

CADTH COMMON DRUG REVIEW

Patient Input

ulipristal acetate (Fibristal)

(Allergan Inc.)

Indication: Uterine fibroids (signs and symptoms)

CADTH received patient input for this review from:

Canadian Women with Fibroids Limited

Women's Health Initiative

July 26, 2017

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Date: July 25, 2017

Objective: To describe patients' experiences and expectations if Fibrystal is used for longer than 3 months. (The impact of this longer use on patients' health & quality of life (both benefits and harms)).

Method: In order to offer input from patients I went to the CANFib members seeking women willing to share how long they have been using Fibrystal as well as the reason, and expectations.

100s of women put their hands up.

The sheer volume of women who were instantly eager to share that they make use of Fibrystal on an extended basis was, to me, a telling sign that there are a number of good reasons it's worth consideration for extended use coverage. In further discussing with a selection of these women, I found that my assumptions were correct.

Included in this submission is a small cross section of case information.

██████████
██████████ was on Fibrystal off and on for 3 years. Where she lives, the wait for surgery is very long, having a defined date is almost impossible. Added to that problem was her constant dip into severe anemia making surgery planning even more difficult. By using Fibrystal over a longer time she was able to work on her blood stores, giving her a leg up when facing surgery. ██████████ worked on her blood stores for these three years and has now reached a time in her condition where her blood levels remain at safer levels most of the time. She is now able to (and has) been put on the list for Hysterectomy.

██████████
██████████ has one child and plans to have more. She opted for Fibrystal in order to keep her body in better form between pregnancies as well as to maintain a quality of life as she builds her family. ██████████ felt this was a more viable option than myomectomy; her fears in this area being that the surgery may cause issues with potential pregnancy down the road. ██████████ prefers an option that does not risk the effectiveness of her uterus until such time as she is finished having children.

██████████ is 52 and waiting for Menopause to make the changes in her body required to calm her fibroids down. Her expectation for longer term use is to make this wait less debilitating while avoiding surgery altogether. At 52 ██████████ is not sure surgery is a good idea unless absolutely necessary yet her quality of life was rather questionable with a consistent blood level under 80 points. She feels that should menopause "drag on" till 54 or 55 that these years should be in good health.

██████████ has stayed on Fibrystal for longer intermittent use because she would like to avoid surgery for many reasons, for her the most important being she simply not take the time off work required to recover. While hysterectomy itself only

requires a few days in hospital, the recovery time can be up to six months. Depending on the type of work a woman does, this is a very long time to have no income. [REDACTED] runs a business and has 2 kids; these are the contributing factors to her hope that surgery can be held off until such time as she can afford the long departure from her business.

[REDACTED] is thankful for Fibrystal because she, is quite overweight. Statistics Canada reports that in 2016, 20% of Canadians are now “obese” leaving a number of women with Fibroids in this category. [REDACTED] says she knows her weight contributes to the level of danger presented by any surgery, but the ability to lose weight when dealing with severe Fibroids is less manageable. [REDACTED] says she has managed to have a quality of life that was not available to her prior to access to the drug.

These patient snapshots underline the figures from a recent Survey of CANFib members in which more 100s of respondents relayed their concerns regarding the current treatment choices.

Supporting Survey

The March 2017 CANFib Survey of women with Fibroids concluded 76% of women want a treatment that allows them to keep their uterus (and 63% of respondents said they want to avoid surgery at all).

In the same survey, those that had opted for Hysterectomy told us the recovery time was 6-9 months, a strong reason why many women (including some in this Patient Snapshot) simply need other options.

Summary

These are all cases of women who have opted to request longer term intermittent use of Fibrystal, each for varying specific reasons. The expectation in each case is that their quality of life will either remain as is or improve during the longer use.

While women who opt for hysterectomy are often quite happy with the outcome, the journey of this procedure extends well beyond a three day stay in the hospital. The impact of abdominal surgery can take a toll on the ability to handle children and family as well as attend work; and as with most Canadians, their income is not disposable.

My own recovery from Hysterectomy was a six-month process. Of these six months, at least two of them made my job difficult, even with the advantage of having a sit down workday. The simple act of lifting a full wastebasket or 2 reams of paper at the office is a potential setback. Often pain medication is also required for an extended time, something which can make attendee at work (or with children) not just difficult but in some instances dangerous.

