

Position Statement for Management of Genitourinary Syndrome of the Menopause (GSM)

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One of the most consistently identified predictors of impaired sexual health in women is the presence of vaginal symptoms. The vast majority of postmenopausal women have symptoms associated with Genitourinary Syndrome of the Menopause (GSM) yet only a minority receive any treatment. Unlike many other symptoms of the menopause, symptoms of GSM often worsen over time.

This guidance is designed to support healthcare professionals in diagnosing and managing this condition.

Terminology

The term Genitourinary Syndrome of Menopause (GSM) was introduced in 2014. GSM is a comprehensive term that includes vulvovaginal symptoms and lower urinary tract symptoms related to low oestrogen levels. The terms *vulvovaginal atrophy* and *atrophic vaginitis* (which were in general use) had a limitation because they did not cover the full spectrum of symptoms and did not indicate that symptoms were directly related to decreased oestrogen levels in the menopausal state. GSM more accurately describes the postmenopausal hypoestrogenic state of the genitourinary tract.¹

Talking about GSM

GSM is very common but often underdiagnosed and undertreated.

Studies have shown that around 70% of women have symptoms of GSM, yet only 7% receive treatment.²

Despite a vast majority of women experiencing symptoms related to this condition, only around 25% of women volunteer this information to their healthcare professional.

70% of healthcare professionals acknowledge they never, or rarely, ask about problems like vaginal dryness².

The prevailing attitude among both women and healthcare professionals is one that considers symptoms of GSM to be a natural and unavoidable part of the aging process.³

NICE menopause guidance gives clear recommendations regarding the optimal management of this condition in menopausal and postmenopausal women.⁴

Treatments for GSM are usually effective, safe and cost effective.⁴ Women need to receive individualised advice and treatment for this debilitating condition as a priority.

Symptoms and Signs

The symptoms and signs of GSM are detailed in Figure 1.

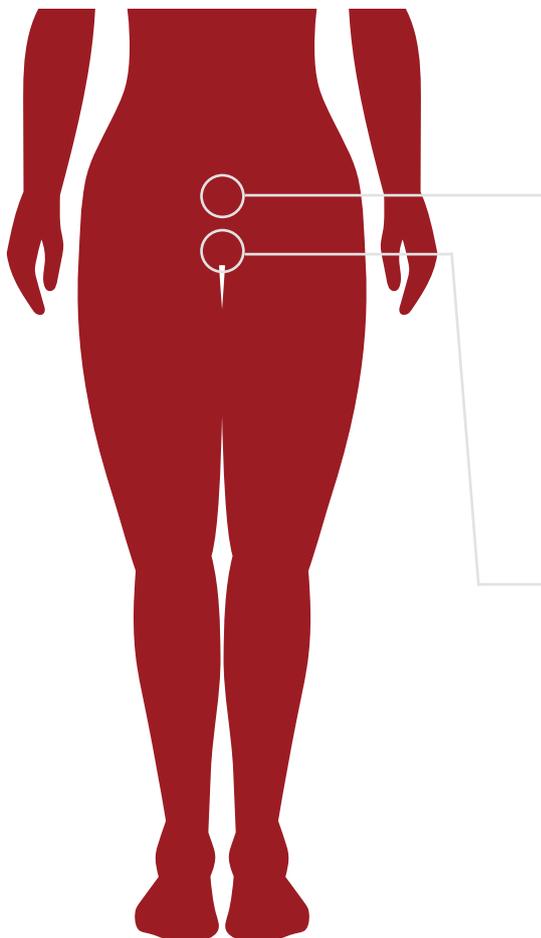
Symptoms	Signs
Genital dryness	Decreased moisture
Decreased lubrication during sexual activity	Decreased elasticity
Discomfort or pain during sexual activity	Labia minora resorption
Post-coital bleeding	Pallor, erythema
Decreased arousal, orgasm, desire	Loss of vaginal rugae
Irritation, burning, or itching of the vulva or vagina	Tissue fragility, fissures, petechiae
Urinary frequency and urgency	Urethral eversion or prolapse
	Prominence of urethral meatus
	Introital retraction
	Recurrent urinary tract infections

