

Dienogest for endometriosis in short-term studies (3–6 months): a systematic review and meta-analysis

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Type: Systematic review / meta-analysis (preprint, version of record) · **Search date:** 9 June 2026 · **Analysis date:** 10 June 2026
· **Version date:** 10 June 2026
Records identified: 411 · **Studies in pain synthesis:** 27 · **Primary outcome:** endometriosis-associated pelvic pain (VAS/VRS, 0–10)
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<https://docs.mdwrt.app/infographics/dienogest-endometriosis-en/>

Abstract

Background. Endometriosis is a chronic, oestrogen-dependent disease affecting about 10% of women of reproductive age, with pelvic pain as its leading and most disabling manifestation. Dienogest is a fourth-generation oral progestin approved at 2 mg/day for endometriosis-associated pain. Because early response (the first 3–6 months) drives adherence and the decision to continue, we focused on the short-term horizon, which most reviews under-report in favour of long-term (≥ 12 -month) outcomes.

Objective. To quantitatively assess the efficacy of dienogest 2 mg/day for endometriosis-associated pain and to characterise its tolerability in short-term (3–6 month) studies.

Methods. A systematic PubMed search combined intervention terms (dienogest and brand names) with disease terms (endometriosis) and returned 411 records. Eligible designs were RCTs and prospective single-arm before–after studies of dienogest 2 mg/day monotherapy in established endometriosis, with a pain assessment (VAS/VRS) at 3–6 months. Pain measures were harmonised to a 0–10 scale. The primary synthesis pooled the within-arm pain change using a random-effects model (DerSimonian–Laird with Knapp–Hartung adjustment), reporting I^2 and a 95% prediction interval; where only baseline and end values were available, the standard error of the change was derived assuming a paired-measurement correlation $r = 0.5$ (robustness checked for $r = 0.3$ – 0.7). Tolerability was pooled as proportions (logit transform). A formal risk-of-bias assessment was not performed in this iteration and is flagged for the full version.

Results. Twenty-seven studies entered the pain synthesis. Dienogest 2 mg/day reduced overall pelvic pain by a pooled -3.64 points on the 0–10 VAS scale (95% CI -4.46 to -2.82 ; $k = 17$; $I^2 = 99\%$), dysmenorrhoea by -3.82 points (95% CI -4.67 to -2.98 ; $k = 14$), and dyspareunia by -1.93 points (95% CI -3.09 to -0.78 ; $k = 10$; $p = 0.004$; $I^2 = 100\%$; prediction interval -6.30 to 2.43). The pelvic-pain estimate was robust to the assumed paired-measurement correlation ($r = 0.3$ – 0.7). Tolerability was favourable: pooled treatment discontinuation from any cause was 11.2% (95% CI 8.1–15.2; $k = 29$) and discontinuation due to adverse events was 6% (95% CI 4.9–8.0; $k = 22$); the most frequent adverse event was a change in bleeding pattern (spotting/irregular bleeding 29%; amenorrhoea 41%), an expected progestin class effect.

Conclusions. Over a 3–6 month horizon, dienogest 2 mg/day produces a clinically meaningful reduction in endometriosis-associated pelvic pain and dysmenorrhoea, with a smaller but significant effect on dyspareunia and favourable tolerability (≈ 89 – 94% continue). The early, sustained pain response supports dienogest as a rational first-line therapy from the start of treatment.

Keywords: endometriosis; dienogest; pelvic pain; dysmenorrhoea; dyspareunia; meta-analysis; systematic review; progestin; tolerability.

1. Introduction

Endometriosis is a chronic, oestrogen-dependent disease affecting about 10% of women of reproductive age. Its leading and most disabling manifestation is pelvic pain: secondary dysmenorrhoea, non-cyclic pelvic pain and dyspareunia. Because radical surgery does not eliminate the risk of recurrence, long-term hormonal therapy that suppresses disease activity remains the mainstay of management for most patients. Dienogest is a fourth-generation oral progestin with selective progestogenic and antiproliferative effects on endometriotic tissue; at 2 mg/day it is approved for endometriosis and has become a first-line option for endometriosis-associated pain. For both clinician and patient the early response is decisive: pain dynamics over the first 3–6 months drive adherence and the decision to continue. From an evidence-based standpoint, the right answer about the magnitude of effect is not a narrative listing of individual studies but their quantitative synthesis.

