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The cost-effectiveness of ulipristal acetate tablets in treating patients with moderate to severe symptoms of uterine fibroids

Balázs Nagy [a,b,*], György Timár [b], Judit Józwiak-Hagymásy [b], Gábor Kovács [b], Gergő Merész [b], István Vámossy [c], Tamás Ágh [c], Ádám László [d], Zoltán Vokó [a,b], Zoltán Kaló [a,b]

[a] Department of Health Policy & Health Economics, Institute of Economics, Faculty of Social Sciences, Eötvös Loránd University, Budapest 1117, Hungary
[b] Syreon Research Institute, Budapest 1146, Hungary
[c] Gedeon Richter Plc., Budapest 1103, Hungary
[d] Bajcsy-Zsilinszky Hospital, Budapest 1106, Hungary

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ABSTRACT

Objectives: Ulipristal acetate is a selective progesterone receptor modulator that has been demonstrated to be an effective 3-month pre-operative treatment for moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The aim of this analysis was to assess the cost-effectiveness of 5 mg ulipristal as an add-on therapy to standard pre-surgical observation and treatment in Hungary.
Study design: A Markov model was developed using a 10-year time horizon. Ulipristal was compared with pre-surgical observation and immediate hysterectomy. The model comprised the following mutually exclusive health states: mild, moderate, severe, or persistent severe excessive bleeding disorder; myomectomy; post-myomectomy with mildly to moderately excessive bleeding disorder; post-myomectomy with severely excessive bleeding disorder; hysterectomy; post-hysterectomy; post-menopause; and death. Transition probabilities and utility values were obtained from clinical trials and the scientific literature. Resource utilisation and unit costs were derived from a consensus panel of clinical experts, National Health Insurance Fund tariffs, and publications.
Results: Adding a 3-month course of ulipristal to pre-operative observation was predicted to achieve an additional 0.021 quality-adjusted life years (QALYs) at an estimated incremental cost of €397, which would result in an incremental cost of €19,200/QALY. When 3 months of ulipristal therapy was compared with immediate hysterectomy, the incremental cost-effectiveness ratio was reduced to €3575/QALY. The results were most sensitive to the utility value of the post-hysterectomy health state but responsive to changes in other model parameters.
Conclusions: The results of this analysis suggest that adding ulipristal treatment to standard pre-surgical therapy represents a good value for money in Hungary. The inclusion of societal benefits may considerably reduce the cost-effectiveness ratio.

Introduction

Uterine fibroids, or leiomyomas, are benign hormone-sensitive tumours that consist of smooth muscle cells and affect approximately 20–40% of women of reproductive age [1,2]. Uterine fibroids are a benign disease, but this condition may have serious pathological consequences. In addition to anaemia caused by abnormal uterine bleeding, dysmenorrhea, pelvic pain, and pelvic pressure are common symptoms that are associated with uterine fibroids and may significantly reduce quality of life and affect fertility [3–6].

The mainstays of treatment for symptomatic uterine fibroids are surgical and radiological interventions. Uterine fibroids are the most common indication for hysterectomy [2]. Less invasive procedures include myomectomy, uterine artery embolisation and other radiological interventions [3,7]. Additionally, medical therapies are available to manage uterine fibroids. However, most of these therapies, such as gonadotropin-releasing hormone (GnRH) agonists, progestins, and levonorgestrel-releasing intrauterine devices, have limitations. GnRH agonists induce a low-oestrogen state, which effectively reduces fibroid size and bleeding, but they frequently cause hot flushes, and because of safety concerns, such as the loss of bone mineral density, the use of

* Corresponding author at: Syreon Research Institute, Thököly Street 119, 1146 Budapest, Hungary. Tel.: +36 1 787 0083; fax: +36 1 220 5768.

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these drugs is limited to short-term therapy [8]. Progestins may actually cause fibroids to grow and can result in breakthrough bleeding, which may limit their use [9,10]. Levonorgestrel-releasing intrauterine devices can only be used in women with no uterine distortion caused by fibroids. These devices control menorrhagia only in certain patients, and their effect on fibroid volume remains controversial [11].

Ulipristal acetate 5 mg (Esmya®, manufactured by Gedeon Richter Plc., Budapest, Hungary) is a novel oral therapy for the pre-operative treatment of symptomatic uterine fibroids in adult women of reproductive age [12]. Ulipristal acetate is a selective progesterone receptor modulator (SPRM) with a direct action on fibroids and the endometrium through the progesterone receptor [5,6,13]. Its clinical benefits include its ability to reduce fibroid-related bleeding, anaemia, pain, and fibroid size [5,6].

Ulipristal acetate has been compared with a placebo (Pearl I) [5] and GnRH agonists (Pearl II) [6] in pivotal clinical trials. In several Central-Eastern European countries, including Hungary, GnRH agonists are not reimbursed for the preoperative treatment of symptomatic uterine fibroids. Therefore, in these countries, GnRH agonists are not appropriate comparators for ulipristal acetate in economic evaluations. The aim of this analysis was to assess the cost-effectiveness of ulipristal acetate 5 mg as an add-on therapy to standard pre-surgical observation (i.e., a placebo) or immediate hysterectomy in a Hungarian healthcare setting.

