

Prescribing information for ulipristal (Esmya®) for pre-operative treatment of uterine fibroids

This prescribing information document outlines the prescribing responsibilities between the specialist and GP. GPs are invited to participate. If the GP feels that such prescribing is outside their area of expertise or has clinical concerns about the safe management of the drug in primary care, then he or she is under no obligation to do so. In such an event, clinical responsibility for the patient's health remains with the specialist.

If a specialist asks the GP to prescribe but the GP is not happy to continue prescribing, they must inform the specialist within 2 weeks of receiving the request.

Consultant details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	NHS Number:
Email:	Email:	Date of birth:
Contact number:	Contact number:	Contact:

Licensed Indication

Ulipristal acetate (Esmya®) is licensed for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. The duration of treatment is limited to 3 months.

Note: Ulipristal acetate is also available as ellaOne® 30mg for use as emergency contraception (which is a different and separate preparation).

It is an orally active synthetic selective progesterone receptor modulator which acts on progesterone receptors in uterine fibroids to reduce fibroid size. It is an alternative to GnRH agonists. It is an oral preparation that can be better tolerated than leuprorelin, the incidence of hot flushes and menopausal symptoms are reduced and there is little effect on bone turnover.

Dosage and administration

One 5mg tablet to be taken orally once daily for up to 3 months. Treatment should be started during the first week of a menstrual cycle. Tablets may be taken with or without food.

There is no data on treatment durations greater than 3 months or on repeat courses of treatment, therefore, treatment duration should not exceed 3 months.

If a patient misses a dose, the dose should be taken as soon as possible. If the dose was missed by more than 12 hours, the missed dose should not be taken and the normal dosing schedule resumed.

Specialist responsibilities

- Discuss benefits and side effects of treatment with patient.
- Initiate and prescribe treatment with ulipristal acetate Esmya® for the first month of therapy
- Give patient a copy of this guideline and ensure patient has given informed consent for their treatment.
- Forward a copy of this guideline to GP with a request for shared care and signed statement that, at initiation, discussions and proper counselling had taken place with the patient.
- If the GP does not accept shared care the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. Ensure appropriate follow-up in conjunction with the GP.
- Advise the GP of the duration of treatment and that the total duration of treatment must not exceed 3 months
- Continue to monitor clinical response and communicate promptly with the GP when treatment is changed
- To be available for advice if the patient's condition changes.
- To ensure that procedures are in place for the rapid re-referral of the patient by the GP.
- To liaise with the GP on any suggested changes in prescribed therapy.
- Review concurrent medication for potential interactions.

- Report adverse events to the MHRA (via Yellow Card)
www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Primary Care responsibilities

- Notify the specialist without undue delay if they agree to share care
- Follow the specialist's advice on any changes in treatment.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment
- Review concurrent medication for potential interactions
- Ask for advice before discontinuing medication.
- To manage general health issues of the patient.
- Report adverse events to the MHRA (via Yellow Card)
www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

Communication

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
Specialist:				
Hospital Pharmacy Dept:				
Other:				

Contra-indications, Special warnings/precautions & adverse effects¹

Contra-indications:

Hypersensitivity to the active substance or to any of the tablet excipients
 Pregnancy and breastfeeding.
 Genital bleeding of unknown aetiology or for reasons other than uterine fibroids.
 Uterine, cervical, ovarian or breast cancer.
 Due to lack of long term safety data, the duration of treatment should not be longer than 3 months

Special warnings/precautions:

Ulipristal acetate should only be prescribed after careful diagnosis.

Pregnancy should be precluded prior to treatment.

Contraception

Concomitant use of progestogen-only pills, a progestogen-releasing intrauterine device or combined oral contraceptive pills is not recommended, and a non-hormonal contraceptive method is recommended during treatment.

Renal impairment

Renal impairment is not expected to significantly alter elimination. In the absence of specific studies, ulipristal acetate is not recommended for patients with severe renal impairment unless the patient is closely monitored.

Hepatic impairment

There is no therapeutic experience in patients with hepatic impairment, but it is expected to alter the elimination, resulting in increased exposure. This is considered not to be clinically relevant for patients with mildly impaired liver function, but ulipristal acetate is not recommended for use in patients with moderate or severe hepatic impairment unless the patient is closely monitored.

Asthma patients

Use in women with severe asthma insufficiently controlled by oral glucocorticoids is not recommended.

Endometrial changes

Ulipristal acetate has a specific pharmacodynamic action on the endometrium. Increase in thickness of the endometrium may occur. If the endometrial thickening persists within 3 months following the end of treatment and return of menstruations, this may need to be investigated as per usual clinical practice to exclude underlying conditions.

Changes in the histology of the endometrium may be observed in patients treated with ulipristal acetate. These changes are reversible after treatment cessation. These histological changes are denoted as “Progesterone Receptor Modulator Associated Endometrial Changes” (PAEC) and should not be mistaken for endometrial hyperplasia. In absence of safety data for a period longer than 3 months or on repeat courses of treatment, the risk of adverse impact on the endometrium is unknown if treatment is continued; therefore, treatment duration should not exceed 3 months.

Bleeding pattern

Patients should be informed that treatment with ulipristal acetate usually leads to a significant reduction in menstrual blood loss or amenorrhoea within the first 10 days of treatment. Should the excessive bleeding persist, patients should notify their physician. Menstrual periods will generally return within 4 weeks after the end of the treatment course

Adverse Effects

The safety of ulipristal acetate has been evaluated in 393 women with uterine fibroids treated with 5mg or 10mg ulipristal acetate during Phase III studies. The most common finding in clinical trials was amenorrhoea (82.2%), which is considered as a desirable outcome for the patients.

The most frequent adverse reaction was hot flush. The vast majority of adverse reactions were mild and moderate (94.9%), did not lead to discontinuation of the medicinal product (99.3%) and resolved spontaneously.

For a full list of adverse effects, refer to Summary of Product Characteristics

Drug Interactions

Potential for other medicinal products to affect ulipristal acetate:

Hormonal contraceptives

Ulipristal acetate has a steroid structure and acts as a selective progesterone receptor modulator with predominantly inhibitory effects on the progesterone receptor. Thus hormonal contraceptives and progestogens are likely to reduce ulipristal acetate efficacy by competitive action on the progesterone receptor. Therefore concomitant administration of medicinal products containing progestogen is not recommended.

CYP3A4 inhibitors

Erythromycin propionate (moderate) and potent CYP3A4 inhibitors (e.g. ketoconazole, ritonavir, nefazodone) may lead to increases in plasma levels of ulipristal.

CYP3A4 inducers

Concomitant use of ulipristal acetate and potent CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St John’s wort) is not recommended as plasma levels of ulipristal acetate may be reduced.

Potential for ulipristal acetate to affect other medicinal products:

Hormonal contraceptives

Products containing progestogen should not be taken concomitantly or within 12 days after cessation of ulipristal acetate treatment.

P-gp substrates

Co-administration of ulipristal acetate may increase the plasma levels of concomitant medicinal products that are substrates of P-gp. In the absence of clinical data, co-administration of ulipristal acetate and P-gp substrates (e.g. dabigatran etexilate, digoxin), is not recommended.

See product SPC for full list of drug interactions (www.medicines.org.uk)

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions. Please refer to full prescribing data in the Summary of Product Characteristics (www.medicines.org.uk) or the British National Formulary (www.bnf.org).

¹ Ulipristal acetate (Esmya) 5mg Tablets – Summary of Product Characteristics. Available at www.medicines.org.uk