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Royal Cornwall Hospitals NHS Trust

Ulipristal (Esmya)

Shared Care Guideline

V2.0

April 2019

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of ulipristal acetate (Esmya) in the treatment of uterine fibroids in women of reproductive age who are not eligible for surgery. As with all shared care guidelines they highlight significant prescribing issues but should be used in conjunction with the BNF, ABPI summary of product characteristics and do not replace them.

1.2. **Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation**

The Trust has a duty under the DPA18 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed and documented. We can't rely on Opt out, it must be Opt in.

The DPA18 covers how the Trust obtains, hold, record, use and store all personal and special category (e.g. Health) information in a secure and confidential manner. This Act covers all data and information whether held electronically or on paper and extends to databases, videos and other automated media about living individuals including but not limited to Human Resources and payroll records, medical records, other manual files, microfilm/fiche, pathology results, images and other sensitive data.

DPA18 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the DPA18 please see the 'information use framework policy', or contact the Information Governance Team rch-tr.infogov@nhs.net

2. The Guidance

2.1. Ulipristal acetate (Esmya) is licensed for the pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age. It is also indicated for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age who are not eligible for surgery (e.g. where the risks of surgery outweigh the benefits or where the woman declines surgical treatment) - this indication is the purpose of this SCG.

2.2. Ulipristal acetate (Esmya) is an orally active synthetic selective progesterone receptor modulator characterised by a tissue-specific partial progesterone antagonist effect. Treatment with ulipristal acetate results in new endometrial changes described as PRM Associated Endometrial Changes (PAEC).

2.3. This SCG supports the use of ulipristal acetate (Esmya) for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age who are not eligible for surgery (e.g. where the risks of surgery outweigh the benefits or where the woman declines surgical treatment) . It is in line with NICE Clinical Guideline 88 as below:-

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

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

2.4. **Preparations And Dosage**

2.4.1. 5 mg (one tablet) to be taken orally once daily for treatment courses of up to 3 months each.

2.4.2. Each treatment course should not exceed 3 months as the risk of adverse effect on the endometrium is unknown if treatment is continued. Repeated intermittent treatment has been studied up to 4 intermittent courses.

2.4.3. Under this shared care guideline, the specialist is responsible for the first course and the GP for the following three courses if they are needed and where referral for surgery is declined.

2.4.4. 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.

2.4.5. Note that ulipristal acetate is also available as ellaOne 30mg for use only as emergency contraception.

2.5. Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy and breastfeeding.
- Genital bleeding of unknown aetiology or for reasons other than uterine fibroids.
- Uterine, cervical, ovarian or breast cancer.

2.6. **Precautions**

- Ulipristal acetate has a specific pharmacodynamic action on the endometrium. Increase in thickness of the endometrium may occur. If the endometrial thickening persists beyond 3 months following the end of treatment or an altered bleeding pattern is noted, this may need to be investigated as per usual clinical practice to exclude underlying conditions, including endometrial malignancy. 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

- 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 specialist. Menstrual periods will generally return within 4 weeks after the end of the treatment course.
- If, during repeated intermittent treatment, after the initial reduction in bleeding or amenorrhea, an altered persistent or unexpected bleeding pattern occurs, such as inter-menstrual bleeding, investigation of the endometrium including endometrial biopsy should be performed in order to exclude other underlying conditions, including endometrial malignancy.
- Use in women with severe asthma insufficiently controlled by oral glucocorticoids is not recommended.
- Concomitant use of progestagen-only pills, a progestagen-releasing intrauterine device or combined oral contraceptive pills is not recommended. Although a majority of women taking a therapeutic dose of ulipristal acetate have anovulation, a non-hormonal contraceptive method is recommended during treatment and for 12 days after stopping treatment.
- No dose adjustment is recommended in patients with mild or moderate renal impairment. In the absence of specific studies, ulipristal acetate is not recommended in patients with severe renal impairment unless the patient is closely monitored.
- No dose adjustment is recommended for patients with mild hepatic impairment. In the absence of specific studies, ulipristal acetate is not recommended in patients with moderate or severe hepatic impairment unless the patient is closely monitored.

