South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**084**
Intervention:	Triple combination therapy inhalers for adults with chronic obstructive pulmonary disease (COPD): **Trelegy® Ellipta®** (fluticasone furoate/umeclidinium bromide/vilanterol) and **Trimbow® /Trimbow® NEXThaler®** (beclometasone dipropionate/formoterol fumarate dihydrate/ glycopyrronium) (These inhalers each deliver a combination of a corticosteroid and two long acting bronchodilators in a single inhaler device)
Date of Decision:	**June 2018. Updated in May 2024 to reflect a change in category from Amber 1 to Green and first line use where specified criteria are met, in line with publication of the SEL COPD Inhaler pathway**
Date of Issue:	**June 2018. Re-issued June 2024**
Recommendation:	**Green- can be prescribed within agreed criteria for use in primary or secondary care**
Further Information	• Trelegy® Ellipta® and Trimbow® (including Trimbow® NEXThaler®) are accepted for use within South East London as an option for the treatment of adults with moderate to severe chronic obstructive pulmonary disease (COPD). • In line with the local COPD inhaler pathway, Trelegy® and Trimbow® may be considered as first line maintenance treatment in people with COPD who: - have had ≥1 severe [hospitalised] or ≥ 2 moderate [required systemic steroids] exacerbations in the last year **AND** - have an eosinophil count ≥100 cells per microlitre. • These inhalers may also be considered for use in patients appropriately receiving triple therapy (inhaled corticosteroid [ICS]/LABA and LAMA) in separate devices. It should be noted that switching of patients who are stable on other triple therapy regimens to Trelegy® or Trimbow® may not always be appropriate. • Whilst the use of Trelegy® and Trimbow® in this setting is in line with the current recommendations from the Global Initiative in Chronic Obstructive Lung Disease (GOLD), their use in this setting is not currently licensed (off-label). • Trelegy® is a dry powder inhaler device, Trimbow® is a metered dose inhaler device and Trimbow® NEXThaler® is a dry powder inhaler device. The device chosen should be based on patient factors, such as inhaler technique. • All patients should be asked to demonstrate their inhaler technique regularly and adherence should be established before initiating/ stepping up therapy. • Treatment with these inhalers can be initiated in line with this recommendation by primary or secondary care clinicians. • If patients experience a further exacerbation after being stabilised on triple therapy management, patients can be referred to a respiratory specialist or advice and guidance sought. • The local SEL COPD Inhaler pathway reflects the criteria for use of these inhalers.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• The application estimates that ~152 patients in SEL would be initiated on triple therapy per annum instead of LABA+ICS or LABA+LAMA. • It is not possible to accurately model the costs, as the current rate of escalation to triple therapy from dual therapy as per criteria in the current SEL guidance is unknown. However, most patients targeted for initial triple inhaler therapy in the COPD inhaler pathway would currently be receiving LABA+ICS treatment rather than LABA+LAMA, either due to a raised eosinophil or other factors suggesting asthmatic features. • If 130 patients and 22 patients are prescribed initial triple therapy rather than LABA+ICS and LABA+LAMA respectively, this equates to approximately £27,250 increased costs per annum for SEL (or ~ £1,400 per 100,000 population). By year 5,

	this would equate to approximately £135,000 (or £6,750 per 100,000 population) costs for SEL by accumulation. • In terms of broader value, availability of these inhalers in the first line setting is expected to reduce hospitalisations or deaths from COPD in the future.
Usage Monitoring & Impact Assessment	**Acute Trusts** • Monitor and submit usage and audit data on request to the Committee
	SEL Borough Medicines Optimisation Teams: • Monitor ePACT2 data • Exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from new evidence evaluation presented in February 2024)** 1. Singh D, Agusti A, Martinez F et al. Blood eosinophils and chronic obstructive pulmonary disease: A Global Initiative for Chronic Obstructive Lung Disease Science Committee 2022 Review. American Journal of Respiratory and Critical Care Medicine 2022 206 1 p17-24. 2. Global strategy for prevention, diagnosis and management of COPD: 2023 Report. Available here [accessed 18/12/2023] 3. NG115: Chronic obstructive pulmonary disease in over 16s: diagnosis and management. National Institute for Health and Care Excellence. Available here [accessed 18/12/2023] 4. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012; 9(9): CD006829. 5. Nannini L, Poole P, Milan S, Kesterton A. Combined corticosteroid and long-acting beta(2)- agonist in one inhaler versus inhaled corticosteroids alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2013; 8(8) CD006826. 6. Agarwal R, Aggarwal A, Gupta D, Jindal S. Inhaled corticosteroids vs placebo for preventing COPD exacerbations: a systematic review and meta regression of randomized controlled trials. Chest 2010; 137: 318–2. 7. Rabe K, Martinez F, Ferguson G et al. Triple inhaled therapy at two glucorticoid doses in monderate-tovery-severe COPD. NEJM 2020 383 (1) p35-48. 8. Lipson D, Barnhart F, Brealey N et al. Once-Daily Single-Inhaler Triple Therapy versus Dual Therapy in Patients with COPD. NEJM 2018 378 (18) p1671-1680. 9. Ferguson G, Rabe K, Martinez F et al. Triple therapy with budesonide/glycopyrrolate/formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel group, multicentre, phase 3 randomised controlled trial. Lancet Respiratory 2018 doi 10.1016/S2213-2600(18)30327-8. 10. van Geffen WH, Tan DJ, Walters JAE, Walters EH. Inhaled corticosteroids with combination inhaled long-acting beta2-agonists and long-acting muscarinic antagonists for chronic obstructive pulmonary disease (Review). Cochrane Database of Systematic Reviews 2023 Issue 12. Art. No.: CD011600. 11. Lipson D, Crim C, Criner G. Reduction in all-cause mortality with fluticasone furoate/umeclidinium/vilanterol in patients with chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine 2020 vol 201 (12) p1508-1516. 12. Vestbo J, Fabbri L, Papi A, et al. Inhaled corticosteroid containing combinations and mortality in COPD. Eur Respir J 2018; 52: 1801230. 13. Bafadhel M, Peterson S, Blas M et al. Predictors of exacerbation risk and response to budesonide in patients with chronic obstructive pulmonary disease: a post-hoc analysis of three randomised trials. Lancet Respiratory 2018 6(2): 117-26. 14. Pascoe S, Lacantore N, Dransfield M et al. Blood eosinophil counts, exacerbations, and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomised controlled trials. Lancet Respir Med 2015; 3(6): 435-42 15. Siddiqui S, Guasconi A, Vestbo J, et al. Blood Eosinophils: A Biomarker of Response to Extrafine Beclomethasone/Formoterol in Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med 2015; 192(4): 523-5.

NOTES:

a) SEL IMOC recommendations and minutes are available publicly via the website.

b) This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**