2. Aim and review question

To quantitatively assess the efficacy of dienogest 2 mg/day for endometriosis-associated pain and to characterise its tolerability in short-term (3–6 month) studies.

PICO. **P** — women with endometriosis · **I** — oral dienogest 2 mg/day · **C** — within-arm change (before → after; controlled comparisons considered additionally) · **O** — primarily pain (VAS/VRS), secondarily tolerability · **Window** — 3–6 months.

3. Methods

3.1 Search

A systematic PubMed search combined intervention terms (dienogest and brand names) and disease terms (endometriosis). Primary reproducible query:

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(dienogest[tiab] OR "Dienogest"[nm] OR Visanne[tiab] OR Dinagest[tiab] OR Visabelle[tiab] OR DNG[tiab]) AND ("Endometriosis"[Mesh] OR endometriosis[tiab] OR endometrioma*[tiab] OR endometriotic[tiab]) NOT (animals[mh] NOT humans[mh])
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The query returned 411 records.

3.2 Eligibility criteria

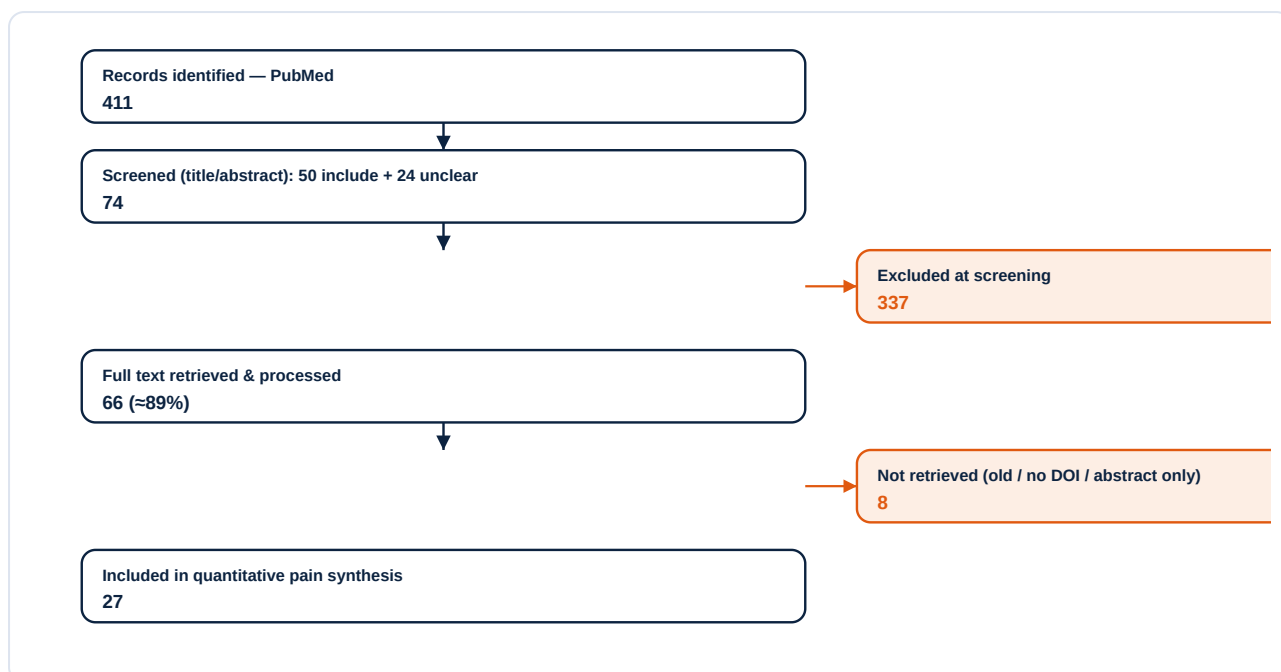
Included: RCT or prospective single-arm before–after study; women with established endometriosis; dienogest 2 mg/day monotherapy; assessment of pain (VAS/VRS) and/or lesions/quality of life; an assessment point within 3–6 months. **Excluded:** reviews and meta-analyses; retrospective studies and case series; combination products (dienogest within a combined oral contraceptive); studies without relevant outcomes or with long-term timepoints only.

