Medical Management of Fibroids Esmya®

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Treatment options for Uterine Fibroids

- ESMYA
- Selective Uterine Artery Embolisation
- Fibroid ablation (hysteroscopic morcellation) for either submucous or pedunculated fibroids
- Laparoscopic morcellation for subserous or possibly intramural fibroids
- Myomectomy
- Hysterectomy

Possible causes of HMB

Dysfunctional Uterine Bleeding [1]
(No obvious physical abnormality 40-60%)

Endometrial lesions[1]
(fibroids 36%, polyps 11.5%, malignancy 1%)

Inflammatory response
(e.g. IUD use, pelvic infection)

Medical disorders
(e.g. hypothyroidism

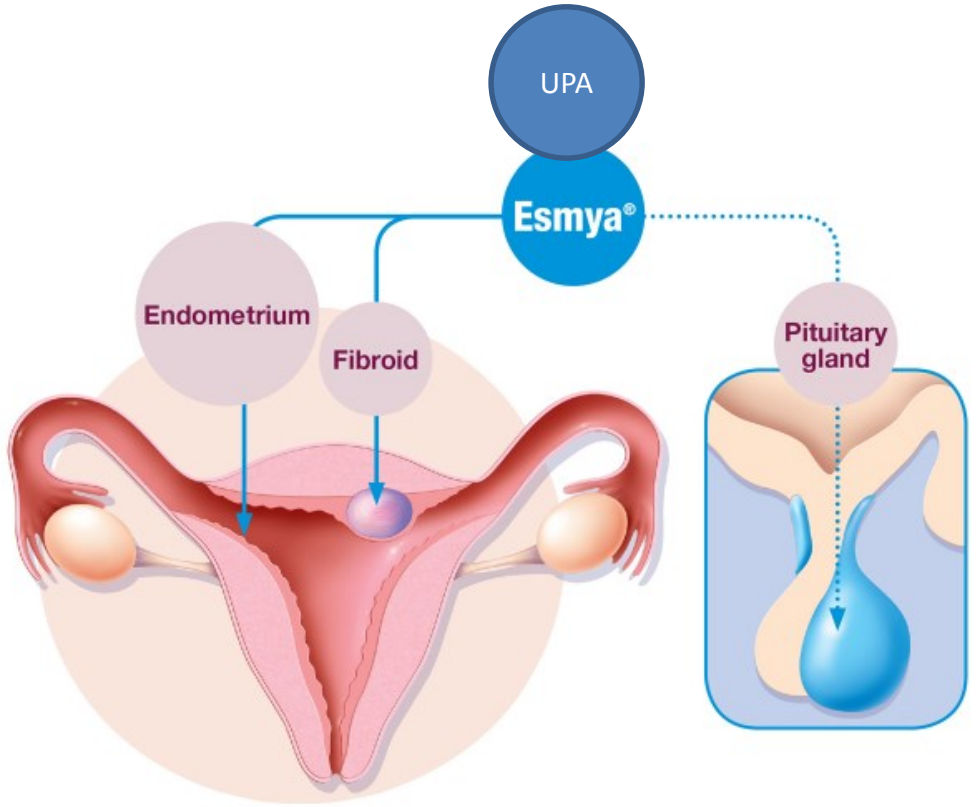
Coagulation defects
(e.g. von Willebrands disease)

