WHAT ARE UTERINE FIBROIDS?

Uterine fibroids are benign tumours that develop in the muscle wall of the uterus. They are made up of muscle and fibrous tissue and may be single or multiple and can vary greatly in size from one millimetre to more than 20 cm in diameter. Uterine fibroids are the most common benign tumours in women of reproductive age with a clinically relevant prevalence in 20-40% of women.1-4

In many women, these are asymptomatic but symptoms can include: heavy menstrual bleeding, anaemia, abdominal pain, pressure on bladder or bowel, subfertility and can cause miscarriage.

NICE’s heavy menstrual bleeding guidelines (CG44) 2016 update, states:

• “Offer ulipristal acetate 5 mg (up to 4 courses) to women with heavy menstrual bleeding and fibroids of 3 cm or more in diameter, and a haemoglobin level of 102 g per litre or below”

• “Consider ulipristal acetate 5 mg (up to 4 courses) for women with heavy menstrual bleeding and fibroids of 3 cm or more in diameter, and a haemoglobin level above 102 g per litre”.

THIS DOCUMENT HAS BEEN DEVELOPED BY A STEERING GROUP OF EXPERTS IN GYNAECOLOGY AND IN PARTNERSHIP WITH GEDION RICHTER TO REVIEW THE MEDICAL MANAGEMENT OF UTERINE FIBROIDS WITH ESMYA®.
ESMYA®
ESMYA® is a selective progesterone receptor modulator (PRM) licensed for the pre-operative or intermittent treatment of moderate-to-severe symptoms of uterine fibroids in adult women of reproductive age. ESMYA® demonstrates rapid control of uterine bleeding and pain, and significant and sustained reduction in fibroid size and restoration of quality of life.

TREATMENT SCHEDULE
Treatment consists of one 5mg tablet to be taken orally, once daily for up to 12 weeks. Treatment should be started within the first week of a period. This 12 week treatment course can be repeated.
Re-treatment courses should start at the earliest during the first week of the second period following the previous treatment course completion. Each treatment course should not exceed 12 weeks. Treatment free intervals are required between courses.
If symptom control is sub-optimal with the first course of ESMYA®, a second course can be considered as symptom control tends to improve with repeated courses. If there is no or poor response to the second course, referral to a specialist for further treatment options is advised.
If there is no improvement after the first course, treatment should be stopped and reviewed.

CONSIDERATIONS
- ESMYA®’s most common treatment-related adverse events include: headache, hot flushes and fatigue. Most side effects are mild or moderate & resolve spontaneously with repeated courses.
- An annual pelvic/trans-vaginal ultrasound scan is recommended to assess the health of the endometrium. Recommend the first scan takes place after completion of the second course of treatment with ESMYA® following at least one period. This equates to approximately one year.
- PRM-associated endometrial changes (PAEC) may be observed with ESMYA®. Evidence indicates PAEC is harmless and quickly reversible6,6. Endometrial thickening reverses when ESMYA® treatment is stopped and periods resume.
- Concomitant use of hormonal contraceptives or Hormone Replacement Therapy (HRT) are not recommended. If contraception is required, non-hormonal contraception options should be discussed. Ensure the woman’s intrauterine system (IUS) has been removed prior to treatment with ESMYA®.
- HRT should not be prescribed, instead seek specialist advice.
- Treatment with ESMYA® is contra-indicated in women who are pregnant or breast-feeding. Pregnancy should be precluded prior to treatment. If pregnancy is suspected prior to initiation of a new treatment course, a pregnancy test should be performed.
Confirmed diagnosis of symptomatic Uterine Fibroids

Medical Management with first course of ESMYA®*

Review after one course

- Positive response
  - Repeat second course
    - Review with pelvic/trans-vaginal ultrasound scan after two courses
      - Additional courses as required
  - Sub-optimal response
    - Consider second course if some symptom improvement
      - Positive response
      - Stop treatment if one or more of the following occur:
        • Unexplained bleeding
        • Woman is asymptomatic
        • Abnormal endometrial thickening
        • Desire to conceive
  - No response
    - Sub-optimal response
      - Refer to specialist for other treatment options e.g. surgery

*Refer to your locality for regional guidance
ESMYA® (ulipristal acetate)

Please refer to the SmPC before prescribing.

