
بسم الله الرحمن الرحيم

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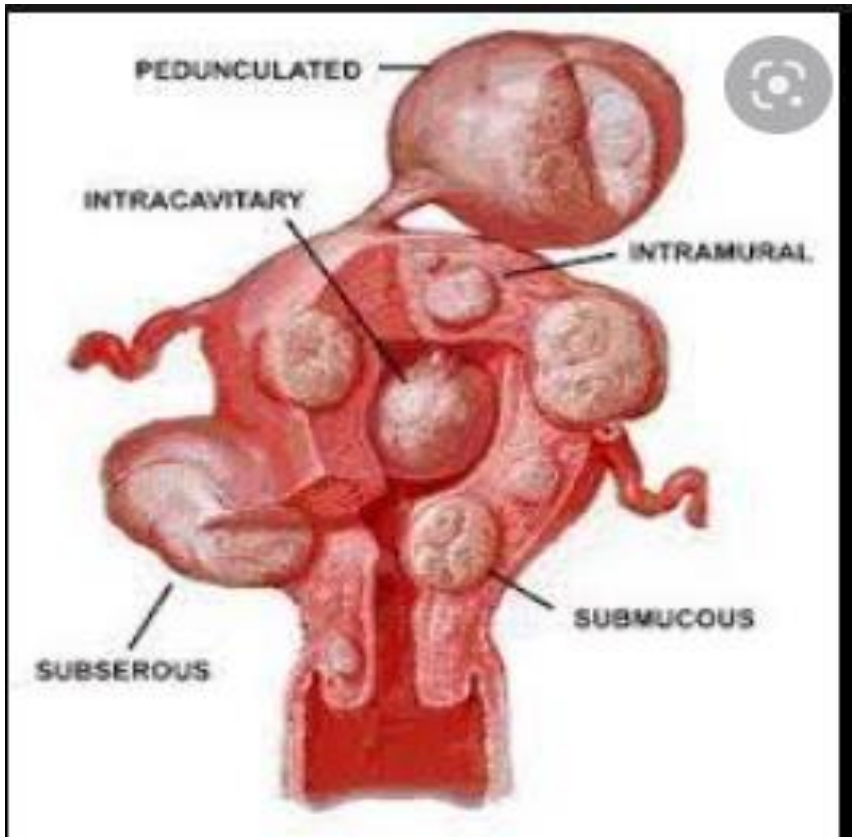
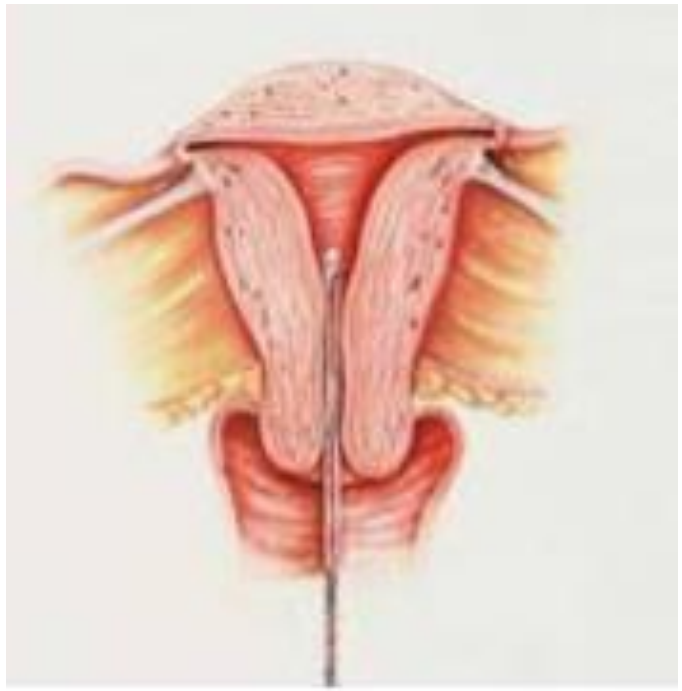
fibroma and Medical therapy



