NHS
Shropshire
Clinical Commissioning Group

NHS
Telford and Wrekin
Clinical Commissioning Group

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

Following MHRA advice (9 February 2018): Ulipristal (Esmya) must not to be started in any new patients or in those who have competed one or more courses. For existing patients who are part way through a course, if after being informed of the risks a decision is made to continue treatment, additional hepatic monitoring is required (see below)

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.

Ulipristal acetate is indicated for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

Note: Ulipristal acetate is also available as ellaOne® 30mg for use as emergency contraception (which is a different and separate preparation). No cases of serious liver injury have been reported with ellaOne and there are no concerns with this medicine at this time.

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

The treatment consists of one tablet of 5 mg to be taken orally once daily for treatment courses of up to 3 months each.
Treatments should only be initiated when menstruation has occurred:
- The first treatment course should start during the first week of menstruation.
- Re-treatment courses should start at the earliest during the first week of the second menstruation following the previous treatment course completion.

The treating physician should explain to the patient the requirement for treatment free intervals.

Repeated intermittent treatment has been studied up to 4 intermittent courses.

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

The specialist responsibilities listed below relate only to patients who are currently taking ulipristal, the drug should not be started in any new patients or restarted in patients who have completed one or more courses.

- Discuss benefits and side effects of treatment with patient.
- Advise women who are currently taking ulipristal acetate (Esmya) of the risks, document the discussion in the patient's notes and if a decision is made to continue treatment, provide information about the signs and symptoms of liver injury (these may include nausea, vomiting, malaise, right hypochondrial pain, anorexia, asthenia, jaundice)
- 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 sharing 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.
- Advise the GP on continuing treatment, if planned surgery is delayed.
- 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

The GP responsibilities listed below relate only to patients who are currently taking ulipristal, the drugs should not be started in any new patients or restarted in patients who have completed one or more courses

- New patients will no longer be initiated – any requests to accept prescribing responsibility should be referred back to the specialist
- Advise women who are currently taking ulipristal acetate (Esmya) of the risks, document the discussion in the patient's notes and if a decision is made to continue treatment, provide information about the signs and symptoms of liver injury (these may include nausea, vomiting, malaise, right hypochondrial pain, anorexia, asthenia, jaundice)
- 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

MONITORING

- Liver function tests (LFTs) must be monitored at least once a month. Treatment should be stopped if transaminase levels are more than 2 times the upper limit of normal– refer to hepatologist as clinically indicated
- Repeat LFTs 2-4 weeks after stopping treatment

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 effects[1]

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 5mg should only be continued for the current treatment course after discussion with the patient about the risks and benefits of ongoing treatment and the requirement for careful monitoring of liver function.

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

Five reports of serious liver injury including four cases of hepatic failure needing liver transplantation have been reported worldwide in women using Esyma for uterine fibroids. No treatment courses should be initiated for Ulipristal acetate 5mg (Esyma)

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 amenorrhea 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 amenorrhea (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