Pharmacological Management of Common Gynecological Pathologies: Comprehensive Review of Therapeutic Strategies and Clinical Applications

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Abstract: Gynecological pathologies represent significant global health challenges affecting women of reproductive age. This comprehensive review examines the pharmacological management of endometriosis, polycystic ovary syndrome (PCOS), uterine fibroids, menorrhagia, dysmenorrhea, and gynecological malignancies. Current therapeutic approaches include hormonal therapies (progestins, GnRH agonists/antagonists, combined oral contraceptives), selective progesterone receptor modulators (SPRMs), insulin sensitizers, and emerging immunotherapies. Recent advances demonstrate superior efficacy of novel agents such as elagolix, linzagolix, ulipristal acetate, and checkpoint inhibitors (pembrolizumab, dostarlimab) in specific pathologies. This review synthesizes current evidence regarding drug mechanisms, comparative efficacy, adverse effects, and emerging treatment paradigms based on 60 recent publications and clinical trials.

Keywords: *gynecological pathologies, pharmacological treatment, endometriosis, PCOS, uterine fibroids, immunotherapy, hormonal therapy, GnRH agonists*

INTRODUCTION

Gynecological pathologies remain among the most prevalent conditions affecting women globally, with significant morbidity and substantial impact on quality of life. In recent decades, gynecology has undergone profound transformation driven by technological, pharmacological, and biotechnological innovations. Endometriosis affects approximately 10-15% of reproductive-age women, with estrogen-dependent mechanisms driving disease progression. The development of hormonal therapies targeting gonadotropin-releasing hormone (GnRH) pathways and novel selective progesterone receptor modulators (SPRMs) has substantially improved clinical outcomes [1-3]. Polycystic ovary syndrome (PCOS), affecting 6-20% of women, represents a complex endocrine-metabolic disorder where insulin resistance and hyperandrogenism drive pathophysiology. Current management employs insulin sensitizers and antiandrogen medications with emerging evidence supporting novel inositol formulations [5, 7]. Uterine fibroids occur in 20-50% of reproductive-age women, and while ulipristal acetate has demonstrated superior efficacy and favorable side-effect profiles compared to traditional GnRH agonists, clinical use remains

variable [9, 11]. Menorrhagia and dysmenorrhea significantly impact daily functioning in a substantial proportion of women, with multiple therapeutic modalities including tranexamic acid, NSAIDs, and intrauterine systems offering effective management [12, 15]. Gynecological malignancies, particularly cervical, ovarian, and endometrial cancers, represent leading causes of cancer-related mortality, though recent breakthroughs in checkpoint inhibitors and PARP inhibitors have transformed treatment landscapes [2, 3, 6]. This comprehensive review synthesizes current pharmacological approaches to these conditions, evaluating therapeutic mechanisms, comparative efficacy, adverse effects, and emerging treatment paradigms.

METHODS

This comprehensive literature review examined pharmacological treatment strategies for gynecological pathologies published between 2022-2026. A systematic search was conducted using PubMed, Cochrane Database, Web of Science, and clinical trial registries (clinicaltrials.gov). Search terms included: endometriosis treatment, PCOS management, uterine fibroids pharmacotherapy, gynecological cancer immunotherapy, menorrhagia treatment, and dysmenorrhea management. Inclusion criteria encompassed randomized controlled trials, systematic reviews, meta-analyses, phase 2-3 clinical trials, and expert consensus guidelines. Exclusion criteria included case reports, animal studies, and publications without English abstracts. A total of 60 recent publications and clinical trials were selected for comprehensive analysis. Data extraction included: drug mechanisms of action, efficacy outcomes (clinical response rates, symptom relief), safety profiles (adverse effects, contraindications), dosing regimens, comparative effectiveness, and biomarker-guided treatment strategies. Quality assessment was performed using GRADE methodology for evidence evaluation.

Table 1. Pharmacological Treatment Comparison: Mechanisms, Efficacy, and Safety Profiles Across Gynecological Pathologies

Pathology	Drug Class/Agent	Mechanism	Efficacy	Key Adverse Effects	Special Notes
Endometriosis	Dienogest (progestin)	↓ FSH/LH, endometrial atrophy	70-80% pain relief; long-term efficacy	Breakthrough bleeding, mood changes	First-line long-term option
Endometriosis	GnRH agonists (leuprolide)	Profound estrogen suppression	60-75% lesion reduction; short-term use	Bone loss, hot flushes, hypoestrogenism	Requires add-back therapy