1. 1. NICE CG44 Heavy Menstrual Bleeding 2007, Full Guideline

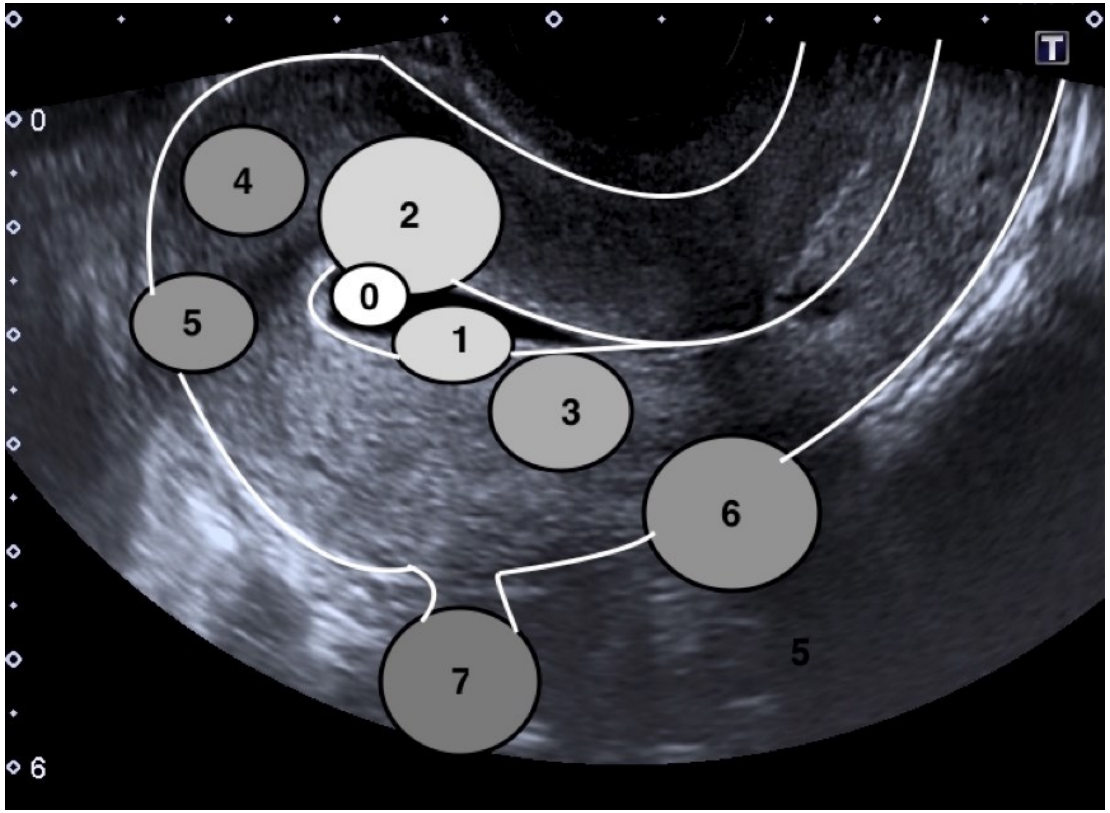
Esmya, a novel, targeted mode of action

- Ulipristal acetate 5mg works both locally and centrally[1-4]

- Acts at the hypothalamus-pituitary level to inhibit ovulation whilst maintaining oestradiol levels in the mid-follicular range in the majority of patients
- Reduces the size of fibroids through the inhibition of cell proliferation and induction of apoptosis
- Exerts a direct effect on the endometrium, rapidly reducing bleeding



1. Bouchard P, Chabbert-Buffet N, Fauser BC. Fertil Steril 2011; 96(5): 1175-89.
2. Donnez J, et al. New Engl J Med 2012; 365(5): 409-420.
3. Donnez J, et al. New Engl J Med 2012; 365(5): 421-432.
4. Chabbert-Buffet N, et al. J CLin Endocrinol Metab 2007; 92:3582-89.