2.7. Monitoring

2.7.1. Specialist Team:

Where ulipristal acetate is prescribed for medical management, periodic monitoring of the endometrium is recommended. This includes annual ultrasound to be performed after resumption of menstruation during an off-treatment period

2.7.2. General Practice:

Liver function tests are to be taken before initiation of each treatment course and every month during the first 2 treatment courses. For further treatment courses, LFT are to be taken once before each new course. Also to be taken 2-4 weeks at the end of each treatment course. Hence the LFT monitoring schedule is as below.

If AST or ALT is over twice the upper limit of normal then treatment should not be started. If it is over three times the upper limit of normal, it should be stopped.

LFT to be taken -

prior to treatment	Undertaken by secondary care
End of first month of course or block 1	Undertaken by GP
End of second month of course or block 1	Undertaken by GP
End of third month of course or block 1	Undertaken by GP
2-4 weeks after completing course or block 1	Undertaken by GP

End of first month of course or block 2	Undertaken by GP
End of second month of course or block 2	Undertaken by GP
End of third month of course or block 2	Undertaken by GP
2-4 weeks after completing course or block 2	Undertaken by GP
Prior to treatment course or block 3	Undertaken by GP
2-4 weeks after completing course or block 3*	Undertaken by GP
Prior to treatment course or block 4	Undertaken by GP
2-4 weeks after completing course or block 4*	Undertaken by GP

***= The test 2-4 weeks after treatment blocks could act as the 'pre-test' for additional treatment blocks if the test is < 3-4 months old and nothing has changed e.g. new medicines**

2.8. Side Effects

- 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 increase.
- Uncommon (≥1/1,000 to <1/100) Anxiety, emotional disorder, dizziness, dry mouth, constipation, alopecia, dry skin, hyperhidrosis, back pain, urinary incontinence, uterine haemorrhage, metrorrhagia, genital discharge, breast discomfort, oedema, asthenia, blood cholesterol increased, blood triglycerides increased.
- Rare (≥1/10,000 to <1/1,000) Epistaxis, dyspepsia, flatulence, ovarian cyst ruptured, breast swelling

2.9. Common/Significant Drug Interactions

- 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 - Co-administration of moderate (e.g. erythromycin, grapefruit juice, verapamil) or potent (e.g. ketoconazole, ritonavir, nefazodone, itraconazole,
- telithromycin, clarithromycin) CYP3A4 inhibitors and ulipristal acetate is not recommended
- CYP3A4 inducers - Concomitant use of ulipristal acetate and potent CYP3A4 inducers (e.g. rifampicin, rifabutin, carbamazepine, oxcarbazepine, phenytoin, fosphenytoin, phenobarbital, primidone, St John´s wort, efavirenz, nevirapine, long term use of ritonavir) is not recommended
- Administration of ulipristal and P-glycoprotein substrates (e.g. dabigatran etexilate, digoxin) should be separated in time by at least 1.5 hours.

2.10. Areas Of Responsibility For The Sharing Of Care

These are suggested ways in which the responsibilities for the management of adult patients with growth hormone deficiency who are prescribed **ulipristal acetate** for the treatment of uterine fibroids can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care

assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.11. Specialist:

- Initiate and prescribe treatment with ulipristal acetate for the first three months of therapy for the first treatment course.
- Discuss the benefits and side effects of treatment with the patient, whilst also taking time to explain the requirement for treatment free intervals, utilising the patient written information.
- Provide patient with written information and / or links to electronic resources and ensure that the patient understands the dosing regimens and monitoring requirements.
- Ask the GP whether he or she is willing to participate in shared care, and discuss the shared care arrangement with the patient, using the shared care agreement letter.
- Advise the GP on the duration of treatment and number of courses to be prescribed, when to stop treatment or consult with the specialist.
- Ensure that clear arrangements exist for GPs to obtain advice and support.
- Where ulipristal acetate is prescribed for medical management, periodic monitoring of the endometrium is recommended. This includes annual ultrasound to be performed after resumption of menstruation during an off-treatment period, preferably in the week after menstruation when endometrial thickness of <10mm is taken as indicative of a low chance of underlying pathology.
- If a fourth treatment course is required this will be prescribed by the GP. However the specialist will be notified so that the specialist will organise and review an ultrasound scan after this fourth treatment course (performed after resumption of menstruation during an off-treatment period, preferably in the week after menstruation when endometrial thickness of <10mm is taken as indicative of a low chance of underlying pathology).
- Report adverse events to the MHRA, the Company and GP.

