Cost-Effectiveness of Linzagolix for Uterine Fibroids in Australia: A Healthcare Payer and Societal Perspective

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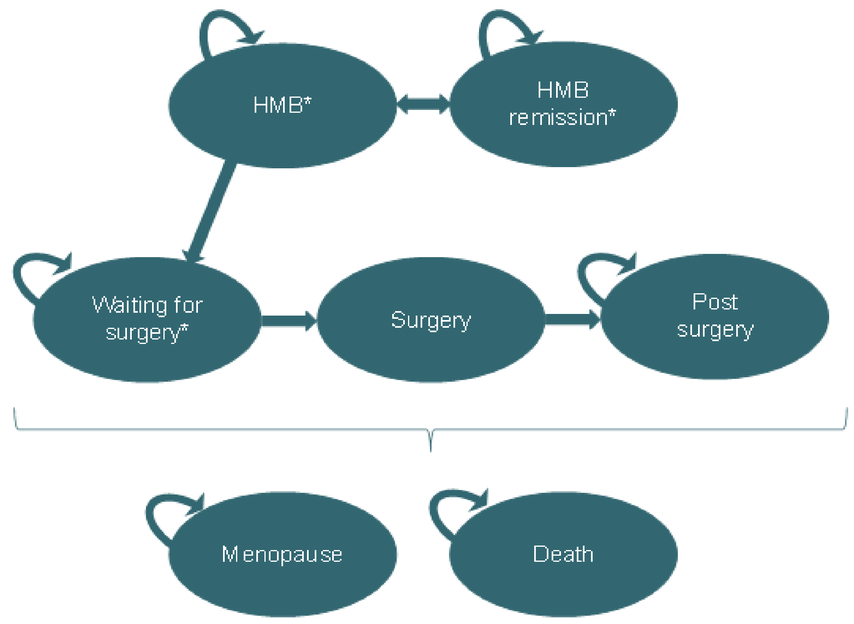
INTRODUCTION

- Uterine fibroids (UFs) are non-cancerous muscle tumours of the uterus and are common in women of reproductive age. Despite their high prevalence, UFs are generally underdiagnosed and under-treated, reflecting the fact that this has been, until recently, a relatively neglected women's health issue.
- In many cases UFs are asymptomatic, or symptoms are successfully treated with first line treatments such as hormonal therapies (eg, oral contraceptives and intrauterine systems) and/or anti-inflammatory medications.
- A proportion of women continue to experience severe symptoms including heavy menstrual bleeding (HMB) despite the use of first line therapies, and the use of hormonal therapies is sometimes limited by contraindications and/or patient preferences.
- In these women, chronic symptoms can lead to anxiety, stress, self-esteem issues, reproductive concerns and increased financial burden, including substantial healthcare costs. These factors contribute to high rates of absenteeism in the workplace[1], depression[2] and a reduced quality of life overall.[3]
- Other treatment options include surgery (eg, hysterectomy and myomectomy); however, in Australia, there is a growing preference for minimally invasive and uterus-preserving approaches to therapy.
- For women who are refractory to, or intolerant to first line therapies, there is a high clinical need for reimbursed non-surgical treatment options.
- Linzagolix (LGX) is a novel oral GnRH antagonist that can reduce HMB associated with UFs and shrink fibroid volume through the suppression of oestrogen. In most markets LGX is available in two doses (100 mg and 200 mg[#]), and each can be used with or without hormonal add-back therapy (ABT), so treatment can be tailored to the needs of the individual.
- The superior clinical efficacy of LGX compared to best supportive care (BSC) is supported by two Phase 3, double-blind, multicentre, randomised placebo-controlled trials: PRIMROSE 1 and PRIMROSE 2[4].

Objective To evaluate the cost-effectiveness of LGX plus BSC compared to BSC alone for the treatment of moderate to severe symptoms of UFs, including HMB, in premenopausal adult women in Australia from a healthcare payer and societal perspective.

Figure 1. Simplified model structure



** In each arm of the model, treatment is either LGX + BSC or BSC alone.*
Surgery includes myomectomy, abdominal hysterectomy and laparoscopic hysterectomy.

METHODS

Model structure

- A cost-utility analysis was conducted using a combined decision tree and Markov model with monthly cycles to estimate costs and health outcomes from treatment initiation to menopause when symptoms naturally resolve.
- The model accounted for varying female age at treatment initiation and menopause, resulting in a variable time horizon of 3-21 years. Costs and health outcomes were discounted at 5% per year.
- The model was analysed from two perspectives: the Australian healthcare system, and a societal perspective in line with previously published models in UFs.
- Both perspectives captured the drug acquisition costs of LGX, direct healthcare costs associated with HMB, and health-related outcomes experienced by patients in the form of QALYs. The societal perspective additionally captured productivity losses due to HMB.
- The model consisted of 17 health states based on treatment received (LGX+BSC; BSC), HMB status, surgery and death. A simplified model structure is provided in Figure 1.
- The model applied a stopping rule at 24 weeks in line with the PRIMROSE trials whereby patients on LGX who failed to show an adequate reduction in menstrual bleeding, discontinued treatment.