Pretreatment assessment

Includes

- **clinical and laboratory evaluation**,
- **imaging**
- **endometrial sampling**
- **Peri- and postmenopausal patients** are evaluated for **sarcoma risk**
- **evaluated for iron deficiency** anemia and the possibility of **coexisting endometrial hyperplasia.**



ROLE OF EXPECTANT

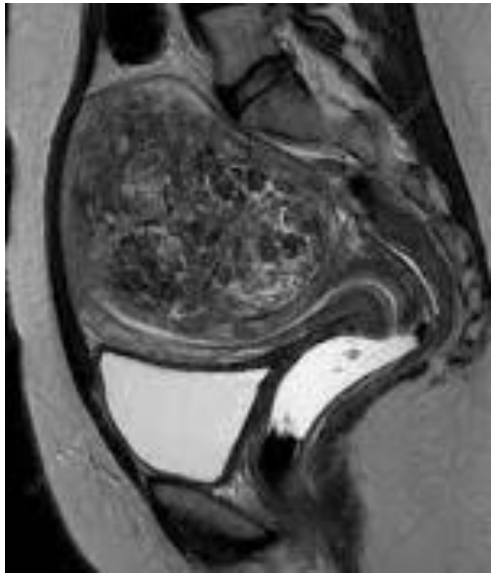
Candidates

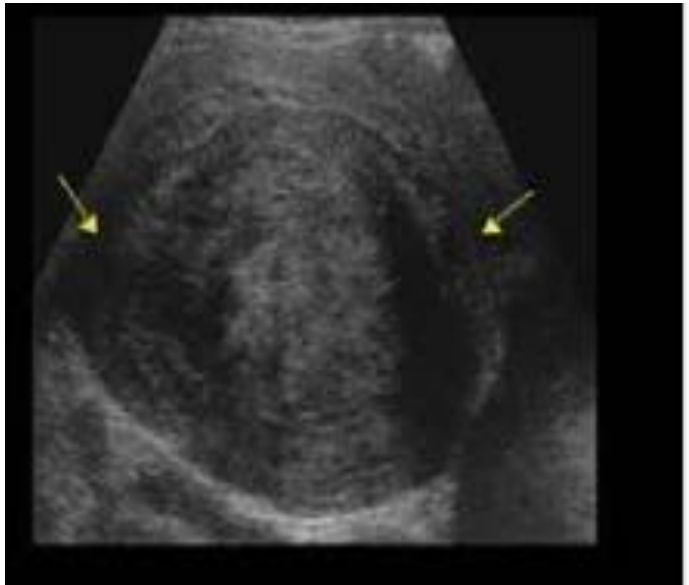
- Asymptomatic
- Attempting pregnancy
- With lesions that are stable in size as demonstrated by serial imaging studies for one year
- Peri- or postmenopausal
- With uteri less than 12 weeks in size (not palpable abdominally)

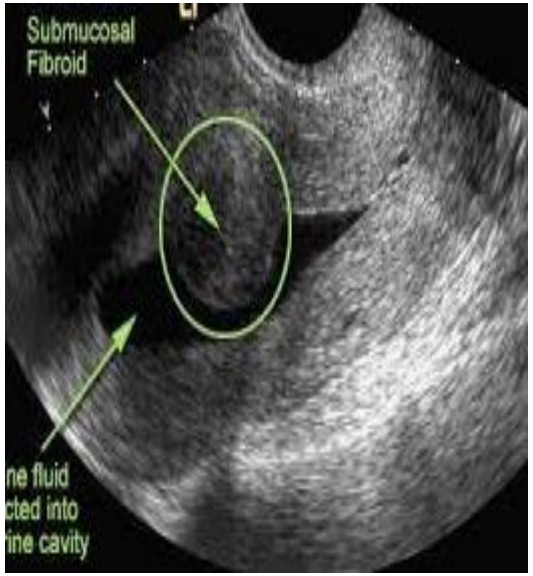
●**Components of expectant management** – Expectant management involves periodic evaluation of the patient for new symptoms that could be related to fibroids and for evidence of fibroid growth.