Endometriosis	GnRH antagonists (elagolix)	Selective GnRH receptor inhibition, oral	65-72% pain improvement; rapid recovery	Hot flushes (reversible), vaginal dryness	No flare-up effect; oral administration
PCOS	Metformin	Insulin sensitizer; ↓ HbA1c	Weight loss, cycle normalization (40-50%)	GI side effects; rare lactic acidosis	Gold standard; 1000-2000 mg/day
PCOS	Myoinositol	Insulin sensitizer; second messenger	Non-inferior to metformin; RCT evidence	Minimal; well tolerated	Natural alternative; 4g daily
Uterine Fibroids	Ulipristal Acetate (SPRM)	Selective progesterone modulation	Bleeding control 90-92%; fibroid volume ↓	Fewer hot flushes vs GnRH agents	Oral; preoperative use preferred
Menorrhagia	Tranexamic Acid	Antifibrinolytic; ↓ plasminogen	34-59% blood loss reduction	Minimal; thromboembolic risk rare	Non-hormonal; 5 days/month
Menorrhagia	LNG-IUS (Mirena)	Local progestin; endometrial atrophy	Gold standard; 90% efficacy	Irregular bleeding initially; minimal systemic	Contraception + treatment; 5-year efficacy
Cervical Cancer	Pembrolizumab + Chemo	PD-1 inhibition; synergistic	OS benefit KEYNOTE-826 trial	Grade 3+ AE: anemia, neutropenia	First-line metastatic disease
Ovarian Cancer	PARP Inhibitors (olaparib)	PARP enzyme inhibition; HRD target	69.2% benefit in BRCA+ platinum-sensitive	Anemia, fatigue, GI disturbance	Maintenance therapy; biomarker-driven
Endometrial Cancer	Dostarlimab + Chemo	PD-1 inhibition;	2-year PFS: 61% vs 74%	Immune-related AE;	Advanced/recurrent disease;

		dMMR target	(chemotherapy)	hepatotoxicity risk	FDA-approved

RESULTS

Endometriosis Management. Current pharmacological strategies for endometriosis center on suppressing estrogen production and activity. Progestins, particularly dienogest, demonstrate superior long-term efficacy with favorable tolerability profiles, achieving pain relief in 70-80% of patients. Dienogest operates through multiple mechanisms including suppression of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), resulting in endometrial atrophy and reduced inflammatory responses. GnRH agonists including leuprolide and goserelin induce profound hypoestrogenism, achieving 60-75% lesion reduction, though side-effect profiles including bone mineral density loss limit long-term use to 6 months without add-back hormone therapy comprising norethisterone acetate or estrogen-progestin combinations. Novel oral GnRH antagonists (elagolix, linzagolix, relugolix) demonstrate 65-72% pain improvement without initial flare-up effects characteristic of agonists, enabling rapid recovery of ovarian function. These agents enable flexible dosing and improved tolerability, though menopausal symptoms including hot flushes persist.

PCOS Management. Management of polycystic ovary syndrome emphasizes insulin sensitization combined with antiandrogen therapy. Metformin remains the gold standard metabolic treatment, improving insulin sensitivity at doses of 1000-2000 mg daily, achieving cycle normalization in 40-50% of women and reducing testosterone levels. Recent meta-analyses encompassing 26 randomized controlled trials demonstrate that myoinositol shows non-inferiority to metformin for cycle normalization while maintaining a more favorable adverse effect profile with minimal gastrointestinal symptoms. Combined therapy with metformin plus spironolactone (50 mg daily) demonstrates superior efficacy for hirsutism management compared to monotherapy, with menstrual cycle improvements from 6.6 cycles annually at baseline to 10.2 cycles at six months. Lifestyle modification including 5% weight loss remains foundational to successful management, potentially sufficient as monotherapy in mild phenotypes.

Uterine Fibroids Pharmacotherapy. Selective progesterone receptor modulators, particularly ulipristal acetate at 5-10 mg daily doses, have revolutionized fibroid management. The PEARL I trial demonstrated bleeding control in 91-92% of women with 13-week treatment courses, compared to 19% placebo response. PEARL II trial showed non-inferiority of ulipristal acetate to monthly leuprolide injections while causing significantly fewer hot flashes (9% versus 67%). Ulipristal acetate achieves fibroid volume reduction of 36-46% after 13 weeks of treatment. Despite hepatotoxicity concerns requiring monitoring, the drug's favorable tolerability profile and oral administration make it preferred for preoperative fibroid downsizing

compared to GnRH agonists, which require depot formulations and demonstrate substantial bone loss during extended use.

Menorrhagia and Dysmenorrhea. Multiple pharmacological options effectively address heavy menstrual bleeding with distinct mechanisms. Tranexamic acid, an antifibrinolytic agent inhibiting plasminogen activation, reduces menstrual blood loss by 34-59% when administered 1 gram four times daily during menses, with efficacy exceeding NSAIDs and scheduled progestins. The levonorgestrel-releasing intrauterine system (LNG-IUS, Mirena) represents gold standard therapy, achieving 90% efficacy through local endometrial atrophy, with combined contraceptive benefits. Combined oral contraceptives demonstrate comparable efficacy to tranexamic acid in selected studies, with 29% reduction in menstrual blood loss through endometrial thinning. NSAIDs including ibuprofen and mefenamic acid effectively manage dysmenorrhea while providing modest blood loss reduction. For dysmenorrhea specifically, first-line pharmacotherapy involves NSAIDs initiating 24-48 hours before expected menstruation, with 80% of patients achieving satisfactory symptom relief.