3.3 Data extraction and analysis

Data were extracted independently over several iterations with disagreement resolution; contested numeric values were checked against the source. Pain measures were harmonised to a single 0–10 scale. The primary synthesis pooled the within-arm pain change using a random-effects model (DerSimonian–Laird, Knapp–Hartung adjustment), with the I^2 heterogeneity statistic and a 95% prediction interval; when only baseline and end values were reported, the standard error of the change was derived assuming a paired-measurement correlation $r = 0.5$ (robustness checked for $r = 0.3$ – 0.7). Tolerability was pooled as proportions (proportion meta-analysis, logit transform). Physically impossible values or those incompatible with the denominator were excluded and flagged for review.

Risk of bias. Within this tender, given the tight timeframe, a formal risk-of-bias assessment (RoB 2 / ROBINS-I) was not performed; it is flagged as a direction for the full version of the review.

4. Study selection (PRISMA 2020)



Stage	n
Identification — PubMed records	411
Screening (title/abstract) — selected	74
of which clear includes / unclear	50 / 24
Excluded at screening (reviews / retrospective / irrelevant / long-term only)	337
Full text retrieved and processed	66 (~89%)
Not retrieved (old / no DOI / niche-language / abstract only)	8
Included in the quantitative pain synthesis	27

5. Characteristics of included studies

The included studies span the full range of short-term evidence — from placebo-controlled and active-comparator RCTs (vs GnRH agonists, COC, LNG-IUS, other progestins) to large prospective single-arm real-world cohorts (Cho 2020, n = 2777; Techatraisak 2022, n = 484).

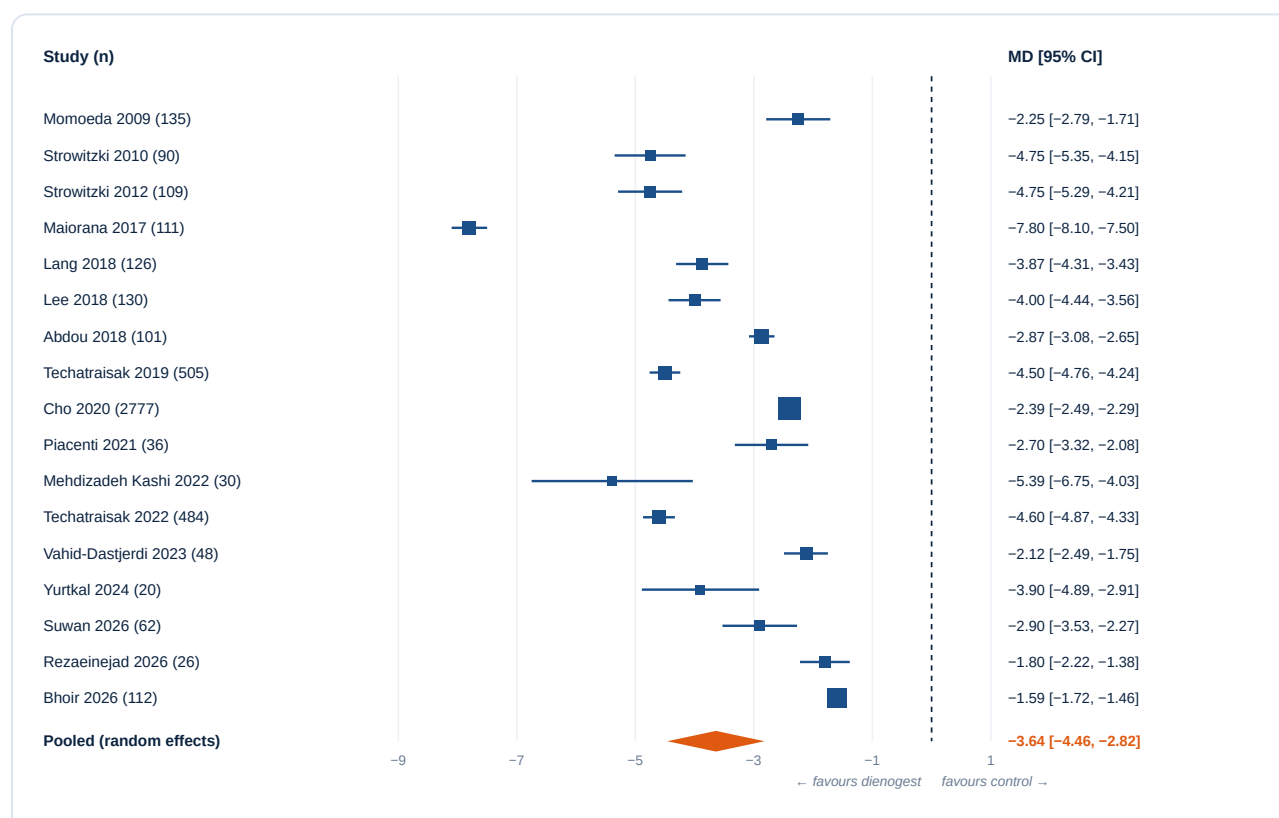
Study	Year	Design	N	Scale	Comparator	Outcomes
Momoeda	2009	prospective single-arm	135	VAS 0–100mm	— (single-arm)	Pelvic
Strowitzki	2010	RCT	90	VAS 0–100mm	GnRH agonist	Pelvic
Strowitzki	2012	RCT	109	VAS 0–100mm	GnRH agonist	Pelvic
Yanase	2014	prospective single-arm	25	VAS 0–10	— (single-arm)	Dysmen.
Maiorana	2017	prospective single-arm	106	VAS 0–10	— (single-arm)	Pelvic/Dyspar.
Lang	2018	RCT	126	VAS 0–100mm	placebo	Pelvic
Lee	2018	non-rand. comparative	130	VAS 0–10	LNG-IUS	Pelvic/Dysmen.
Abdou	2018	RCT	55	VAS 0–100mm	GnRH agonist	Pelvic/Dyspar.
Lee	2018	single-arm	61	VAS 0–10	— (single-arm)	Dysmen.
Techatraisak	2019	prospective single-arm	505	NRS 0–10	— (single-arm)	Pelvic
Cho	2020	prospective single-arm	2777	VAS 0–100mm	— (single-arm)	Pelvic
Osuga	2020	prospective single-arm	147	VAS 0–100mm	— (single-arm)	Dysmen.
Piacenti	2021	non-rand. comparative	36	VAS 0–10	COC	Pelvic/Dyspar.