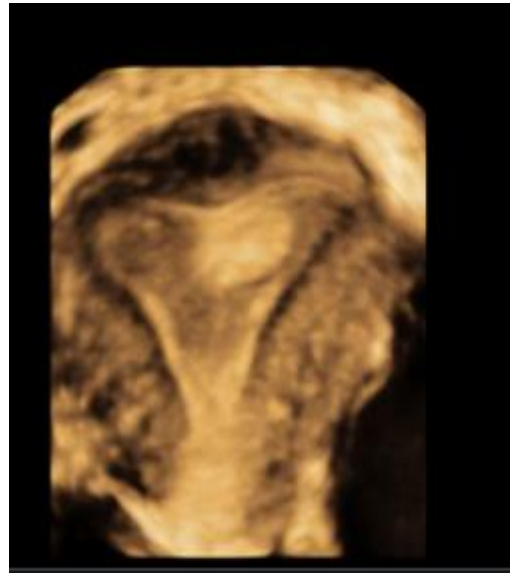
Such evaluation may be limited to history and physical examination or may require imaging or laboratory studies, typically with pelvic ultrasound and assessment for anemia.

- In patients with no other symptoms or concerns, yearly evaluation is reasonable.
- Patients are encouraged to contact their clinicians if new pelvic symptoms develop.









expectant management for patients with uterine fibroids, there is little evidence of documented harm over 6 to 12 months of observation, and expectant management can be employed.

Patients who desire fertility – For patients who **desire pregnancy** and **present with symptoms** that are reasonably attributed to fibroids (bleeding, bulk, infertility), **myomectomy is typically the first option.**

- hysteroscopic resection
- open abdominal
- laparoscopic myomectomy

Most medical therapies are not used in patients desiring pregnancy because

- **preclude conception**
- **adverse effects when employed long-term**
- **rapid symptom rebound when discontinued**.

Last line – For patients who do not desire future fertility and have persistent fibroid-related symptoms despite the above treatments or who desire surgical therapy, options include

- hysterectomy
- myomectomy.

While hysterectomy is the definitive procedure for **relief of symptoms** and prevention of recurrent fibroid-related problems **(eg, hydronephrosis),** it is also associated with **long-term morbidity**.

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Selection of medication, embolization, or surgery depends on patient preferences around

- side effects,
- invasiveness,
- recovery time,
- need for prolonged treatment,
- and risk of the treatment compared with risk of symptom recurrence.

the treatment order considers the

- efficacy,
- safety,
- tolerability,
- ease of use,
- ancillary benefits (eg, contraception), and
- cost.
- patient preferences and other factors, such as
- desire for contraceptive efficacy or
- local availability.

First tier

1. For patients with **HMB** likely from **submucosal fibroids**, we recommend **hysteroscopic myomectomy**
2. **For patients with all other types of fibroids** (ie, not exclusively submucosal) who do not desire pregnancy, we suggest initial treatment with **a**

➢**combined estrogen-progestin contraceptive** (oral pills, transdermal patch, or vaginal ring)

- work quickly and are
- widely available
- low in cost
- well-tolerated

➢levonorgestrel-releasing intrauterine devices,

➢tranexamic acid,

➢progestin-only pills.

treatment selection

- efficacy,
- safety,
- tolerability,
- ease of usecost.

Patients with all other types of fibroids (not exclusively submucosal) who do not desire pregnancy are offered medical management to reduce their HMB.

- **First-tier** agents for HMB do not reduce the fibroid size but improve the bleeding parameters.
- **Second tier** Patients who also have bulk or pressure symptoms are directed to treatment options that are considered second tier for HMB as these agents reduce fibroid size as well.