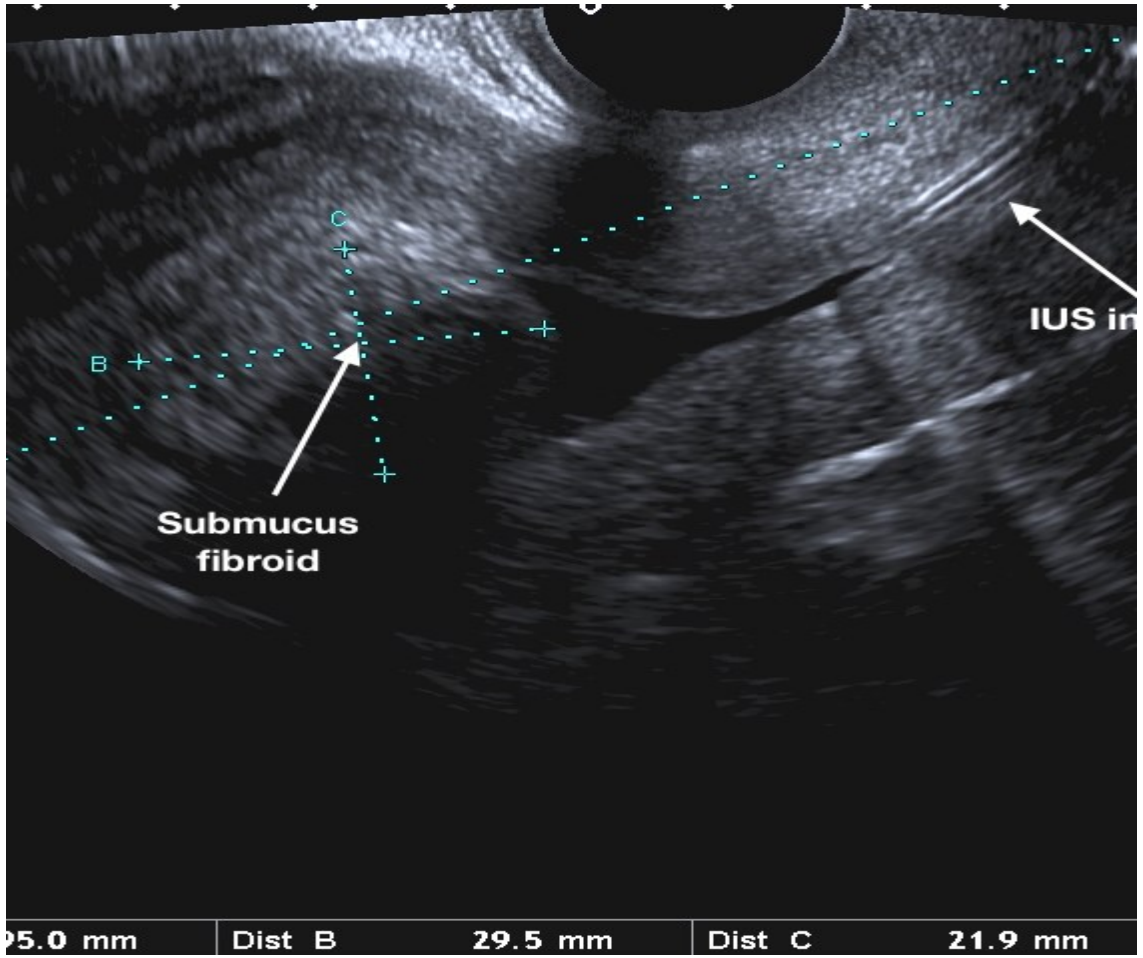
0. Pedunculated intracavity
1. < 50% intramural
2. > 50 % intramural