Malik	2021	prospective single-arm	56	NRS 0–10	— (single-arm)	Dysmen.
Niakan	2021	RCT	30	VAS 0–10	placebo	Dyspar.
Mehdizadeh Kashi	2022	RCT	30	VAS 0–10	placebo	Pelvic/Dyspar.
Techatraisak	2022	prospective single-arm	484	NRS 0–10	— (single-arm)	Pelvic
Vahid-Dastjerdi	2023	non-rand. comparative	48	VAS 0–10	other progestin	Pelvic/Dysmen./Dyspar.
Saglik Gokmen	2023	prospective single-arm	64	VAS 0–10	— (single-arm)	Dysmen./Dyspar.
Yurtkal	2024	non-rand. comparative	20	VAS 0–10	COC	Pelvic/Dysmen.
Chaichian	2024	prospective single-arm	15	VAS 0–10	other	Dysmen.
Long	2024	prospective single-arm	22	VAS 0–10	— (single-arm)	Dyspar.
Park	2025	prospective single-arm	30	VAS 0–10	— (single-arm)	Dysmen.
Kikuno	2025	RCT	44	VAS 0–100mm	other progestin	Dysmen.
Suwan	2026	prospective single-arm	62	VAS 0–10	— (single-arm)	Pelvic/Dysmen./Dyspar.
Rezaeinejad	2026	RCT	26	VAS 0–10	placebo	Pelvic/Dysmen./Dyspar.
Bhoir	2026	RCT	112	NRS 0–10	other (elagolix)	Pelvic/Dysmen.