Presentation: 5mg tablet

Indication: Pre-operative or intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

Dose and administration: One tablet of 5mg to be taken orally once a day for a maximum of 3 months, starting during first week of menstrual cycle. This 3 month treatment course can be repeated. Re-treatment courses should start at the earliest during the first week of the second menstruation following the previous treatment course completion. Each treatment course should not exceed 3 months. Treatment free intervals are required between courses. Repeated intermittent treatment has been studied for up to 4 intermittent treatment courses. Please refer to SmPC for missed dose information.

Patients with renal or hepatic impairment: No dose adjustment in mild to moderate renal impairment or mild hepatic impairment. Not recommended for patients with severe renal impairment and moderate or severe hepatic impairment unless patient is closely monitored. Children and adolescent under 18 years: No relevant use.

Contraindications: Pregnancy, Breastfeeding, Genital bleeding of unknown aetiology. Uterine, Cervical, Ovarian or Breast cancer. Hypersensitivity to active substance or any excipients.

Drug interactions: Hormonal contraceptives and progestogens are likely to reduce the efficacy of ulipristal acetate by competitive action on progesterone receptors, hence co-administration is not recommended. Concomitant use of oral glucocorticoids is not recommended. Concomitant use of hormonal contraceptives is not recommended hence a non-hormonal contraceptive method should be used. Reversible histological changes of the endometrium ‘Progestrone Receptor Modulator Associated Endometrial Changes’ (PAEC) may be observed in patients. Also, reversible thickening of the endometrium may occur (during) treatment. If it persists beyond 3 months following the end of treatment and return of menstruations, and/or an altered bleeding pattern is noted, this may need to be investigated as per usual clinical practice.

Drug interactions: Concomitantly used estrogenic or antiestrogenic drugs, such as hormone replacement therapy or tamoxifen, may reduce the effect of ulipristal acetate. Concomitant use of oral contraceptives, progestogens, and/or progestogens containing estrogen is not recommended. Use in women with severe asthma insufficiently controlled by oral glucocorticoids is not recommended. Concomitant use of hormone replacement therapy and ulipristal acetate is not recommended. Concomitant use of hormone replacement therapy and ulipristal acetate is not recommended. Concomitant use of hormone replacement therapy and ulipristal acetate is not recommended.

Undesirable effects: The following adverse reactions have been reported during first treatment courses: Very Common (>1/10): Amenorrhea, Endometrial thickening. Common (>1/100 to <1/10): Headache, Vertigo, Abdominal pain, Nausea, Acne, Musculoskeletal pain, Hot flush, Pelvic pain, Ovarian cyst, Breast tenderness/pain, Fatigue, Weight gain, Uncommon (<1/1000 to <1/100): Drug hypersensitivity, Anxiety, Emotional disorder, Dizziness, Dry mouth, Constipation, Alopecia, Dry skin, Hyperhidrosis, Back pain, Urinary incontinence, Uterine haemorrhage, Metrorrhagia, Genital discharge, Breast discomfort, Oedema, Asthenia, Increase in cholesterol level increased triglycerides, Rare (<1/10,000 to <1/1,000): Epistaxis, Dyspepsia, Flatulence, Rupture of ovarian cyst, Breast swelling. Frequency not known Angioedema.

When comparing repeated treatment courses, overall adverse reaction rates were less frequent in subsequent treatment courses than during the first one and each adverse reaction was less frequent or remained in the same frequency category (except dyspepsia which was classified as uncommon).

Overdose: Limited experience. Single doses of up to 200mg and daily doses of 50mg for 10 consecutive days administered to a limited number of subjects, and no serious or severe adverse reactions were reported.

Special precautions for storage: Keep the blisters in the outer carton to protect from light.

Legal Category: POM

Basic UK NHS cost: £114.13 per pack of 28 tabs

Marketing Authorisation Numbers: EU/1/12/750/001, EU/1/12/750/002, EU/1/12/750/003, EU/1/12/750/004, EU/1/12/750/005


FURTHER INFORMATION IS AVAILABLE FROM:

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For further information, please refer to:

• Summary of ESMYA® Product Characteristics
  • esmya.co.uk

Richter Resource Centre
Education & Support in Women’s Health
richterresourcecentre.co.uk