3-4 intramural:
3. 100% intramural – contacts endometrium
4.intramural

5-7 subserosal:
5. > 50% intramural
6. < 50% intramural
7. Peduculated

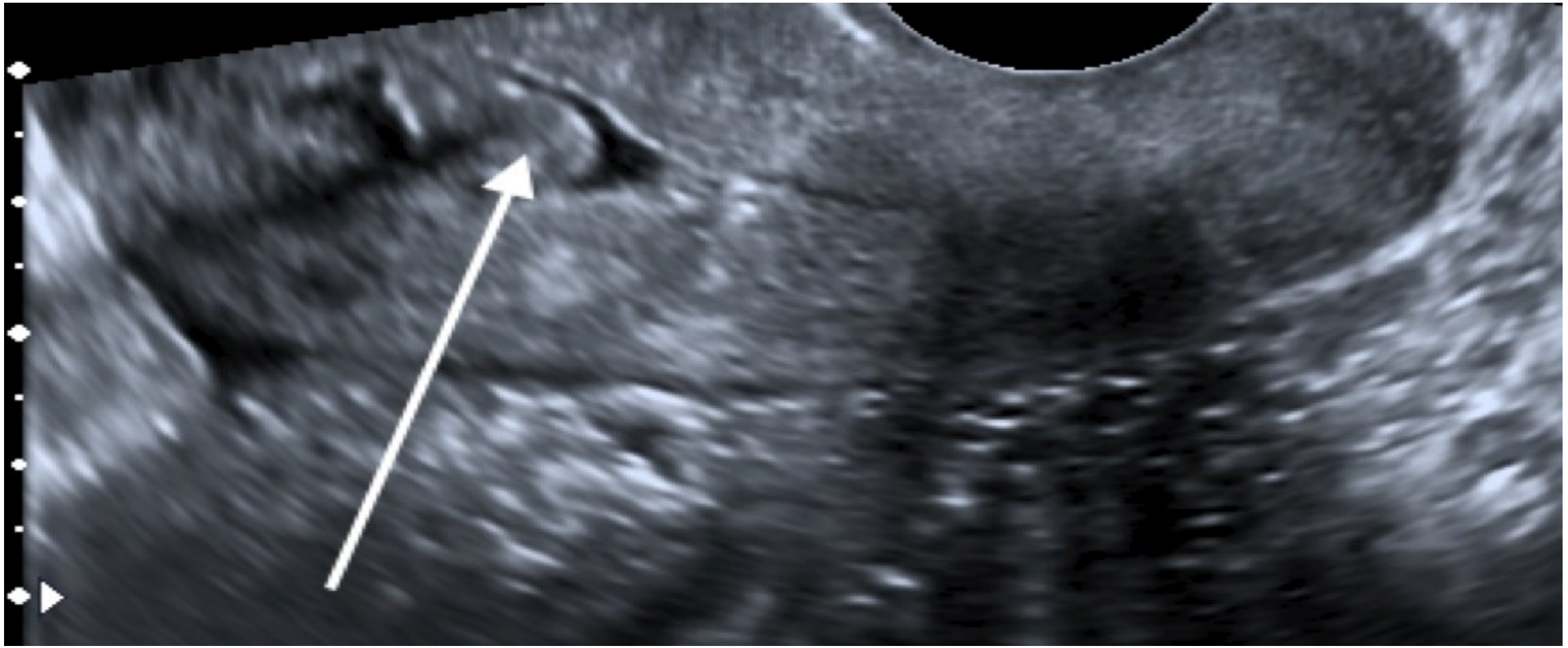
8. Other e.g. cervical

Transvaginal ultrasound

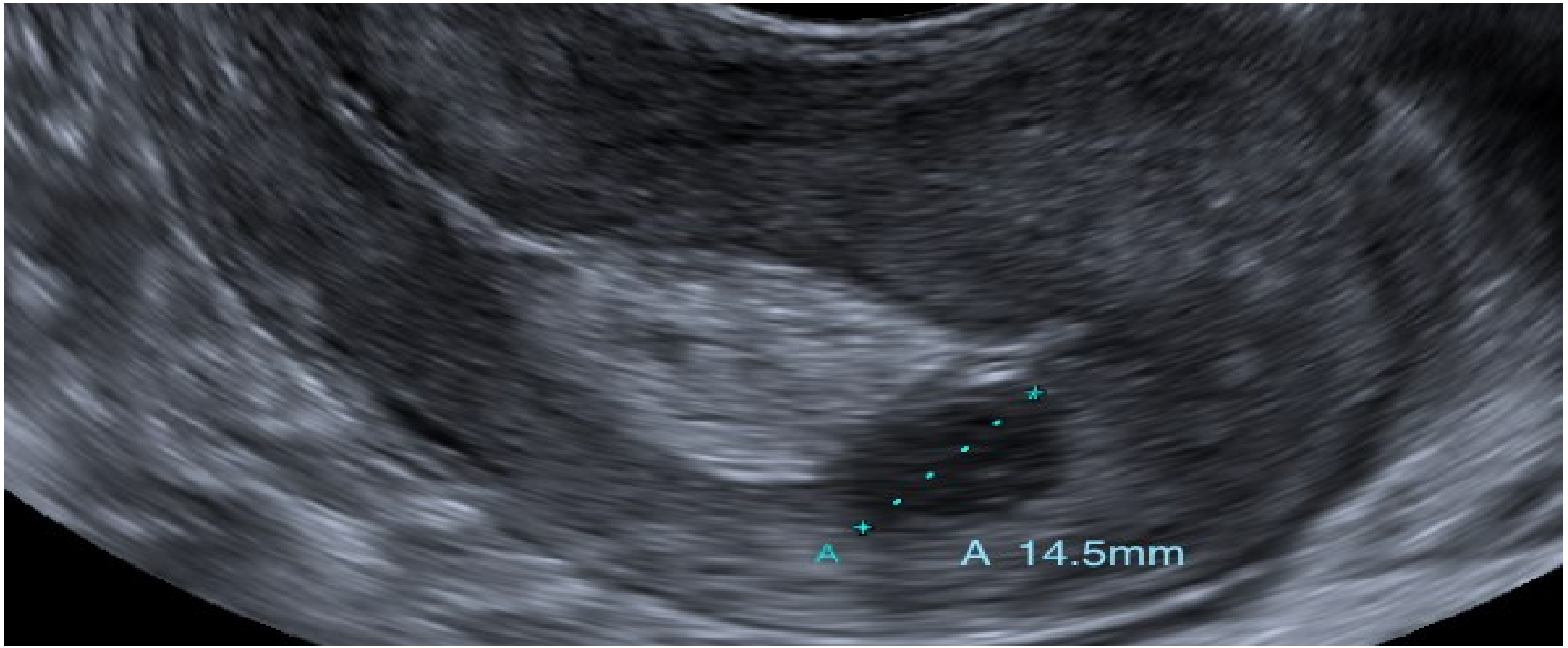


- Submucous fibroid (distorting endometrial cavity)
- Heavy menstrual bleeding despite treatment (sub-optimal placement)
- IUS should be removed prior to commencing Rx with UPA 5mg daily for 12 weeks initially