Patients with HMB who do not desire future fertility

For patients who do not desire future fertility, treatment is aimed at the presenting symptoms and performed in a stepwise approach until the symptoms are adequately controlled.

As there are limited comparative studies demonstrating superiority of one treatment option over another, patient preference and shared decision-making are used to create the optimal management strategy.

Estrogen-progestin contraceptives

Combined estrogen-progestin contraceptives

- oral contraceptive pills
- vaginal ring
- transdermal patch

benefits

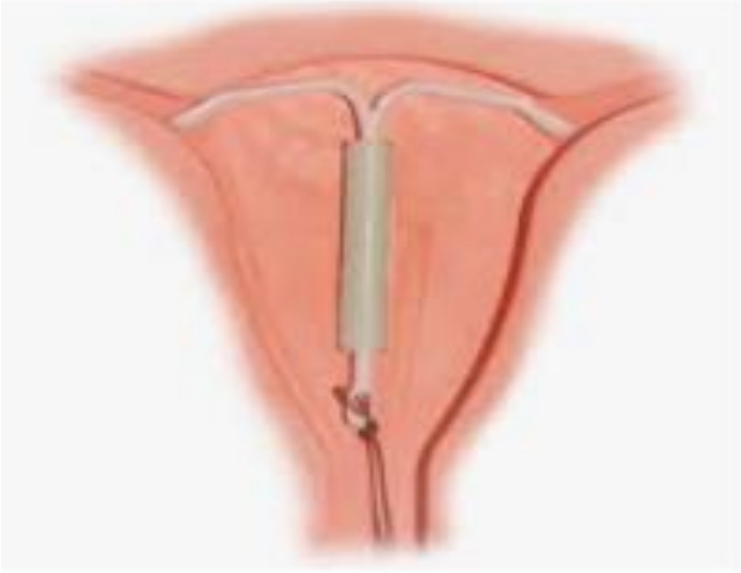
- ➢contraception
- ➢reduction of iron deficiency anemia,
- ➢reduction of uterine cancer ovarian cancer;
- ➢a long clinical history of use
- ➢inexpensive

<u>combined estrogen-progestin contraceptives as first-line therapy</u>

Patients must be appropriate candidates for exogenous estrogen use.

Progestin-releasing intrauterine devices (IUDs) –

- For patients who cannot use do not want estrogen-containing contraceptives,
- the levonorgestrel (LNG)-releasing IUDs are the main progestin-only contraceptive for fibroid-related HMB
- most guidelines support the use of LNG IUDs as a first-line agent for fibroid-related HMB
- IUDs also provide highly effective long-acting contraception.
- the risk of expulsion of the IUD is greater in patients with **fibroids that distort** the endometrial cavity.



Tranexamic acid

- a nonhormonal oral medication
- during menses or during the heavy days of menses.
- more effective than **oral progestins**
- Tranexamic acid is available as an oral 1.3 gram dose given three times daily
- It is **started with the onset of HMB.**