Women planning families feel they are best to avoid surgeries that bring any sharp objects near their uterus, citing the ability to accomplish similar results with a medication is a better option and should be there for them should they need it.

Conclusion

Women want/need a non-surgical option that allows them to significantly reduce bleeding in order to maintain their quality of life while preserving their uterus.

Thank you for this opportunity to contribute to your process.

Patricia C Lee, Founder: CANFib (Canadian Women with Fibroids Limited)

1. About Your Patient Group

Women's Health Initiative Network is a national not-for-profit organization that aims to change the way we educate women about the following quality of life health conditions that are rarely discussed:

Uterine Health – Fibroids

Vaginal Health

Sexual Health

Bladder Health

We are a registered, non-profit organization that exists for the enhancement of women's health to provide awareness, policy change, influence patient engagement and lead consumer research to ultimately empower women.

<http://whin.ca>.

2. Information Gathering

We gathered the information through a combination of personal and professional experience and a consumer survey of 1117 respondents. The data from the survey was gathered in Canada from both English and French speaking participants. Three physicians and 2 RN's contributed their insights to me as well.

3. Disease Experience

Fibroids are benign uterine tumours. The symptoms may be very distressing for women and occur at what is often the busiest time in their lives between the ages of 30 and 50. This is at a time when women are desiring to or starting a family and/or raising children and may also be at a critical time in their career. Many women in this age bracket are also helping with their aging parents. The most common symptoms of uterine fibroids are heavy menstrual bleeding, prolonged periods, pelvic pressure, pelvic pain, frequent urination, urgency, difficulty emptying the bladder, constipation, backache and/or leg pains. Walking may be an issue for many women. Women may suffer fatigue & anemia from heavy blood clots and require iron supplements and/or blood transfusions. Fibroids may interfere with fertility; result in pregnancy loss or preterm birth. Patients may have difficulty with activities of daily living due to pain/bloating and bleeding. Patients may not be able to care for children, work, exercise or socialize both of which are so helpful for mental health and/or maintenance of a healthy weight. Patients may not be able to exercise due to any one of the symptoms of uterine fibroids. Sex may be painful for women with uterine fibroids and impact their relationship and general sense of well-being. Bleeding and pain are likely the most important symptoms to control. Women may experience insomnia and are at risk for depression due to the lack of sleep and/or chronic pain.

4. Experiences with Currently Available Treatments

There are many treatment options. Those women that are symptom-free may be under watchful waiting. Other treatments include medications that target hormones that regulate a woman's menstrual cycle which treats heavy menstrual bleeding and pelvic pressure. They don't eliminate fibroids, but may shrink them. Medications include:

- **Gonadotropin-releasing hormone (Gn-RH) agonists** treat fibroids by blocking the production of estrogen and progesterone, shrinking fibroids prior to surgery. One of the side effects is significant hot flashes and it also can't be used for more than 3-6 months as long term uses may lead to loss of bone.
- **Progestin-releasing intrauterine device (IUD).** A progestin-releasing IUD can relieve heavy bleeding caused by fibroids. A progestin-releasing IUD provides symptom relief only and doesn't shrink fibroids or make them disappear. It also prevents pregnancy.
- **Tranexamic acid (Lysteda).** This non-hormonal medication is taken to ease heavy menstrual periods. It's taken only on heavy bleeding days.
- Oral contraceptives or progestins can help control menstrual bleeding, but won't reduce fibroid size. Many women experience bloating, weight gain, headaches and nausea for this medication.

Nonsteroidal anti-inflammatory drugs (NSAIDs), which are not hormonal medications, may be effective in relieving pain related to fibroids, but they don't reduce bleeding caused by fibroids.

MRI-guided focused ultrasound surgery (FUS) is a **noninvasive treatment option** for uterine fibroids that preserves the uterus and is done on an outpatient basis.

