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**Our reference**
2025024660

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Date 10 October 2025
Re: Expansion additional conditions sildenafil and tadalafil for Raynaud's secondary phenomenon

Dear Mr Bruijn,

The National Health Care Institute is advising you on the extension of the further conditions for sildenafil and tadalafil for secondary Raynaud's phenomenon. Both medicinal products are included in the Medicine Reimbursement System (GVS). The reason for this advice was an application from the professional associations, the Dutch Association for Rheumatology (NVR) and the Netherlands Society of Internal Medicine (NIV). The National Health Care Institute advises you to expand the additional conditions for sildenafil and tadalafil.

Raynaud's phenomenon is a common vascular disorder, often affecting the fingers and toes. Temporary cramping of the blood vessels reduces the flow of blood through them. This can cause severe pain and sometimes sores and wounds. Secondary Raynaud's phenomenon has an underlying cause. It is usually associated with connective tissue disease, such as systemic sclerosis. Some patients with secondary Raynaud's phenomenon are therapy-resistant, which means that they no longer respond to standard treatment with calcium channel blockers. However, therapy-resistant secondary Raynaud's phenomenon is rare: the professional group estimates that this occurs in 1 in 260,000 people. In the Netherlands, patients with secondary Raynaud's phenomenon are usually treated with the calcium channel blocker nifedipine. If this treatment is not or no longer effective, off-label treatment with phosphodiesterase-5 inhibitors is administered. In severe cases, the patient is treated intravenously with iloprost in the hospital. To receive reimbursement for phosphodiesterase-5 inhibitors, an application must be submitted to each patient's healthcare insurer. This is happening now for dozens of patients each year and entails a significant administrative burden.

<u>Request professional group</u>
The Dutch Association for Rheumatology and the Netherlands Society of Internal Medicine are requesting reimbursement for all phosphodiesterase-5 inhibitors for patients with secondary Raynaud's phenomenon associated with connective tissue disease, where nifedipine is not sufficiently effective. These include sildenadil, tadalafil, avanafil and vardenafil. Only sildenafil and tadalafil are already included in the GVS (for the indication of pulmonary arterial hypertension). Therefore, the National Health Care Institute has assessed whether the additional conditions of these two medicinal products could be extended. The professional groups expect

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that the use of phosphodiesterase-5 inhibitors for the above indication will prevent patients from being hospitalised for 3-5 days to receive intravenous iloprost treatment.

Registered indications
Sildenafil and tadalafil have been registered for use in certain adult men with erectile dysfunction and in addition for certain patients with pulmonary arterial hypertension.

Current reimbursement status
Sildenafil and tadalafil have not been registered as therapy for secondary Raynaud phenomenon associated with connective tissue disease, but are already being used off-label for this indication in practice. Since this indication is outside the applicable List-2 conditions, in principle, sildenafil and tadalafil are reimbursed from the GVS. The National Health Care Institute has now assessed whether both medicinal products can be reimbursed on a permanent basis from the GVS for the above indication.

Both products are available in tablets taken daily for 6 to 12 months for this indication.

Current additional conditions for sildenafil and tadalafil
Only for insured persons who:

1. Suffer from pulmonary arterial hypertension New York Heart Association Class II and who are prescribed ambrisentan, bosentan, macitentan, riociguat, selexipag, sildenafil or tadalafil for this
2. Suffer from pulmonary arterial hypertension New York Heart Association class III or IV and who are prescribed:
    1. one of the oral medicinal products ambrisentan, bosentan, macitentan, riociguat, selexipag, sildenafil or tadalafil, or a combination of two oral medicinal products from different pharmacological groups

Sildenafil and tadalafil are included on List 1A of the GVS in cluster 0G04BEA.

**Advisory report**
For sildenafil and tadalafil, the National Health Care Institute recommends that List 2 of the GVS be extended to include the following further conditions:

Only for insured persons who:

3. Suffer from secondary Raynaud's phenomenon associated with connective tissue disease and who are prescribed sildenafil or tadalafil and are insufficiently responsive to or cannot be treated with dihydropyridine calcium channel blockers.

The expansion of the additional conditions is accompanied by minor additional costs from the pharmaceutical budget, estimated at between €421,575 and €599,235 per year at most. The National Health Care Institute considers these minor additional costs acceptable, given the expected savings in medical specialist care.

We have explained below how we reached this advisory report.

Substantive assessment

*Therapeutic value*
The National Health Care Institute has concluded that sildenafil and tadalafil meet the established medical science and medical practice for the treatment of therapy-resistant secondary Raynaud's phenomenon associated with connective tissue disease. Both products, like iloprost and nifedipine, reduce the frequency and severity of seizures and thus have a positive effect on secondary Raynaud's phenomenon.

*Budget impact analysis*
Based on the input from the professional group, the National Health Care Institute estimates that up to 700 patients are eligible for sildenafil or tadalafil for the above-mentioned indication by year 3 after inclusion in the package. The total cost per patient per year is €602.25 for sildenafil treatment at a dose of 3x 20 mg per day with a pharmacy purchase price (PPP) of €0.55 per tablet. For tadalafil, the total cost per patient is €863.23 at a dose of 20 mg every other day with a PPP of €4.73 per tablet. If all 700 patients were treated with sildenafil or tadalafil, this would result in a macro cost of €421,575 to €605,535 per year, depending on the ratio of sildenafil and tadalafil. As usual in a budget impact analysis, potential savings due to the prevention of hospitalisations for intravenous iloprost treatment have not been taken into account. There is uncertainty about the number of patients who will actually be treated with sildenafil or tadalafil, and about the duration of treatment.

Should you need any further information, please do not hesitate to contact us.
The assessment report is attached as an annex (pharmacotherapeutic report).

Yours sincerely,

M.J. Janssen
Chairperson of the Executive Board