Progestin-only contraceptives

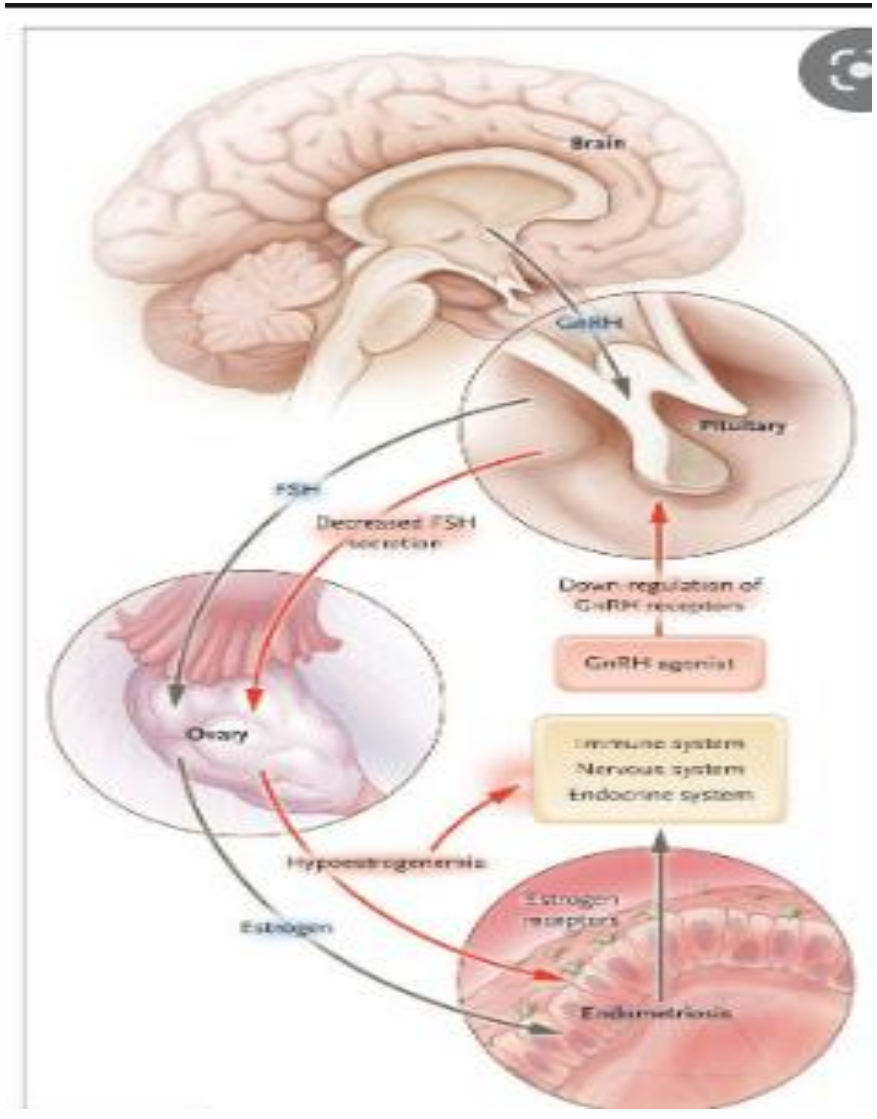
- Oral progestin-only contraceptives
- progestin implants
- progestin injections

do not appear to be effective for fibroid-related **HMB**

- **Second tier**
- GnRH agonists
- GnRH antagonists .
- Uterine artery embolization is a minimally invasive treatment option that treats both bleeding and bulk symptoms [24].
- progesterone receptor modulators

GnRH analogs

GnRH analogs, including antagonists and agonists, can reduce HMB Agonists also **reduce fibroid volume** but have potential **adverse effects** that limit use.



For patients who do not have an adequate response to first-tier treatment, the author prefers to **initiate GnRH antagonists,**

because they are orally dosed and generally better tolerated compared with agonists, and then moves to a trial of depot GnRH agonists **if** the antagonist therapy is not adequate to control symptoms.

However, patients and clinicians who prefer to initiate GnRH agonists may reasonably do so.

GnRH agonists likely result in a **greater reduction in fibroid volume compared with GnRH antagonists.**

GnRH antagonists – Oral GnRH antagonists are a relatively new generation of medical therapy. Like GnRH agonists,

these agents act centrally and are associated with hypoestrogenic side effects,

but they are available as oral formulations rather than injections.

GnRH antagonists are often formulated with low-dose steroidal add-back to limit hypoestrogenic side effects,

so separate add-back therapy is not required.

Elagolix – Elagolix, in combination with estradiol and norethindrone acetate

This preparation is available as two co-packaged capsules:

one contains elagolix 300 mg plus estradiol 1 mg plus norethindrone 0.5 mg to be taken in the morning

the other contains elagolix 300 mg alone to be taken in the evening.

