



> Return address PO Box 320, 1110 AH Diemen

To the Minister of Health, Welfare and Sport  
PO Box 20350  
2500 EJ THE HAGUE

2024036530

Date 25 October 2024  
Re: Expansion further condition relugolix + estradiol and norethisterone acetate (Ryeqo®)

**National Health Care Institute**

Care  
Medicinal Products

Willem Dudokhof 1  
1112 ZA Diemen  
PO Box 320  
1110 AH Diemen  
[www.zorginstituutnederland.nl](http://www.zorginstituutnederland.nl)  
[info@zinl.nl](mailto:info@zinl.nl)

T +31 (0)20 797 85 55

**Contact**

K. Watson

[warcg@zinl.nl](mailto:warcg@zinl.nl)

**Our reference**

2024036530

Dear Ms Agema,

In the letter of 24 June 2024 (CIBG-24-07072), you asked the National Health Care Institute to assess the possibility of expanding the List 2 condition for the combination preparation *relugolix + estradiol and norethisterone acetate* (Ryeqo®).

This combination therapy is currently used to treat patients with severe menstrual bleeding due to uterine fibroids.

**Background**

*The combination tablet relugolix + estradiol and norethisterone acetate* (Ryeqo®) is already listed in the Medicine Reimbursement System (GVS). It is included in List 1B of the Health Insurance Regulation (Rzv) with the following List 2 condition:

Only for adult insured persons of reproductive age with severe menstrual bleeding due to uterine fibroids for whom menopause is expected to start within 2 – 3 years and where conservative primary line medication has failed and surgical treatment/invasive procedure is not desired or possible.

**Current request**

The current request is for the expansion of this reimbursement condition to include the treatment of endometriosis-associated pain in adult women of reproductive age, where previous hormone and/or surgical treatment has been insufficient. It is based on the registration granted by the European Medicines Agency (EMA) in 2023 for the treatment of endometriosis symptoms.<sup>1</sup>

**Assessment of therapeutic value**

The standard treatment of endometriosis-related pain in women for whom first-line hormone medication has had insufficient effect and who do not choose surgery consists of off-label use of a *gonadotropin-releasing hormone agonist* (GnRH agonist) combined with hormone suppletion therapy. In the Netherlands, the most commonly prescribed GnRH agonist is leuprorelin, which is administered

<sup>1</sup> Endometriosis is a condition in which tissue similar to the lining of the uterus grows elsewhere in the body.

via subcutaneous injection.

The National Health Care Institute concluded that the combination preparation *relugolix + estradiol and norethisterone acetate* complies with the established medical science and medical practice for the present indication. The combination preparation has an equivalent clinical value to long-term use of a GnRH agonist (such as leuprorelin) + hormone suppletion therapy.

**National Health Care  
Institute**  
Care  
Medicinal Products

**Date**  
25 October 2024

**Our reference**  
2024036530

### **Budget impact analysis**

Taking into account the assumptions regarding patient numbers, duration of treatment, and comparative treatment, the above-mentioned expansion of the *relugolix + estradiol and norethisterone acetate* combination preparation in an insured adult patient with endometriosis-related pain will result in savings of approximately €0.1 million in the third year after inclusion in the package. A total of 1,672 patients will be treated with this medicinal product in the third year. The annual costs per patient are €1,285.06. This is slightly lower than the treatment costs for a GnRH agonist + hormone suppletion therapy: €1,362.49 There is uncertainty about the number of patients, the costs of replacement treatment and market penetration.

### **Cost-effectiveness**

Based on the estimated macro costs, the product is exempt from pharmacoeconomic analysis.

### **Advice**

Based on the above considerations, the National Health Care Institute recommends amending the current List 2 condition for the combination preparation of *relugolix + estradiol and norethisterone acetate* as follows:

Only for an adult insured person of reproductive age

1. with severe menstrual bleeding due to uterine fibroids for whom menopause is expected to start within 2 – 3 years and for whom conservative primary line medication has failed and surgical treatment/invasive procedure is not desired or possible; **or**
2. **with endometriosis-associated pain, where previous hormone therapy and/or surgery has been insufficient.**

Should you need any further information, please do not hesitate to contact us. The assessment reports (pharmacotherapeutic report & budget impact analysis) are attached as annexes.

Yours sincerely,

Mark Janssen  
*Chairperson of the Executive Board*