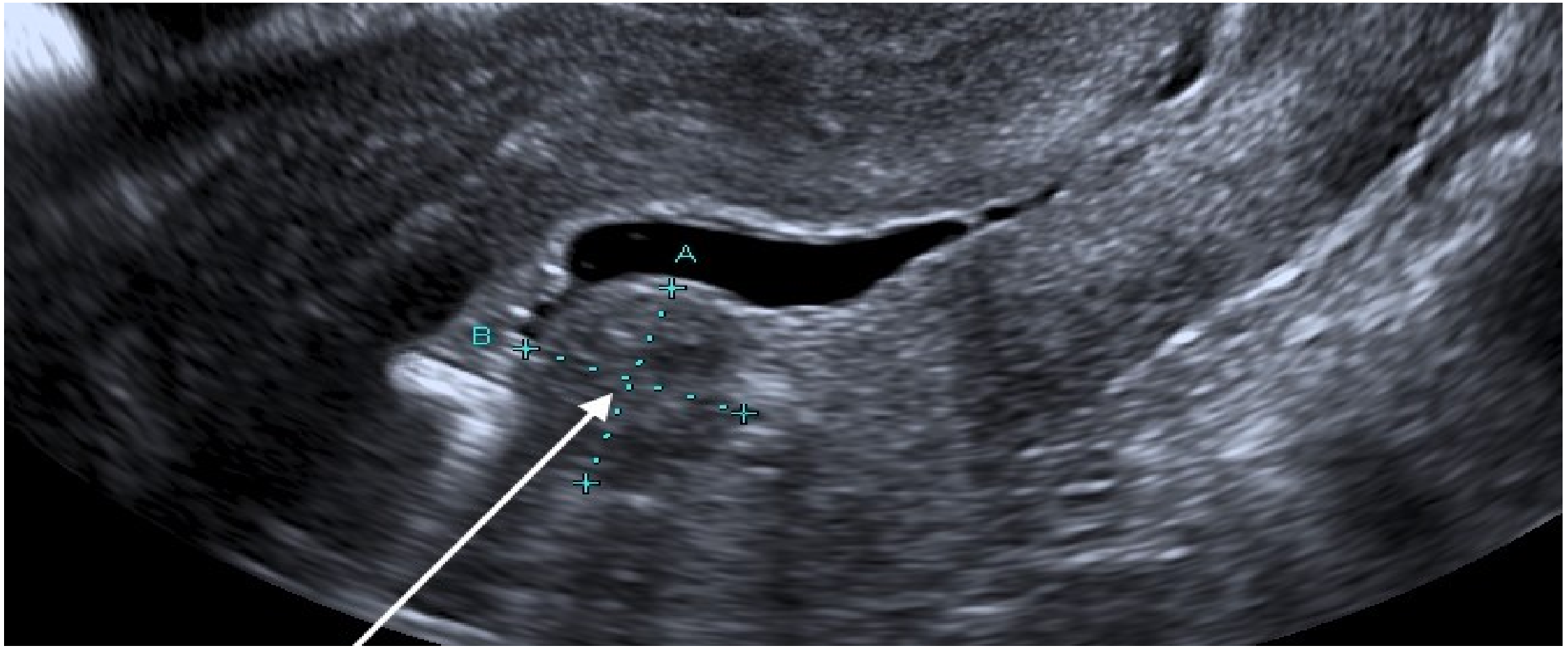
Type 0 fibroid – small fibroids may undergo complete regression in association with Rx with Esmya®



