Roflumilast (Daxas®) for maintenance treatment of severe chronic obstructive lung disease (COPD)

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 31 July 2018.

Zorginstituut Nederland has carried out an assessment of the medicinal product roflumilast (Daxas®), whereby the following conclusion was reached.

In a letter dated 15 May 2018 (CIBG-18-06295), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* to assess whether roflumilast (Daxas®) is interchangeable with a medicinal product already included in the Medicine Reimbursement System (GVS). The *Zorginstituut* has completed its assessment. Its deliberations can be found in the GVS report, the pharmacotherapeutic report and budget impact analysis that were sent to the Minister.

Roflumilast is available as 500 microgram film-coated tablets. The maintenance dose is one 500 microgram tablet once a day.
Roflumilast is registered as an addition to treatment with bronchodilators for the maintenance treatment of severe chronic obstructive lung disease (COPD) associated with chronic bronchitis in adults whose COPD flares up frequently. The *Zorginstituut* assessed roflumilast (Daxas®) in 2010 and advised that the product should not be included in the basic package for the registered indication.

Since 2010 new studies have been carried out in which roflumilast was studied with a limited indication. Based on this, the manufacturer is asking for a reassessment of the reimbursement of roflumilast, not for the registered indication, but for a limited indication, namely as additional maintenance treatment of severe COPD associated with chronic bronchitis in adults whose COPD, despite optimum inhalation of triple-therapy (LABA/LAMA/ICS), still flares up frequently (≥ 2 moderate to severe flare-ups or ≥ 1 hospital admission in the previous year).

Assessment of interchangeability

In 2010 the (former) *College voor zorgverzekeringen* (Health Care Insurance Board (CVZ) established – based on the GVS criteria for interchangeability – that the GVS includes no product that is interchangeable with roflumilast (CFH-report 10/21). Since 2010 no new products have been included in the GVS with a similar field of indication and the same administration route as roflumilast.

Based on the above, roflumilast (Daxas®) cannot be placed on List 1A. What must be examined is whether roflumilast is eligible for placing on List 1B of the Health Insurance Decree.

Therapeutic value
Zorginstituut Nederland, advised by the Scientific Advisory Board (WAR), concluded that for the treatment of patients with severe and very severe chronic obstructive lung disease (COPD) associated with chronic bronchitis in adults whose COPD flares up frequently, roflumilast has a therapeutic added value for reducing severe flare-ups compared to other optimal triple therapy.

Budget impact analysis (BIA)

Taking into account assumptions regarding numbers of patients, market penetration and therapeutic value, including roflumilast for severe COPD with chronic bronchitis on list 1B of the GVS will be accompanied by additional costs to the pharmacy budget of about €2.4 million in 2021.
Uncertainty exists about the percentage of patients who fulfil the sub-indication, the percentage of patients with chronic bronchitis and the percentage of patients treated with triple-therapy. Uncertainty also exists about the percentage of market penetration.
The product was granted exemption from performing a pharmacoeconomic analysis based on the estimated budget impact.

Appropriate use
Reimbursement is being requested for a sub-group of the registered indication. The BIA was calculated over this sub-group, though based on maximum assumptions. Clearly the budget impact would be larger if roflumilast were to be used in clinical practice for the entire registered indication. The professional group has indicated that – based on the REACT study mentioned in the report – the requested sub-indication is the only correct indication for using roflumilast. Furthermore, this sub-indication is also advised in the international GOLD guidelines. They do not expect roflumilast to be used more broadly, i.e., as suggested in the registered indication. National experts in the field of COPD share this opinion. The professional group feels therefore that the budget impact analysis is a realistic representation of the expected costs.

Advice on inclusion in the GVS
Roflumilast is not interchangeable with any other product included in the GVS. Based on the above-mentioned considerations, we advised the Minister of VWS to include roflumilast on List 1B and List 2 of the Health Insurance Decree. Inclusion on List 1B will involve additional costs.

Condition
Only for an insured person aged 18 years and older:
- who has severe chronic obstructive lung disease (FEV1 <50% of predicted) associated with chronic bronchitis, and,
- as an addition to maintenance treatment (a corticosteroid, a long-acting β2-sympathicomimetic and a long-acting parasympathicolytic agent) for an insured person who, despite this optimum (maximum dosage of) triple inhalation therapy, still suffers frequent flare-ups (≥ 2 moderate to severe flare-ups or ≥ 1 hospital admission in the year prior to starting treatment).

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.