

**South East London Integrated Medicines Optimisation Committee
Formulary recommendation**

Reference:	135
Intervention:	Dienogest (Zalkya™) 2mg film-coated tablets for the treatment of endometriosis (Dienogest is a testosterone derivative with antiandrogenic activity)
Date of Decision:	August 2022, updated January 2024 following report on outcomes data-time limit to the approval removed
Date of Issue:	September 2022, re-issued March 2024
Recommendation:	Amber 2 – initiation and first prescription from the specialist team
Further Information	<ul style="list-style-type: none"> • Dienogest 2mg film-coated tablets (Zalkya™) are accepted for use in South East London as a second line pharmacological treatment option for the treatment of endometriosis related pain • Use is restricted in adults who: <ul style="list-style-type: none"> - Have been referred to specialist obstetric and gynaecology services and have confirmed endometriosis (laparoscopy or MRI or scanned in endometriosis ultrasound clinic) AND - Analgesia and established, conventional hormonal treatments (e.g. combined oral contraceptives or progestogens) have been ineffective or not tolerated • Patients may or may not be under consideration for surgery. In patients who are being considered for surgery or are not suitable for surgery, dienogest may provide an alternative option to gonadotropin hormone-releasing hormone (GnRH) agonists. This includes: <ul style="list-style-type: none"> - Treatment for pre-surgery reduction of endometrioma size - Treatment for post-surgical suppression of endometriosis • Dienogest and GnRH agonists are both second line pharmacological treatment options for the management of endometriosis before or after surgery. • Patients should be offered the option of either dienogest or a GnRH agonist if they meet the above criteria. The decision to initiate dienogest or a GnRH agonist will be made based on an informed decision between the initiating clinician and the patient and will include patient factors and preference. • It should be noted that at the time of approval, data exist for use of dienogest up to 15 months. The continued need for dienogest should be regularly reassessed and reviewed by the prescriber. • Patients must be counselled on the appropriate administration as described in the product information. • The initial prescription and supply will come from the initiating specialist team. Prescribing can then be continued in primary care under “Amber 2” arrangements. • January 2024: In September 2022 the Committee approved the inclusion of dienogest (Zalkya™) for a time limited period to enable experience of use with dienogest. A report summarising outcomes with the use of dienogest in this setting was requested by the Committee after 12 months. It was reported by the acute Trusts that approximately two-thirds of patients treated with dienogest reported a reduction in pain with improved symptoms. Additionally, two-thirds of patients continued treatment. The adverse effects experienced were in line with those noted as “common” or “very common” in the product literature.
Shared Care/ Transfer of care required:	N/A.
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • Local experts estimate there will be approximately 80 - 90 patients per year initiated on dienogest from SEL. • Whilst this equates to an additional cost of approximately £21,510 – £24,200 per annum (~ £1,132 - £1,275 per 100,000 population), compared to GnRH agonists,

	<p>this would equate to savings of around £60,000 - £67,500 in SEL (up to ~£3,500 per 100,000 population). There could also be savings through reduced resource required to administer injections (time/staff capacity).</p> <ul style="list-style-type: none"> The cost impact is therefore likely to be negligible if used in line with this recommendation.
<p>Usage Monitoring & Impact Assessment</p>	<p>Acute Trusts: Monitor and audit usage and outcomes from use of dienogest in this setting (against this recommendation) and report back to the Committee if requested</p> <p>SEL Borough Medicines Optimisation Teams: Monitor ePACT2 data and exception reports from GPs if inappropriate prescribing requests are made to primary care.</p>
<p>Evidence reviewed</p>	<p>References (from evidence evaluation)</p> <ol style="list-style-type: none"> Endometriosis: diagnosis and management (NG73). NICE 2017 [online] Available here [Accessed 18/07/2022] Endometriosis - Guideline of European Society of Human Reproduction and Embryology (ESHRE) 2021. [online] Available here [Accessed 18/07/2022] Zalkya (dienogest), Summary of Product Characteristics. [online] Available here [accessed 18/07/2022]. Strowitzki T, Faustmann T, Gerlinger C et al. Dienogest in the treatment of endometriosis-associated pelvic pain: a 12 week randomised double blind placebo controlled study. European Journal of Obstetrics & Gynaecology and Reproductive Biology 2010 151 p193-198. Petraglia F, Hornung D, Seitz C et al. Reduced pelvic pain in women with endometriosis: efficacy of long-term dienogest treatment. Archives of Gynaecology and Obstetrics 2012 285 p167-173. Strowitzki T, Marr J, Gerlinger C. Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomised multicentre open-label study. Human reproduction 2010 25 (3) p633-641. Lin S, Wang X, Fu X et al. Systematic review and meta-analysis of efficacy and safety of dienogest in treatment of endometriosis. World Journal of Meta-analysis 2021 9 (4) p377-388. Samy A, Taher A, Sileem S et al. Medical therapy options for endometriosis related pain, which is better? A systematic review and network meta-analysis of randomised controlled trials. Gynaecology, Obstetrics and Human Reproduction 2020 doi.org/10/1016/j.jogoh.2020.101798 Lukac M, Knight C, Bielik J et al. Endometriosis associated pelvic pain treated with dienogest or GnRH analogues: cost-utility comparison with 5 year time horizon. Value in Health 2011 (14) Supplement A233-510. Avxentyeva M. Cost-minimisation analysis of dienogest versus gonadotrophin releasing hormone analogues or dydrogesterone for endometriosis treatment in Russia. Value in Health 2013 (16) A323-636. Ferracini M, Nakada C. Cost minimisation analysis of the dienogest use in patients with endometriosis under Brazilian public and private perspective. Value in Health 2013 (16) A323-636. Lukac M, Knight C, Bielik J et al. Cost-utility analysis of dienogest versus GNRH analogue in the treatment of endometriosis associated pelvic pain in Slovakia. Value in Health 14 (2011) A1-214. Martin R, Nelson A, Camilo A et al. Cost minimisation analysis of the dienogest use in patients with endometriosis in Columbia and Argentina. Value in Health 2012 A1-256.

NOTES:

- SEL IMOC recommendations and minutes are available publicly via the [website](#).
- This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
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