

North Staffordshire and Stoke-on-Trent Area Prescribing Committee

Medicine Review Summary

Trimbow® (Fluticasone 87mcg/Formoterol 5mcg/ Glycopyrronium 9mcg /inhalation) pressurised inhalation solution

Verdict:	
Formulary inclusion:	Trimbow® is to be included in the North Staffs Joint Formulary
Formulary category:	Green
Restrictions:	To be used in accordance with Global Initiative for Chronic Obstructive Lung Disease (GOLD) global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease. Accessed via www.goldcopd.org (Accessed online 9 th January 2018) (At a glance guide: stable COPD)
Reason for inclusion:	The New Medicines Committee was satisfied with the evidence to support the safety and efficacy of Trimbow® and acknowledged the fact that the individual components were already well established in clinical practice. The improvement in patient compliance associated with a single inhaler and cost saving when compared to the individual components were noted. The New Medicines Committee acknowledged that locally approved guidelines reflect the GOLD guidelines for management of COPD whereas the licensed indication for Trimbow® places its use after ICS and LABA. The Area Prescribing Committee considered this and supported the use of Trimbow® in line with GOLD and local guidelines; prescribers need to be aware of this.
Link to formulary:	Stoke-on-Trent CCG website: https://www.stokeccg.nhs.uk/stoke-governance/policies/medicines-optimisation/joint-formulary North Staffordshire CCG website: https://www.northstaffscg.nhs.uk/governance/policies/medicines-optimisation/joint-formulary Secondary care: Trust Intranet → Clinicians → Support services → Pharmacy → North Staffordshire Joint Formulary
Link to medicine review summary:	Stoke-on-Trent CCG website: https://www.stokeccg.nhs.uk/stoke-governance/policies/medicines-optimisation/formulary-review-and-verdict-sheets North Staffordshire CCG website: https://www.northstaffscg.nhs.uk/governance/policies/medicines-optimisation/formulary-review-and-verdict-sheets Secondary care: Trust Intranet → Clinicians → Support services → Pharmacy → Joint Formulary Related Documentation → North Staffordshire & Stoke-on-Trent Area Prescribing Committee Medicine Review Summary Verdict Sheets
Link to full review:	Stoke-on-Trent CCG website: https://www.stokeccg.nhs.uk/stoke-governance/policies/medicines-optimisation/formulary-review-and-verdict-sheets North Staffordshire CCG website: https://www.northstaffscg.nhs.uk/governance/policies/medicines-optimisation/formulary-review-and-verdict-sheets Secondary care: Trust Intranet → Clinicians → Support Services → Pharmacy → Joint Formulary Related Documentation → New Medicine Committee (NMC) Medicines Reviews

Review summary:

Formulary Application:

Trimbow® pressurised inhalation solution was reviewed for inclusion in the North Staffordshire Joint Formulary for maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid (ICS) and a long-acting β_2 -agonist (LABA). Dr Imran Hussain (consultant in respiratory medicine) attended the meeting on 10th January 2017 to support the application.

Licensed indications ¹:

Maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting beta2-agonist.

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Related Guidance:

NICE²: www.nice.org.uk

Global Initiative for Chronic Obstructive Lung Disease (GOLD)³: www.goldcopd.org.

Efficacy and safety:

Results from the Trilogy⁴ and Trinity⁵ studies support the benefit of single-inhaler triple therapy compared with ICS/LABA therapy in patients with advanced COPD.

TRIOLOGY was a 52 week, double-blind, randomised, multicentre, two-arm, active-controlled clinical trial to test the superiority of Trimbow® over a fixed combination of beclometasone dipropionate and formoterol 100/6 micrograms (Fostair®) two puffs twice daily administered via pMDI (1,368 randomised patients).