2.12. General Practitioner:

- If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter.
- Prescribe ulipristal acetate at the dose recommended and for the duration specified.
- Do not continue to prescribe if the previous course was not effective in relieving symptoms – each treatment course should have a cumulative effect
- 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 e.g. Advise if symptoms continue or if menstruation fails to be suppressed after 2 months treatment.
- Communicate back to specialist as per agreed treatment plan, if the patient's condition deteriorates, loss efficacy or intolerance occurs.
- Undertake LFT as per the schedule in the SCG
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.

- As the specialist will have prescribed the first course (of 3 months duration), the GP should not prescribe ulipristal for more than a further **THREE** courses in total (where a course is treatment for up to 3 months).
- If a fourth treatment course is required this will be prescribed by the GP who will advise the specialist that the hospital needs to organise an ultrasound scan.
- Report adverse events to the specialist, MHRA and company.

2.13. Patient responsibilities

- Sign the shared care agreement letter.
- The patient undertakes to adhere to the recommended dose and attend follow up appointments and report any unexpected outcomes of treatment.
- To follow the advice of the package insert and the Trust provided information leaflet.
- To be aware of their test results and symptoms that could indicate liver injury.
- To note the requirement for an ultrasound after any fourth treatment course so that the patient can share responsibility for reminding the GP of this recommendation.

BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Diversity & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Ulipristal (Esmya) Shared Care Guideline V2.0		
Date Issued/Approved:	January 2019		
Date Valid From:	April 2019		
Date Valid To:	April 2022		
Directorate / Department responsible (author/owner):	Gynaecology Team / Pharmacy - Head of Prescribing Support Unit		
Contact details:	01872 253548		
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists		
Suggested Keywords:	Ulipristal		
Target Audience	RCHT	CFT	KCCG
	✓		✓
Executive Director responsible for Policy:	Medical Director		
Date revised:	Jan'19		
This document replaces (exact title of previous version):	Shared care guideline for ulipristal (Esmya)		
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee		
Divisional Manager confirming approval processes	Karen Jarvill		
Name and Post Title of additional signatories	Not required		
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}		
	Name: Kevin Wright		
Signature of Executive Director giving approval	{Original Copy Signed}		

Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only	
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards				
Related Documents:	Summary of Product Characteristics. NICE Clinical Guideline 88 (March 2018) to provide guidance on the assessment and management of heavy menstrual bleeding An information site on ulipristal acetate (Esmya) developed by Gedeon Richter, the products manufacturer for health care professional use http://esmya.co.uk/home/.			
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
Sept 2017	V1.0	Original document	M Wilcock, Head of Prescribing Support Unit
Jan'2019	V2.0	New format and slight text amendments	M Wilcock, Head of Prescribing Support Unit

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document

This document has been created following the Royal Cornwall Hospitals NHS Trust Policy on Document Production. It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Initial Equality Impact Assessment Form

<table>
<tr><td colspan="6">Ulipristal (Esmya) Shared Care Guideline V2.0</td></tr>
<tr><td colspan="3">Directorate and service area:
Pharmacy</td><td colspan="3">Is this a new or existing Policy:
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="3">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="5">To provide information on prescribing of ulipristal (Esmya) to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="5">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="5">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="5">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="5">General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td>Other</td></tr>
<tr><td>X</td><td></td><td>X</td><td></td><td></td></tr>
<tr><td colspan="5">Please record specific names of groups
Cornwall Area Prescribing Committee</td></tr>
<tr><td>What was the outcome of the consultation?</td><td colspan="5">Agreed.</td></tr>
</table>

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:

Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No X**	

9. If you are **not** recommending a Full Impact assessment please explain why.

Not required

Signature of policy developer / lead manager / director		Date of completion and submission
M Wilcock		28/11/18
Names and signatures of members carrying out the Screening Assessment	1. M Wilcock 2. Policy Review Group (PRG)	**PRG APPROVED**

Keep one copy and send a copy to the Human Rights, Equality and Inclusion Lead
c/o Royal Cornwall Hospitals NHS Trust, Human Resources Department, Knowledge Spa, Truro, Cornwall, TR1 3HD

This EIA will not be uploaded to the Trust website without the signature of the Human Rights, Equality & Inclusion Lead.

A summary of the results will be published on the Trust's web site.

Signed __M Wilcock _____

Date _____28/11/18_____