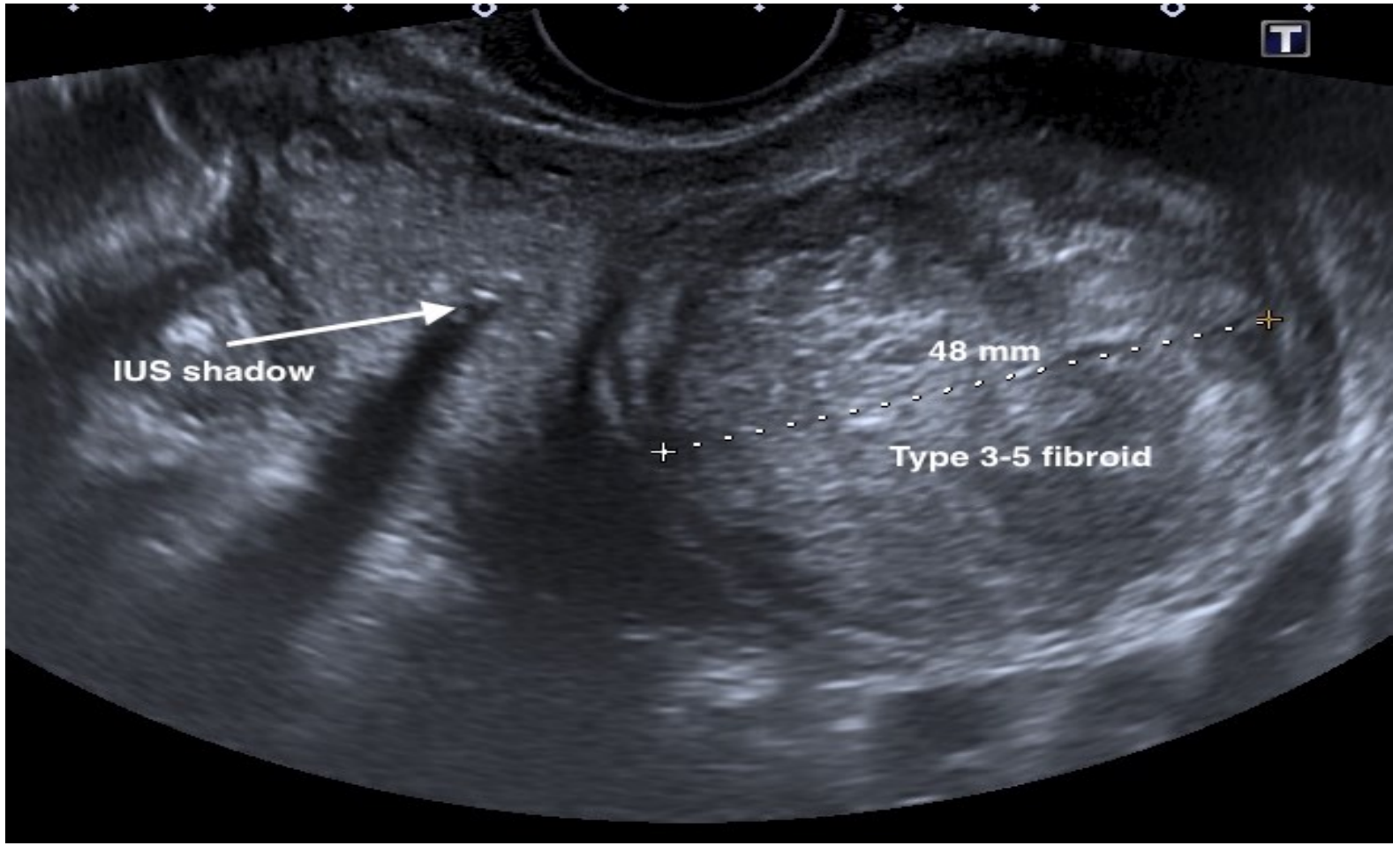
Coincidental finding of a type 3 fibroid pre IUS (52 mg LNG) to manage HMB



Small type 2 fibroid



Asymptomatic intramural fibroid



Prediction of malignancy

- Awareness raised due to debate regarding laparoscopic morcellation
- Uterine sarcomas
  - Myometrial
  - Typically single large tumours
  - Ultrasound appearance may be indistinct from ordinary fibroids
  - May appear as irregular vascularized mass with irregular anenchoeic areas due to necrosis

Clinical guideline 44 been updated?