- **Uterine artery embolization.** Small particles (embolic agents) are injected into the arteries supplying the uterus, cutting off blood flow to fibroids, causing them to shrink and die. This technique can be effective in shrinking fibroids and relieving the symptoms they cause. Complications may occur if the blood supply to your ovaries or other organs is compromised.
- **Myolysis.** In this laparoscopic procedure, radiofrequency energy, an electric current or laser destroys the fibroids and shrinks the blood vessels that feed them. A similar procedure called cryomyolysis freezes the fibroids.
- **Laparoscopic or robotic myomectomy.** In a myomectomy, the fibroids are removed, leaving the uterus in place. If the fibroids are few in number a laparoscopic or robotic procedure may be in order as it uses slender instruments inserted through small incisions in the abdomen to remove the fibroids from the uterus.
- **Hysteroscopic myomectomy is** an option if the fibroids are contained inside the uterus (submucosal).
- **Endometrial ablation** is invasive but effective in stopping abnormal bleeding. Submucosal fibroids can be removed at the time of hysteroscopy for endometrial ablation, but this doesn't affect fibroids outside the interior lining of the uterus and therefore symptoms may be persistent.
- **Abdominal myomectomy is an** open abdominal surgical procedure to remove fibroids. Scarring after surgery can affect future fertility.
- **Hysterectomy is** the removal of the uterus and the only proven permanent solution for uterine fibroids. Hysterectomy is major surgery, requires hospitalization from 1-5 days has a concomitant risk of bleeding and infection and renders a woman infertile. If a woman also has her ovaries removed, it brings on menopause and she may require hormone therapy.

5. Improved Outcomes

Patients would like to see more conservative measures to treat uterine fibroids. Patients always appreciate choice. Patients would like treatments that treat the symptoms such as reduction or elimination of vaginal bleeding, elimination of pain and bulking symptoms (bloating, abdominal pressure and pain). Patients would like treatments that are easy to

take. Patients would like conservative measures to treat their symptoms while they await surgery. Patients would like bridge treatments so they may avoid surgery and its complications altogether.

6. Experience with Drug Under Review

In our 2017 consumer survey of women that said they were currently using Fibrystal® (ulipristal acetate) to treat Uterine Fibroids, 12.5% rated their quality of life on a Lykert scale during treatment as Excellent. 37.5% said their quality of life was very good and 50% said their quality of life was good.

Patients have accessed the medication under review through clinical trials, private insurance and compassionate use. Patients have also paid for the medication out of their own pocket. Patients have had elimination of vaginal bleeding, reduction in size of fibroids and decreased and resolution of pain. Patients were able to plan their lives better. Patients who were anemic but were planning surgery were able to take the medication under review Fibrystal and resolve their anemia and be healthier for their surgery. Many patients were able to delay surgery until the menopause which naturally reduced the size of their uterine fibroids and therefore were able to forego surgery and its inherent risks altogether. Many patients were able to return quickly to a healthy lifestyle, one where they could exercise and socialize. Many women no longer missed work due to pain and bleeding of uterine fibroids. The benefits of Fibrystal were many. Taking a medication is much less interruptive to one's life as opposed to any type of procedure or surgery. The side effects are minimal compared with the oral contraceptive pill or other GnRH agonists which puts a woman into early menopause. As for subgroups, those women who have not completed their families, Fibrystal is a nice option that preserves fertility. Also pre-menopausal women may benefit as Fibrystal may provide a bridge to menopause and may prevent surgery

7. Companion Diagnostic Test

Fibrystal does require testing with companion diagnostics prior to being prescribed

8. Anything Else?

It is clear from my conversations with women with uterine fibroids who've had treatment or who require treatment, treating physicians and our 2017 consumer survey that women want choice and Fibrystal® provides that to women.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No, I completed this submission in it's entirety on my own.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

Yes, I used information from a consumer survey that our patient group did. Epsilon administered the consumer survey. An interim analysis was performed by James F. McGrath

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

1. Tyros BioPharma has provided funding as has Allergan.
2. Allergan may have interest in this medication.

Company	Check Appropriate Dollar Range			
	\$0 to 5,000	\$5,001 to 10,000	\$10,001 to 50,000	In Excess of \$50,000
Tyros Biopharma	X			
Allergan			X	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name:Maureen MCGrath

Position:Executive Director

Patient Group:Women's Health Initiative Network

Date: 2017-07-25