The study showed that triple therapy with Trimbow® had a greater effect on pre-dose and 2 hr post-dose FEV1 than Fostair in patients with COPD who have severe or very severe airflow limitation, symptoms and exacerbation history. There was no superiority shown in relation to TDI and there was a significant prolonged time to first exacerbation with Trimbow®. Thus, the greater improvement in lung function with Trimbow® compared with Fostair® was more clearly accompanied by a reduction in exacerbations than an improvement in breathlessness in this group of patients. Furthermore, Trimbow® had a greater effect on health related quality of life than Fostair®. Limitation: Most patients will progress from LABA +LAMA to triple therapy hence the comparator arm bears little relevance to this recommendation by GOLD. The authors did recognise this as they stated that their study did not address the benefit of escalation to triple therapy from LABA+LAMA. Patients already on triple therapy as two separate inhalers were excluded from the study hence there was no direct comparison made.

TRINITY was a double-blind, parallel-group, randomised, controlled trial across 15 countries in 224 sites. The study compared Trimbow® with tiotropium 18 micrograms inhalation powder, hard capsule, one inhalation once daily; in addition, effects were compared with an extemporaneous triple combination made of a fixed combination of Fostair® 100/6 micrograms two inhalations twice daily plus tiotropium 18 micrograms inhalation powder, hard capsule, one inhalation once daily.

The study showed that Trimbow® reduced the rate of moderate to severe COPD exacerbations by 20% compared to tiotropium with 61mL mean improvement in pre-dose FEV1. There was non-inferiority in pre-dose FEV1 between Trimbow® and open triple therapy. There was general similarity between Trimbow® and open triple therapy in moderate and severe exacerbation rates, use of rescue medication, SGRQ responders but superior to tiotropium monotherapy.

Costs:

LabelDescription	Tradename	Pack size (doses)	Price exc VAT	UHNM Price inc VAT	Price comparison incl VAT	Price difference incl VAT
TRIMBOW 87microgram/ 5microgram/9microgram INHALER (120)	TRIMBOW	120				£9.13
FOSTAIR 200/6 INHALER (120-dose)	FOSTAIR	120				
FOSTAIR 100/6 INHALER (120-dose)	FOSTAIR	120				
GLYCOPYRRONIUM 44microgram BREEZHALER & 30 CAPSULES	SEEBRI BREEZHALER	30				
TRELEGY 92/55/22 INHALER	TRELEGY ELLIPTA	30				£6.00
RELVAR ELLIPTA 92/22 INHALER (30-dose)	RELVAR ELLIPTA	30				
RELVAR ELLIPTA 184/22 INHALER (30-dose)	RELVAR ELLIPTA	30				
UMECLIDINIUM 55microgram INHALER (30 dose)	INCRUSE ELLIPTA	30				

References:

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¹ Summary of Product Characteristics Trimbow® (Fluticasone 87mcg/Formoterol 5mcg/ Glycopyrronium 9mcg /inhalation) pressurised inhalation solution. Last Updated on eMC 26th Jul 2017

<https://www.medicines.org.uk/emc/product/761> (Accessed online 12th Jan 2017)

² NICE Clinical guideline CG101: Chronic obstructive pulmonary disease in over 16s: diagnosis and management. June 2010. Accessed via www.nice.org.uk (Accessed online 12th January 2018)

³ Global Initiative for Chronic Obstructive Lung Disease global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease 2017 report. Accessed via www.goldcopd.org (Accessed online 9th January 2018)

⁴ Single inhaler triple therapy versus inhaled corticosteroid plus long-acting β 2-agonist therapy for chronic obstructive pulmonary disease (TRILOGY): a double-blind, parallel group, randomised controlled trial. Singh D et al; The Lancet, Vol 388 September 3, 2016; 963 – 973.

⁵ Single inhaler extrafine triple therapy versus long-acting muscarinic antagonist therapy for chronic obstructive pulmonary disease (TRINITY): a double-blind, parallel group, randomised controlled trial. Vestbo J et al; www.thelancet.com Published online April 3, 2017 [http://dx.doi.org/10.1016/S0140-6736\(17\)30188-5](http://dx.doi.org/10.1016/S0140-6736(17)30188-5).