Gynecological Malignancy Treatment. Recent years have witnessed revolutionary advances in cancer immunotherapy transforming treatment paradigms. Cervical cancer demonstrates improved outcomes with checkpoint inhibitor-based combinations: pembrolizumab plus platinum-based chemotherapy (cisplatin or carboplatin) with bevacizumab represents current first-line standard for metastatic/recurrent disease. The KEYNOTE-826 trial established median overall survival benefit with pembrolizumab addition, while atezolizumab combinations demonstrate median progression-free survival of 13.7 months versus 10.4 months without immunotherapy. Ovarian cancer benefits from PARP inhibitors targeting homologous recombination deficiency: olaparib achieves 69.2% clinical benefit rate in BRCA1/2-mutated platinum-sensitive disease versus 23.1% in platinum-refractory tumors, while niraparib and rucaparib demonstrate efficacy regardless of BRCA status. Endometrial cancer treatment has evolved with dostarlimab achieving 2-year progression-free survival of 61% when combined with carboplatin-paclitaxel in dMMR tumors, substantially improving upon chemotherapy alone. Lenvatinib combined with pembrolizumab provides second-line options for pMMR tumors with response rates of 35-50%.

DISCUSSION

Contemporary management of gynecological pathologies reflects paradigm shifts toward personalized, mechanism-based pharmacotherapy. The shift from high-dose estrogen-based 'pseudopregnancy' regimens toward selective endocrine and immunological targeting exemplifies evidence-based evolution. For endometriosis, progestins have emerged as optimal long-term first-line therapy given superior efficacy-tolerability balance compared to GnRH agonists, which maintain important roles in second-line management with structured add-back protocols mitigating adverse effects. The emergence of oral GnRH antagonists addresses previous agonist limitations, providing flexibility and improved adherence compared to depot formulations [1, 3]. PCOS management increasingly recognizes heterogeneity across

phenotypes, supporting individualized approaches: insulin-sensitizing agents alone may suffice for ovulatory dysfunction, while combined metformin-spironolactone therapy optimally addresses hyperandrogenic manifestations. Natural alternatives including myoinositol warrant consideration given comparable efficacy and superior tolerability [5, 7]. Uterine fibroid management has benefited substantially from SPRM development, with ulipristal acetate providing effective preoperative downsizing enabling less invasive interventions. The 2023-2024 regulatory approvals accelerated ulipristal acetate adoption despite hepatotoxicity surveillance requirements [9, 11]. Heavy menstrual bleeding management remains multifaceted: tranexamic acid offers non-hormonal efficacy preferred by patients desiring non-contraceptive methods, while LNG-IUS provides gold-standard efficacy with contraceptive co-benefits [12, 15]. Immunotherapy represents transformative advance in gynecological malignancy treatment, with checkpoint inhibitor combinations demonstrating consistent survival improvements across cervical, ovarian, and endometrial cancers. PARP inhibitor efficacy in ovarian cancer is firmly established, though emerging resistance mechanisms increasingly receiving attention [2, 3, 6]. Biomarker-driven strategies including PD-L1 expression, mismatch repair status, homologous recombination deficiency, and tumor mutational burden increasingly guide therapeutic selection. Future research priorities include resistance mechanism characterization, biomarker refinement, and optimal combination strategies.

CONCLUSION

Pharmacological management of gynecological pathologies has undergone substantial advancement through precision medicine approaches targeting specific disease mechanisms. For endometriosis, dienogest-based progestin therapy and novel GnRH antagonists provide superior first-line options balancing efficacy and tolerability. Polycystic ovary syndrome management benefits from insulin sensitization strategies including metformin and myoinositol, with emerging evidence supporting combination antiandrogen therapy for complex phenotypes. Uterine fibroid treatment increasingly favors ulipristal acetate over GnRH agonists for preoperative symptom management given superior side-effect profiles. Menorrhagia management employs multimodal approaches including tranexamic acid, NSAIDs, and levonorgestrel intrauterine systems, with selection individualized to patient preferences and comorbidities. Gynecological cancer treatment has been revolutionized by checkpoint inhibitors and PARP inhibitors, substantially improving survival outcomes across cervical, ovarian, and endometrial malignancies through rational biomarker-guided strategies. Continued research focusing on resistance mechanisms, optimal combination strategies, and biomarker refinement will further enhance therapeutic efficacy and tolerability. Implementation of these evidence-based approaches in clinical practice promises improved quality of life, enhanced reproductive outcomes, and superior cancer survival across diverse populations of women with gynecological pathologies.

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