- In two identical phase III trials comparing six months of elagolix plus hormonal add-back therapy (elagolix 300 mg twice a day with daily estradiol 1 mg and norethindrone acetate 0.5 mg

During treatment with elagolix plus add-back, side effects were modest, including hot flushes (7 percent), night sweats (3 percent), headache (5.5 percent), and nausea (4 percent).

Bone mineral density was also affected

With add-back therapy the effect on fibroid volume reduction is also attenuated.

As ovulation suppression with elagolix plus add-back is variable, it should not be considered a contraceptive.

- Relugolix – Relugolix, in combination with estradiol and norethindrone acetate, was approved by the US FDA

This preparation (commercial name Myfembree) is available as one copackaged capsule containing relugolix 40 mg plus estradiol 1 mg plus norethindrone acetate 0.5 mg in a single daily dose

patients in the relugolix treatment

reduction in pain, anemia, bulk-related symptoms, and uterine volume [reduction of approximately 12 to 15 percent

while preserving bone mineral density.

GnRH agonists are primarily used

1. preoperative therapy (typically 3 to 6 months in duration)
2. As transitional therapy for patients **in late perimenopause** as they move to meno pause.
3. For patients with fibroids and anemia who are planning surgery for fibroids but have not responded adequately to iron-only therapy, a short course of preoperative GnRH agonist treatment plus iron is an established option.
4. Goals of preoperative therapy can include induction of amenorrhea to improve anemia and volume reduction to facilitate a less invasive procedure, such as allowing a vaginal rather than an abdominal hysterectomy.
5. **without hormonal add-back** treatment the parenteral forms of GnRH agonists (**one- and three-month depot formulations** given as an intramuscular injection)

Progesterone receptor modulators (PRMs)

Despite evidence supporting use of the PRMs ulipristal acetate (UPA) and mifepristone as daily medical therapy for fibroid-related bleeding

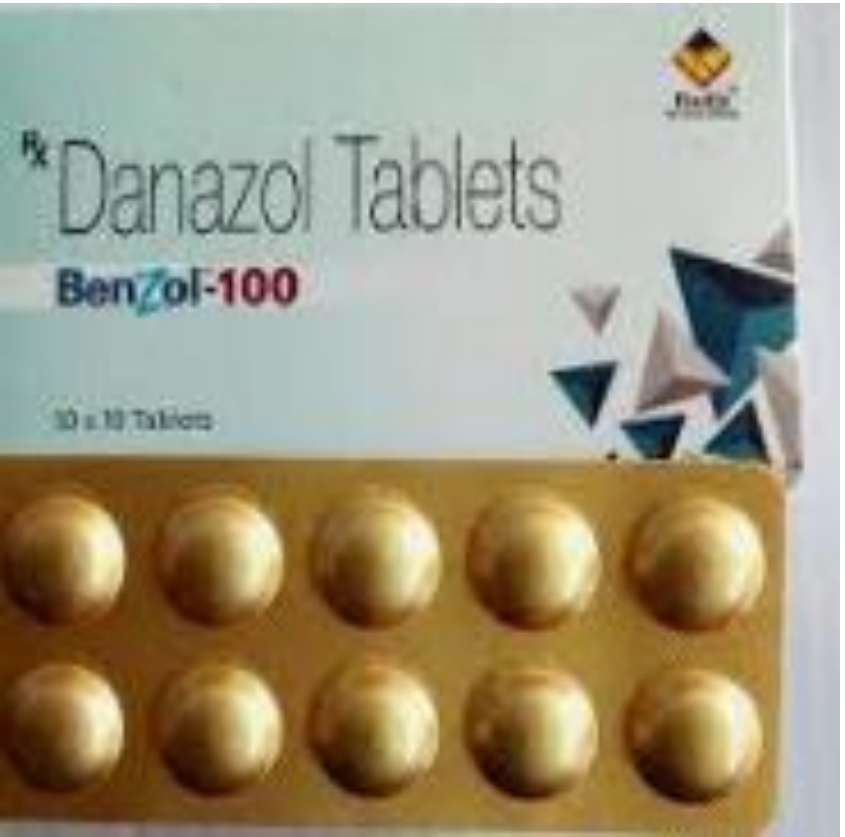
neither is currently available in most countries for fibroid treatment.