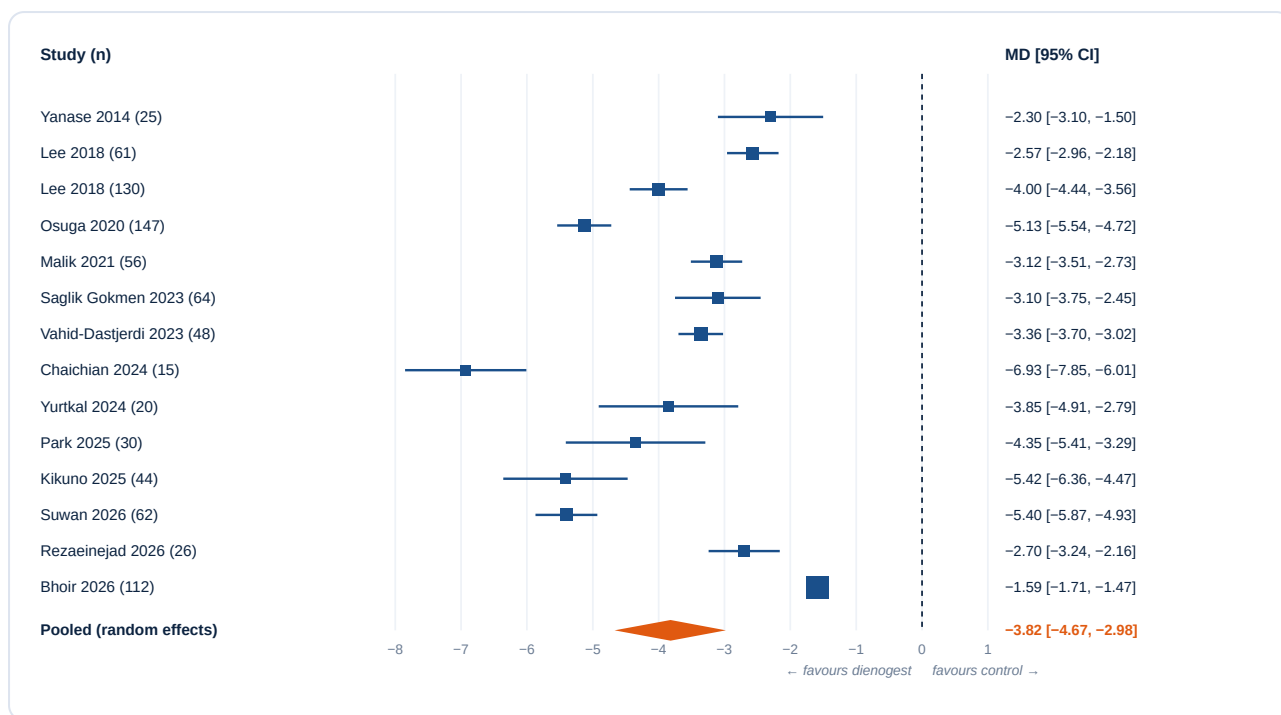
6. Primary outcome — pain (before–after change)

Values are mean differences (MD) in points on the 0–10 VAS scale; negative values indicate a reduction in pain. Pooled estimates are random-effects (DerSimonian–Laird, Knapp–Hartung).

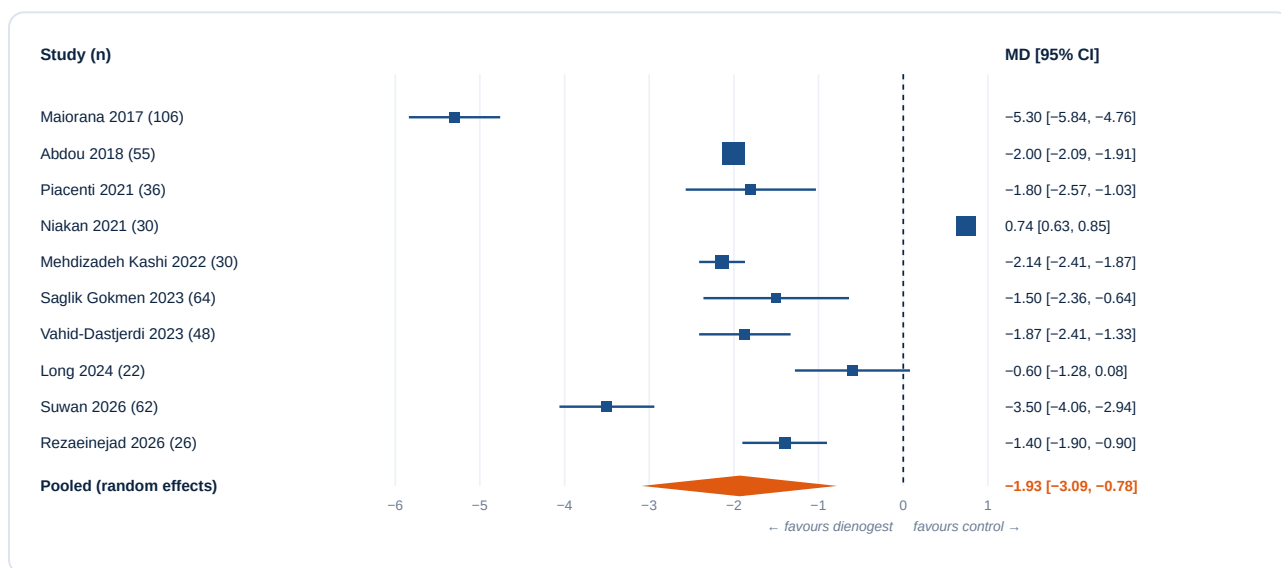
6.1 Pelvic pain (overall) — pooled -3.64 $[-4.46, -2.82]$, $k = 17$, $I^2 = 99\%$



