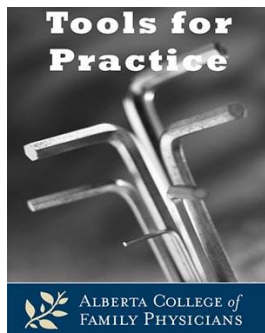


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Evidence Updated: Updated Cochrane review
Bottom Line: Unchanged
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Roflumilast – COPD relief at last?

Clinical Question: Is roflumilast (Daxas®) beneficial as an add-on therapy in the management of COPD?

Bottom Line: Roflumilast decreases the risk of COPD exacerbations for one in 24, with no effect on mortality and no clinically important improvements in quality of life. Roflumilast increases the risk of various adverse effects, including psychiatric (one in 28), diarrhea (one in 15), and weight loss (one in 17). The net benefit of roflumilast is questionable.

Evidence:

- 2017 Cochrane systematic review¹ of 20 randomized trials (17,627 patients) of roflumilast, with follow-up ranging from 12 to 52 weeks:
 - Statistically significant benefit:
 - Reduced likelihood of one or more COPD exacerbations of moderate (requiring corticosteroids) or severe (requiring admission) severity: 31.7% in placebo versus 27.4% in roflumilast, Number Needed to Treat (NNT)=24.
 - Benefit similar regardless of other COPD treatments.
 - Not statistically and/or clinically significant:
 - No reduction in mortality.
 - Multiple quality of life and symptom scores with few reaching statistical significance and none reaching clinical importance.
 - Statistically but not clinically important improvement in FEV₁ with roflumilast (56 mL).
 - Harms:
 - More participants in the roflumilast groups experienced:
 - Psychiatric adverse events, including anxiety, depression, and insomnia, Number Needed to Harm (NNH)=28.
 - Weight loss NNH=17.
 - Diarrhea NNH=15.
 - Nausea NNH=31.

- Headache NNH=44.
- Weight loss is on average 2 kg over 24-52 weeks,^{2,3} though one study found this same weight loss within one month after starting roflumilast following a COPD exacerbation.⁴

Context:

- Roflumilast is an oral phosphodiesterase 4 (PDE₄) inhibitor that reduces the airway inflammation and bronchoconstriction seen in COPD.
- Change in FEV₁ of 100 mL is considered the minimum clinically important difference.⁵
 - However, the observed FEV₁ improvement with roflumilast is similar to that for salmeterol or fluticasone in the TORCH trial.⁵
- In patients with previous COPD exacerbation, weight loss is a risk factor for re-hospitalization and death.⁷⁻⁹

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