be smoking. LTOT should be ordered for a minimum of 15hrs a day and up to 24 hours may be of additional benefit.

• Contacts for oxygen referrals:

- See Wiltshire website for appropriate referral forms: <https://prescribing.wiltshireccg.nhs.uk/prescribing-guidance-by-bnf-chapter/respiratory>
- For BaNES patients: <http://www.virgincare.co.uk/vc-providers/bnes-breathing-problems-service/#>
- For Swindon patients: Brenda Robinson: brenda.robinson@nhs.net or alternatively 01793 646436
- For South Wilts patients: Please use the referral proforma on ICID to the respiratory department at SFT

Patients with excessive, viscous mucous

• For symptom control use as a trial and stop if no benefit:

- Try 2 Carbocisteine 375mg capsules TDS for 4 weeks. Mucolytic therapy should be stopped after a 4 week trial if there is no benefit. Reduce to 2 capsules BD, as condition improves
- Review 3 months after initiation and regularly thereafter - **Stop if no symptomatic benefit**
- DO NOT use to prevent exacerbations (long term use)

MRC Dyspnoea Scale

Grade		Degree of breathlessness related to activities
Mild COPD ($FEV_1 > 80\%$)	1	Not troubled by breathlessness except on strenuous exercise
	2	Short of breath when hurrying or walking up a steep hill
Moderate COPD ($FEV_1 50-79\%$)	3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace
	4	Stops for breath after walking about 100m or after a few minutes on level ground
Severe/Very severe COPD ($FEV_1 < 50\%$)	5	Too breathless to leave the house, or breathless when dressing or undressing

When to refer to secondary care for expert opinion

- FEV1 40% or less (moderate/severe COPD)
- Onset of cor pulmonale
- Assessment for surgery: Bullous lung disease
- Frequent infections or increase of frequency of infections e.g. greater than 3 per year
- Rapid decline in FEV1
- COPD in a patient less than 40 years or FH of alfa 1 antitrypsin deficiency
- For palliative care
- Uncontrolled severe COPD
 - Haemoptysis
 - Low smoking history (i.e. <20 pack years)
 - Uncertain diagnosis
 - Symptoms don't match lung function tests

Resources for patients

- Self management advice in the form of a written plan should be given to patients regarding how to respond to the symptoms of exacerbations.
- Sputum cards
- See the local community pharmacist for a Medication Usage Review
- British Lung Foundation Breatheeasy groups: <http://www.blf.org.uk> and patient passport: <https://passport.blf.org.uk/>

Further information on COPD

- NICE COPD guidance (June 2010): <http://guidance.nice.org.uk/CG101>
- BTS guidance: <https://www.brit-thoracic.org.uk/clinical-information/copd/>
- COPD assessment test on-line: <http://www.catestonline.co.uk/>
- Diagnosis & management of COPD in primary care (Dec 2014) www.pcrs-uk.org/resource/Guidelines-and-guidance/QGCOPD
- Drug Safety Update Feb 2015: Tiotropium delivered via Respimat compared with Handihaler: no significant difference in mortality in TIOSPIR trial <https://www.gov.uk/drug-safety-update/tiotropium-delivered-via-respimat-compared-with-handihaler-no-significant-difference-in-mortality-in-tiospir-trial>
- GOLD 2017 Global Strategy for the Diagnosis, Management and Prevention of COPD: <http://goldcopd.org/gold-2017-global-strategy-diagnosis-management-prevention-copd/>
- Treatment flowchart on page 1 reproduced from: Treatment guidelines for COPD- Going for GOLD? Mak V, Keeley D, Gruffyd Jones K, Stonham C. Primary Care Respiratory Update Vol 4, Issue 2, Autumn 2017. <https://pcrs-uk.org/treatment-guidelines-copd-going-gold> October 2017

COPD Matrons/ Clinical leads

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- IMPACT team for BaNES: 01225 831808
- Swindon Community COPD Service: Amanda Horton  01793 646436

Roflumilast (Daxas®▼) for COPD treatment (AMBER)

Background

[NICE TA461](#) (July 2017) recommends Roflumilast, as an add-on to bronchodilator therapy, is recommended as an option for treating severe chronic obstructive pulmonary disease in adults with chronic bronchitis, only if:

- **The disease is severe, defined as a forced expiratory volume in 1 second (FEV1) after a bronchodilator of less than 50% of predicted normal, AND**
- **The person has had 2 or more exacerbations in the previous 12 months despite triple inhaled therapy with a long-acting muscarinic antagonist, a long-acting beta-2 agonist and an inhaled corticosteroid.**
- **Treatment with roflumilast should be started by a specialist in respiratory medicine.**

Referral Information

Our local respiratory specialists have suggested that COPD patients should only be referred to secondary care for consideration of roflumilast if they meet the above NICE criteria plus have all the following characteristics:

- a) Have a chronic bronchitic phenotype (ie chronic productive cough)
- b) Have good inhaler technique and compliance with their triple inhaled therapy
- c) Have completed pulmonary rehabilitation within the last 3 years
- d) Are not underweight (ie BMI >20)

Patients should be aware that roflumilast is not always well tolerated, typically due to gastrointestinal side effects. They should also be aware that, following assessment in secondary care, they may not be offered roflumilast if this is not felt to be an appropriate choice for them.