NICE clinical guideline 44 was reviewed in 2015 as part of routine surveillance to decide whether an update was needed.[1,2]

New evidence was identified including that related to the medical treatment of fibroids (the effectiveness of progesterone receptor modulators [PRMs]).[1]

As a result of the review, a proposal was made to consider updating guidance relating to:[2]
The diagnosis and management of women with heavy menstrual bleeding (full review expected end of 2017)
The medical management of women with uterine fibroids – *"What is the clinical and cost effectiveness of medical treatments for fibroids greater than 3cm in diameter."* **(Immediate topic update by standing committee)**

References: 1. National Institute for Health and Care Excellence. Addendum to Clinical Guideline 44, Heavy Menstrual Bleeding: assessment and management, May 2016.
2. National Institute for Health and Care Excellence. Centre for Clinical Practice – Surveillance Programme, Recommendation for Guidance Executive. Clinical guideline CG44: Heavy menstrual bleeding: investigation and treatment.

How will the CG44 topic update affect clinical practice?

According to the NICE guideline:[1]

- Treatment with ulipristal acetate is recommended for women with uterine fibroids (greater than 3cm diameter), and for no more than 4 courses

According to its licence and indications:[2]

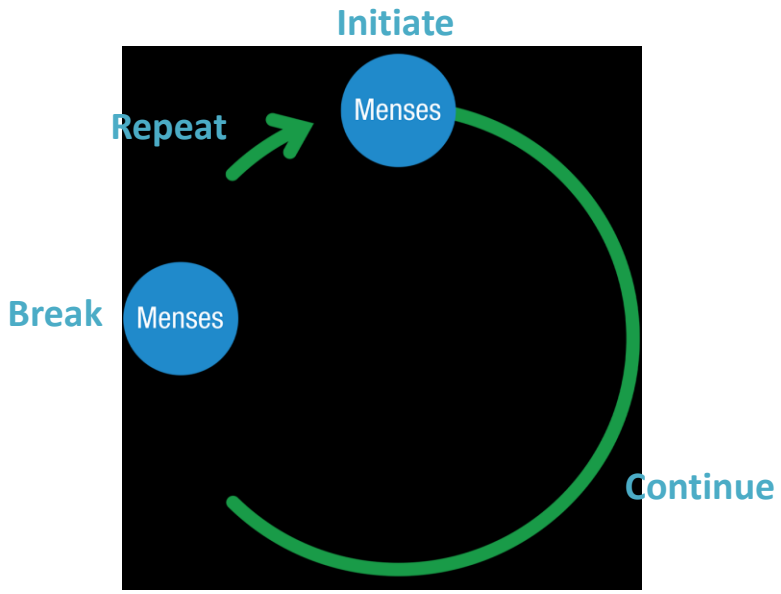
- ESMYA® can be prescribed pre-operatively for women with moderate to severe symptoms of uterine fibroids
  - ESMYA® can correct anaemia and reduce fibroid size before surgery
- ESMYA® can be prescribed in women with moderate to severe symptoms of uterine fibroids, regardless of plans for later lines of treatment

References: 1. National Institute for Health and Care Excellence. Addendum to Clinical Guideline 44, Heavy Menstrual Bleeding: assessment and management, May 2016.
2. Esmya® Summary of Product Characteristics, April 2016.

How will the CG44 topic update affect clinical practice?

Dosing schedule:[1]

- One course is one 5mg tablet daily for 3 months
- The first course should be started during the first week of menstruation
- Subsequent courses should start during the first week of the second menstruation after the previous course ended