6.2 Dysmenorrhoea — pooled -3.82 $[-4.67, -2.98]$, $k = 14$



6.3 Dyspareunia — pooled -1.93 $[-3.09, -0.78]$, $k = 10$, $p = 0.004$, $I^2 = 100\%$, PI $[-6.30, 2.43]$



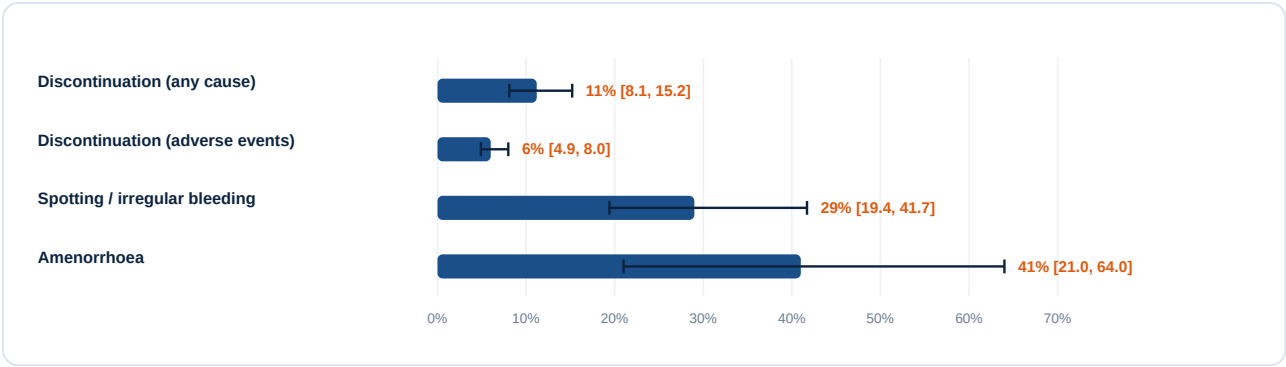
7. Sensitivity analysis

The pelvic-pain result is robust to the assumed correlation of paired measurements:

Correlation r	k	MD	95% CI	I ²
0.3	17	-3.64	[-4.46, -2.82]	99%
0.5	17	-3.64	[-4.46, -2.82]	99%
0.7	17	-3.64	[-4.46, -2.83]	99%

8. Tolerability

Tolerability over 3–6 months was favourable: about 89–94% of patients continued treatment. The most frequent adverse events were changes in the menstrual bleeding pattern — an expected progestin class effect that generally warrants counselling rather than discontinuation. Frequencies are pooled proportions (logit) with 95% CI.



Outcome	Pooled %	95% CI	k
Treatment discontinuation (any cause)	11.2%	[8.1, 15.2]	29
Discontinuation due to adverse events	6.0%	[4.9, 8.0]	22
Spotting / irregular bleeding	29%	[19.4, 41.7]	29
Amenorrhoea	41%	[21.0, 64.0]	10

9. Discussion, limitations and conclusions

Limitations. A single search source (PubMed) was used in this iteration; 8 of 74 candidate full texts were unavailable; and a formal risk-of-bias assessment was not performed — the key direction for the full version. Statistical heterogeneity was high (I^2 up to 100%), reflecting the mix of designs, scales and populations pooled to estimate the short-term effect size.

Conclusions. In the short term (3–6 months), dienogest 2 mg/day produces a clinically meaningful reduction in endometriosis-associated pelvic pain (pooled reduction of about 3.6 points on a 0–10 scale) and dysmenorrhoea (about 3.8 points), with a smaller but statistically significant effect on dyspareunia. Treatment shows favourable tolerability (about 89–94% of patients continue). The early, sustained pain response supports the use of dienogest as a rational first-line therapy from the start of treatment.

References — studies included in the quantitative pain synthesis (n = 27)

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