Model inputs

- Starting age in the model reflected the lower threshold of each of the four age groups considered in PRIMROSE (35-year-old: 22.3%; 39-year-old: 25.2%; 43-year-old: 21.8%; 46-year-old: 30.8%). Age at natural menopause was approximately grouped into quartiles based on an Australian cohort study.[5]
- Transition probabilities and utility weights were obtained from the PRIMROSE trials and literature.
- Health state utility values were estimated based on PRIMROSE data, using mapped UFS-QoL to EQ-5D-3L values. The resulting utility values were 0.7159 for patients with HMB and 0.8421 for patients in HMB remission.
- Direct cost inputs, including costs for BSC, bone mineral density monitoring, and hospitalisations, were obtained based on Medicare Benefits Schedule and Pharmaceutical Benefits Scheme item fees as well as AR-DRGs. LGX treatment costs were informed by the manufacturer. Productivity costs were informed by the literature.
- Transition probabilities were based on the 200 mg dose of LGX plus ABT, however the model also considered that ultimately there would be a proportion of patients on 100 mg LGX, a proportion on 200 mg LGX and a proportion of each of those cohorts with or without ABT.

Table 1. Base case results

Component	LGX	BSC	Incremental
Healthcare payer perspective			
Cost	$15,095.59	$7,472.58	$7,623.01
QALY	6.1860	6.0187	0.1673
Total			$45,567
Societal perspective			
Cost	$35,482.06	$34,932.84	$549.22
QALY	6.1860	6.0187	0.1673
Total			$3,283

RESULTS

- LGX is associated with a 0.1673 QALY gain and additional cost of $7,623 compared to BSC, resulting in an ICER of $45,567/QALY gained from a healthcare payer perspective.
- From a societal perspective, incremental costs associated with LGX decrease to $549 compared to BSC. Due to significant productivity costs associated with UFs, a societal perspective suggests an ICER as low as $3,283/QALY gained.
- Regardless of the perspective utilised, this model demonstrates the cost-effectiveness of LGX for the treatment of UFs, producing ICERs which are generally within an acceptable range in Australia (see Table 1).
- Sensitivity analyses from a healthcare payer perspective suggest that results are sensitive to the probability of progressing to surgery (ICER range: $39,004 to $98,055) and the utility gain from achieving remission (ICER range: $26,193 to $409,430).
- The impact of varying the treatment response rates was modest with ICERs ranging between $50,008 to $64,054 (see Table 2)

Table 2. Results of sensitivity analyses from a healthcare payer perspective

Parameter (base case value)	Description	Incremental costs	Incremental QALYs	ICER
Base case		**$7,623.01**	**0.1673**	**$45,567**
Probability of progressing to surgery (0.602 over 10-year period i.e., 0.0076)	Assume 0.602 over 1-year period (0.0739 per cycle)	$6,322.31	0.0645	$98,055
	Assume 0.602 over max. time horizon of 21 years (0.0036 per cycle)	$8,307.44	0.1983	$41,885
	Removed (0.0000 per cycle)	$9,326.09	0.2391	$39,004
Utility gain in remission (based on pooled PRIMROSE 1 and 2 UFS-QoL results (unadjusted): 0.1262)	Based on pooled PRIMROSE 1 and 2 UFS-QoL results (baseline-adjusted): 0.0572	$7,623.01	0.0763	$99,951
	Based on pooled PRIMROSE 1 and 2 EQ-5D results (baseline-adjusted): 0.0135	$7,623.01	0.0186	$409,430
	Based on Hux (2015)[6]: 0.18	$7,623.01	0.2383	$31,994
	Based on Daniels (2022)[7]: 0.2200	$7,623.01	0.2910	$26,193
LGX efficacy (pooled PRIMROSE 1 and 2 response rate for LGX 200 mg + ABT: 0.845)	Pooled PRIMROSE 1 and 2 response rate for LGX 100 mg: 0.565	$5,755.33	0.0899	$64,054
	Pooled PRIMROSE 1 and 2 response rate for LGX 100 mg + ABT: 0.716	$6,756.82	0.1310	$51,597
	Pooled PRIMROSE 1 and 2 response rate for LGX 200 mg: 0.745	$6,950.03	0.1390	$50,008

CONCLUSIONS

- There is an urgent clinical need for reimbursed non-surgical treatments for moderate to severe symptoms of UFs in women who are refractory or intolerant to first-line hormonal therapies.
- This analysis indicates that LGX reduces HMB, providing a meaningful QoL improvement at a reliably estimated and reasonable level of cost-effectiveness – even more so when a societal perspective is considered.
- The model should be considered in light of certain assumptions, many of which were conservative. For example, it does not account for the fertility risks associated with myomectomy; or the treatment impact of reducing fibroid volume and its potential to simplify or improve the outcomes of surgery. Limitations include a lack of long-term data and low use of prior hormonal therapies in the study population. Nevertheless, the model was shown to be generally robust based on sensitivity analyses.
- To the knowledge of the authors, this is the first peer-reviewed economic evaluation of LGX versus BSC for the treatment of UFs.

References

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Conflict of interest: Study sponsored by Theramex.

Abbreviations: ABT, add back therapy; BSC, best supportive care; HMB, heavy menstrual bleeding; ICER, incremental cost-effectiveness ratio; LGX, Linzagolix; QALY, quality adjusted life year; UF, uterine fibroids.
 # In Australia, LGX 100 mg is currently approved by the Therapeutic Goods Administration.