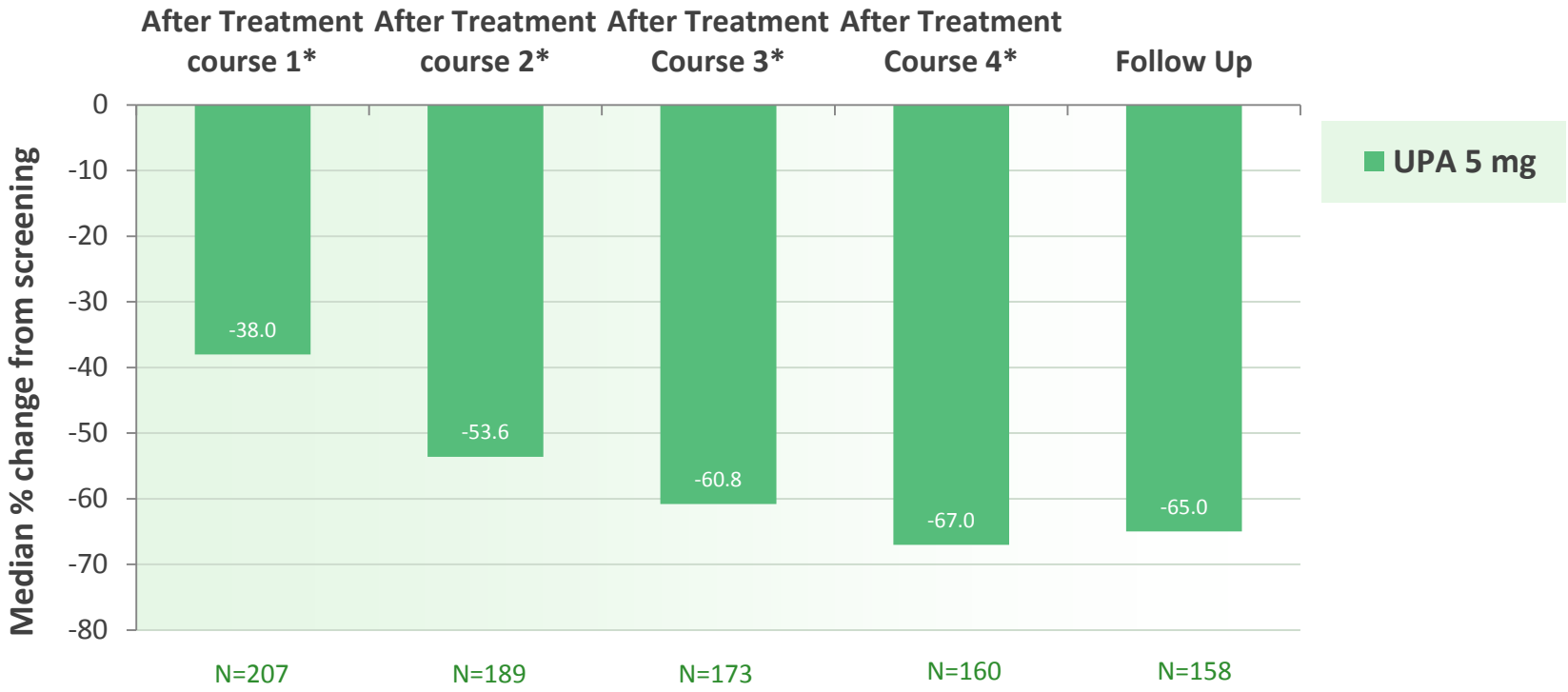


Reference: 1. Esmya® Summary of Product Characteristics, April 2016.

PEARL IV

Efficacy: **Fibroid volume reduction**

Median change from screening in total fibroid volume[a] (FAS1)



[a]Volume of 3 largest fibroids combined
* After treatment course + 1 bleed
UPA, ulipristal acetate

UPA 5mg is the licensed dose

1. Donnez J, et al. Fertil Steril, 2016;105 (1): 165-173.e4

Cystic degeneration of uterine leiomyoma during treatment with UPA

- Potential reduction in volume of degenerated myoma
  - Down-regulation of angiogenic factors
  - Reduction in fibroid vascularisation noted with power doppler
- Medical treatment of uterine leiomyomas is a realistic option for the future
  - Possibility of complete regression

PM, age 48

- Irregular heavy periods – presented to community sexual health service
- Fibroid detected in posterior wall of anteverted uterus (6 cm x 6 cm)
  - No distortion of the endometrial cavity
- Endometrial biopsy taken
  - Early proliferative phase, no endometritis or glandular hyperplasia
- Mirena inserted

PM, age 48

- Mirena expelled 8 months later
- Commenced UPA 5mg daily for 3 months
- Amenorrhoeic
- Reduction in fibroid to 3 cm x 3 cm
- Mirena inserted and retained with optimal bleeding profile

UPA 5 mg is an effective and well tolerated treatment for fibroids

In patients with symptomatic fibroids, a 12-week courses of oral **ulipristal acetate 5 mg** once daily effectively controls

- bleeding and pain,
- reduces fibroid volume
- restores quality of life

and has an established safety profile.

The results of repeat course studies indicate that the use of more than one course of UPA potentially has additional benefits

- The current approved posology is courses each of 3 months duration, separated by off-treatment periods of at least 2 menstrual bleeds
  - Subsequent courses of treatment should commence at the earliest in the second menstrual bleed following completion of the previous course of treatment.

Discussion