This policy statement is approved by Halton, Knowsley, Liverpool, South Sefton, Southport and Formby, St Helens, Warrington, West Lancashire, and Wirral CCGs

Ha Kn Li SS SF SH Wa WL Wi

NHS
Pan Mersey
Area Prescribing Committee

# ROFLUMILAST tablets (Daxas® ▼) for COPD

**The Pan Mersey Area Prescribing Committee recommends the prescribing of ROFLUMILAST tablets (Daxas® ▼) following specialist recommendation as an add-on to bronchodilator therapy, for treating severe chronic obstructive pulmonary disease in adults with chronic bronchitis and in accordance with NICE TA461**

**AMBER following specialist recommendation**

NICE TA461 (26 July 2017) recommends Roflumilast, as an add-on to bronchodilator therapy as an option for treating severe chronic obstructive pulmonary disease (COPD) 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.

The decision to start treatment with roflumilast should be made by a specialist in respiratory medicine.

For further guidance on the recommended treatment of COPD please refer to:

> Pan Mersey APC (2018) COPD Guidelines for Inhaled Therapy

> NICE NG115 Chronic obstructive pulmonary disease in over 16s: diagnosis and management December 2018

**Note**: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Supporting information

# ROFLUMILAST tablets (Daxas® ▼) for COPD

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| **Effectiveness**[1]<br>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).<br>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 RE$^2$SPOND, 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.<br>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]<br>Contra-indications - Cancer (except basal cell carcinoma); concomitant treatment with immunosuppressive drugs (except short-term systemic corticosteroids); history of depression associated with suicidal ideation or behaviour; moderate to severe cardiac failure; severe acute infectious disease; severe immunological disease. Most common adverse reactions include diarrhoea, weight loss, nausea, abdominal pain and headache, decreased appetite.<br>Roflumilast is generally well-tolerated but weight loss and gastrointestinal adverse effects can lead to discontinuation of treatment in some people.<br>Roflumilast is subject to additional monitoring for weight loss.<br>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. In clinical studies and post-marketing experience, rare instances of suicidal ideation and behaviour, including suicide, were reported. Patients and caregivers should be instructed to notify the prescriber of any suicidal ideation<br>For full details of adverse reactions and contraindications, see the SPC. |
| **Cost**<br>Roflumilast 250mcg - £35.20 (28 tablets)<br>Roflumilast 500mcg - £37.71 (30 tablets)<br>(NHSBSA dm+d accessed 10/06/2019)<br>**Annual cost per patient: £458.81**<br><br>NICE estimated that costs were not expected to be significant and expected uptake to be small as only started by specialists in secondary care.[3]<br>Total spend for Pan Mersey CCGs April 2018-March 2019 = £3,557. | **Patient factors**[2]<br>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).<br>Not recommended during pregnancy or breastfeeding.<br>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 information**[2]

The recommended starting dose is one tablet of 250 micrograms roflumilast to be taken once daily, for 28 days. This starting dose is intended to reduce adverse events and patient discontinuation when initiating therapy, but it is a sub-therapeutic dose. Therefore, the 250 micrograms dose should be used only as a starting dose. After 28 days of treatment with the 250 micrograms starting dose, patients must be up-titrated to one tablet of 500 micrograms roflumilast, to be taken once daily. Roflumilast 500 micrograms may need to be taken for several weeks to achieve its full effect. The tablet should be swallowed with water and taken at the same time every day. The tablet can be taken with or without food. 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.

**References**


1. National Institute for Health and Care Excellence. TA461: Roflumilast for treating chronic obstructive pulmonary disease, 26 July 2017. Accessed 22 May 2019.
2. AstraZeneca UK Limited. Summary of Product Characteristics: DAXAS 500 micrograms film-coated tablets, 23 April 2018. Accessed 22/05/2019
3. National Institute for Health and Care Excellence. Roflumilast TA461 Resource impact statement, July 2017. Accessed 22 May 2019.