Both UPA and mifepristone remain on the market for one-time use as emergency contraceptives.

- Mifepristone – Mifepristone at doses of 5 to 50 mg for three to six months has been reported to decrease heavy menstrual bleeding and, in some studies, fibroid volume
- However, some studies reported abnormal endometrial histology at the conclusion of therapy

- **Androgenic compounds** – Use of the androgens danazol and gestrinone

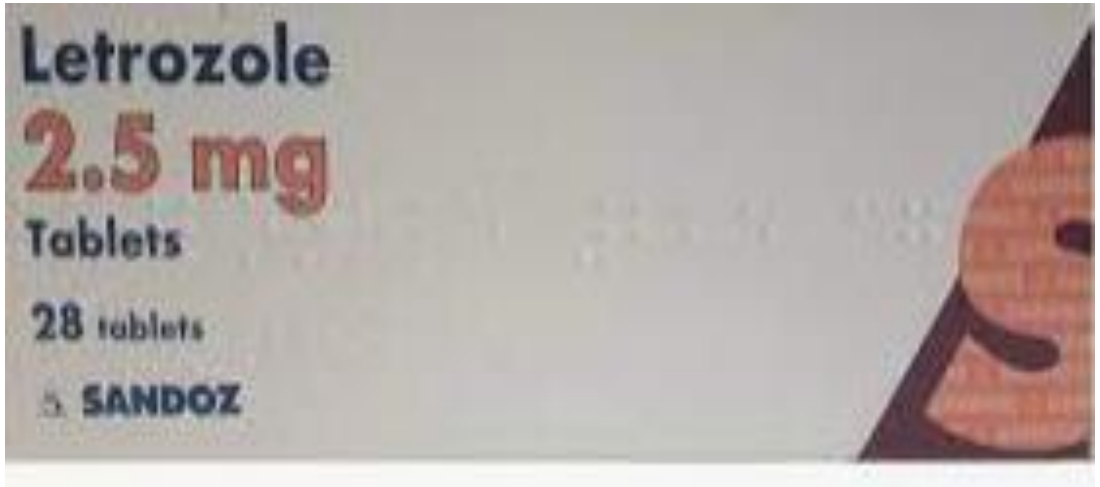
we do not advise using these agents for fibroid-related symptoms.



- **Aromatase inhibitors** –

letrozole reported decreased fibroid volume following treatment

, the trial did not assess fibroid-related symptoms, and the volume reduction was similar to that achieved with GnRH agonist therapy



Selective estrogen reuptake modulators (SERMs)

Studies of the SERM raloxifene have reported mixed outcomes for fibroid treatment

Use of raloxifene as hormonal add-back with GnRH analog treatment for fibroids appeared to reduce bone loss but did not improve quality of life or other fibroid-related symptoms.

Complementary medicine

Herbal supplements – Limited data do not support use of herbal supplements, including black cohosh and Chinese herbal medicine, for fibroid-related symptoms.

Acupuncture we do not advise these interventions as primary treatment of fibroid-related symptoms.

However, as risks associated with acupuncture are low

Herb Drug Safety #4 for Acupuncture ...
healthcmi.com

Peri-and postmenopause

- perimenopausal patients can typically be managed expectantly.
- Postmenopausal patients with fibroids should be **evaluated periodically to ensure that the fibroid or fibroids have not increased** in size.

There is no consensus as to the frequency of evaluation, but every one to two years seems reasonable in the absence of new symptoms.

Postmenopausal patients with new symptoms, particularly

- uterine bleeding
- Enlargement

malignancy, including leiomyosarcoma, should be excluded.