Materials and methods

A Markov state-transition economic model was developed using a 10-year time horizon to estimate the cost-effectiveness of ulipristal acetate compared with either pre-surgical observation or immediate hysterectomy. The model comprised the following mutually exclusive health states: mild to moderate excessive bleeding disorder, severe excessive bleeding disorder, persistent severe excessive bleeding disorder, myomectomy, post-myomectomy with mild to moderate excessive bleeding disorder, post-myomectomy with severe excessive bleeding disorder, post-myomectomy with persistent severe excessive bleeding disorder, hysterectomy, post-hysterectomy, post-menopause, and death (Fig. 1).

In the ulipristal acetate and pre-surgical observation arms, the patient pathways (Fig. 1) followed the Pearl I clinical trial pattern. Pearl I was a randomised, parallel-group, double-blind, placebo-controlled, phase 3 trial that was conducted to assess the efficacy and safety of ulipristal acetate treatment for up to 13 weeks in women with symptomatic uterine fibroids and excessive uterine bleeding. All patients were eligible to undergo fibroid surgery at the end of the treatment period. Uterine bleeding was evaluated using the Pictorial Blood Assessment Chart (PBAC) [14]. The PBAC is a validated self-reporting tool that is used to estimate menstrual blood loss. The 28-day PBAC scores range from 0 (amenorrhea) to more than 500, and higher scores indicate increased bleeding. In the Pearl I clinical trial, women with a PBAC score >100 during days 1–8 of menstruation were included in the study. The mean 28-day PBAC score for all patients on a placebo and on ulipristal acetate 5 mg was 478.2 at baseline. Additional details on the Pearl I clinical trial's study design, methods, and results have been previously reported [5]. The patient characteristics that were used in the current study model were consistent with the study population in the Pearl I clinical trial. In the economic model, a minimum 50% reduction in the PBAC score was considered to be a clinically significant outcome. Therefore, "mild to moderate excessive bleeding" was defined by a PBAC score <225 over 28 days, whereas "severe excessive bleeding" was defined by a PBAC score ≥ 225 over 28 days.

Our model included potential patient health states. Patients either received 5 mg ulipristal acetate or were observed without special therapy for 3 months. In the first 13 weeks, patients stayed in one of the bleeding-related health states, the post-menopause health state, or death occurred. After the 13th week (i.e., the end of

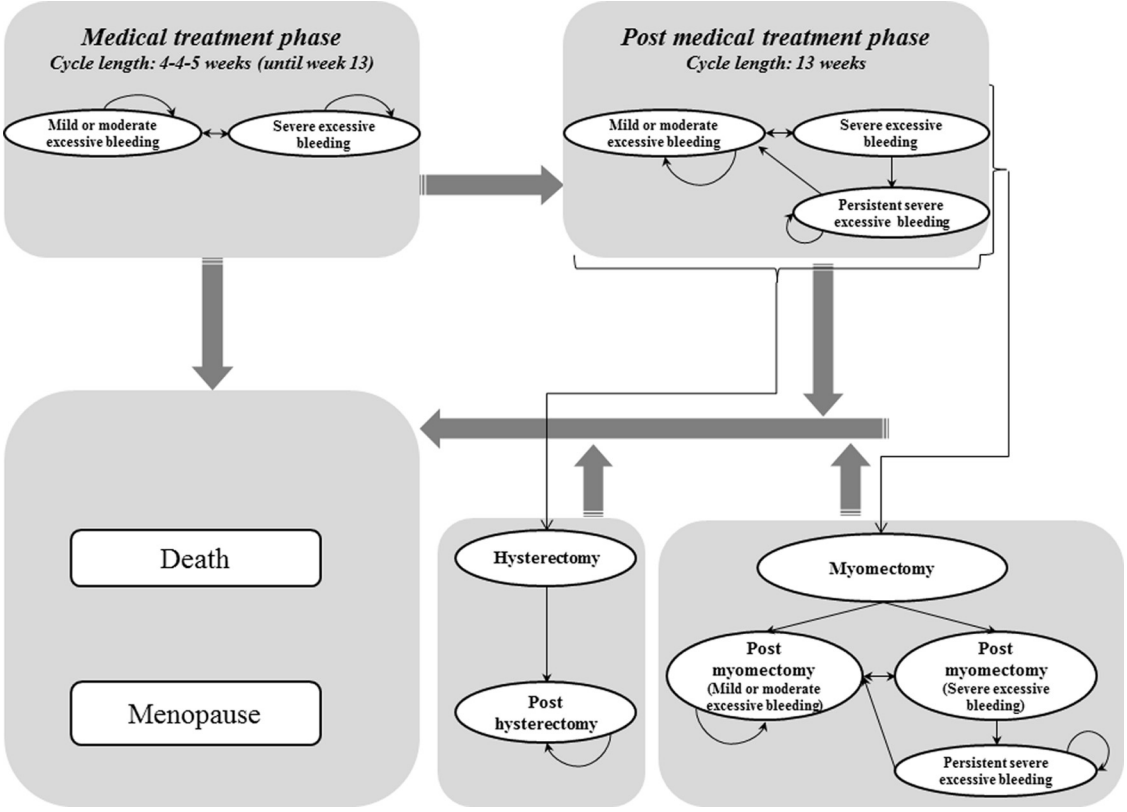

Fig. 1. Patient pathways in the economic model.

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