Effectiveness¹

Roflumilast is an orally administered long-acting selective phosphodiesterase-4 enzyme inhibitor. It targets cells and mediators believed to be important in chronic obstructive pulmonary disease (COPD).

Evidence came from REACT, a large, multicentre double-blind RCT of patients with severe COPD, chronic bronchitis and 2 or more exacerbations in last 12 months, comparing roflumilast plus inhaled combination therapy with placebo plus inhaled combination therapy and RE2SPOND, a large multicentre double-blind trial of patients with severe COPD, chronic bronchitis and 2 or more exacerbations and/or hospitalisations in previous 12 months. It was concluded that the company's pooled analyses provided sufficient evidence of the clinical efficacy of roflumilast compared with placebo in the subgroup of patients with severe COPD having exacerbations despite triple inhaled therapy.

Safety^{1,2}

Most common adverse reactions include diarrhoea, weight loss, nausea, abdominal pain and headache.

Roflumilast is generally well-tolerated but weight loss and gastrointestinal adverse effects can lead to discontinuation of treatment in some people. Roflumilast is subject to additional monitoring for weight loss and the weight of underweight patients should be checked at each GP appointment.

While adverse reactions like diarrhoea, nausea, abdominal pain and headache mainly occur within the first weeks of therapy and mostly resolve on continued treatment, roflumilast treatment should be reassessed in case of persistent intolerance.

Roflumilast is associated with an increased risk of psychiatric disorders such as insomnia, anxiety, nervousness & depression. In clinical studies and post-marketing experience, rare instances of suicidal ideation and behaviour, including suicide, were reported. Roflumilast is therefore not recommended in patients with a history of depression associated

Safety continued^{1,2}

with suicidal ideation or behaviour. Patients and caregivers should be instructed to notify the prescriber of any suicidal ideation. For full details of adverse reactions and contraindications, see the SPC.

Body weight <60 kg:

Treatment with roflumilast may lead to a higher risk of sleep disorders (mainly insomnia) in patients with a baseline body weight of <60 kg, due to a higher total PDE4 inhibitory activity found in these patients.

Health professionals information from the manufacturer can be found here: <http://www.medicines.org.uk/emc/RMM.817.pdf>

Patient Factors²

Hepatic Impairment - Roflumilast should be used with caution in patients with mild hepatic impairment (Child-Pugh A) and contra-indicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C).

Not recommended during pregnancy or breastfeeding.

Women of childbearing age should be advised to use an effective method of contraception during treatment. Roflumilast is not recommended in women of childbearing potential not using contraception.

Prescribing information²

The recommended dose is 250 micrograms (1 tablet) of roflumilast once daily for the first 28 days. Then increase to maintenance dose of 500mcg once daily. The tablet should be swallowed with water and taken at the same time every day. The tablet can be taken with or without food. Roflumilast may need to be taken for several weeks to achieve its effect. All patients should be informed about the risks of roflumilast and the precautions for safe use and should be given a patient card before starting roflumilast. This resource for patients can be found here:

<https://www.medicines.org.uk/emc/rmm/816/Document>

Interactions of note² (See SPC for full details²)

- The use of strong cytochrome P450 enzyme inducers (e.g. phenobarbital, carbamazepine, phenytoin) may reduce the therapeutic efficacy of roflumilast. Thus, roflumilast treatment is not recommended in patients receiving strong cytochrome P450 enzyme inducers.
- There are no clinical data to support the concomitant treatment with theophylline for maintenance therapy. Therefore, the concomitant treatment with theophylline is not recommended.

Stopping criteria

No specific stopping criteria are suggested in the NICE TA for roflumilast or in the license. Pragmatically, when these patients are reviewed, if there has been no change in the number of exacerbations or hospital admissions they have in a year it might be worth considering whether it is worth continuing.

Cost

Roflumilast costs £37.71 for 30 tablets. Annual cost: £459

References

1. NICE TA461 Roflumilast for treating chronic obstructive pulmonary disease 26th July2017 <https://www.nice.org.uk/guidance/ta461>
2. DAXAS 500 micrograms film-coated tablets SPC <http://www.medicines.org.uk/emc/medicine/23416>