Figure 1: Symptoms and Signs of GSM¹

Impact of GSM

GSM leads many women to needlessly suffer with unbearable symptoms. It can affect women of all ages and is not solely related to the menopause. Low oestrogen states also exist in women who are breast feeding or women using progestogen-only contraceptives. Symptoms associated with GSM can have a very negative effect on interpersonal relationships, quality of life and daily activities.⁵

Oestrogen receptors are present in the vagina, urethra, bladder trigone and pelvic floor. All these areas can be affected by a lack of oestrogen during the perimenopause and menopause.⁶



Atrophy of the urethra, with a relative increase in urethral epithelial transitional cells – and a corresponding decrease in intermediate and superficial squamous cells – occurs after menopause.⁷

The smooth muscle in the lower urogenital tract atrophies, affecting the superficial muscle layers of the trigone, the proximal and distal urethra, and the lamina propria of the trigone and proximal urethra.⁸

A fall in oestrogen can result in the loss of superficial epithelial cells, collagen and elastin, resulting in loss of vaginal rugae.⁹

The vaginal epithelium becomes pale and friable and can tear and bleed, particularly during intercourse.

As a result of these changes, women can experience symptoms of:

vulval and vaginal dryness
itching
dyspareunia

urinary frequency and urgency
dysuria
nocturia
recurrent UTIs^{2,10}

These symptoms are reported to affect self-esteem and reduce QOL, including in women who are not sexually active.¹¹

Women who have received chemotherapy, surgery, and/or radiotherapy for certain types of malignancies have a higher risk of developing GSM.¹²

Other conditions, such as inflammatory bowel disease, diabetes mellitus, multiple sclerosis and stress can be associated with vaginal dryness.¹³ In addition, some medications, such as tamoxifen, antihistamines, decongestants and some antidepressants can also cause symptoms.⁹

Understanding the history

Women need to be asked the appropriate questions during consultations for the diagnosis of GSM to be made. If the right questions are asked, in the right clinical setting, women are more likely to be open about their symptoms.

Questions need to be asked in a sensitive manner and women should be given time to reflect and talk about this problem which, understandably, can be very embarrassing and awkward to discuss.

Menopausal women who present with urinary symptoms such as increased urinary frequency, urgency or recurrent urinary tract infections should also be asked if they experience any local vaginal symptoms.

Although pain and discomfort may be present during sexual intercourse, many women find they experience symptoms at other times, for example when they are walking, cycling, horse riding or simply just sitting down.¹⁰

It is also important to gain an understanding of whether the patient is likely to be at risk of a sexually transmitted infection by asking appropriate questions.

All postmenopausal women should be asked about any symptoms regardless of their presentation.¹⁴

Nurses undertaking cervical screening are well placed to enquire about any symptoms – as are all healthcare professionals who see postmenopausal women as part of their clinical work. Many women avoid having cervical screening because a speculum examination is too painful in view of their untreated GSM.

Useful questions to ask:

Does it feel different in any way around your vulva or vaginal area?

Have you noticed any vaginal dryness or less discharge than you used to have?

Have you experienced any vaginal soreness, burning or irritation?

Do you have any itching around your vagina or vulval area?

Is sexual intercourse painful or uncomfortable?

Have you noticed changes in any vaginal discharge (either increased or reduced)?

Have you noticed any symptoms such as increased urinary frequency or being less able to hold on to urine?

Do you have any discomfort on passing urine?

Examination

The decision regarding examination of women with GSM should be individualised and often depends on the clinical setting. Treatment does not need to be delayed if an examination is not possible during the initial consultation, for example a remote consultation.

Women should be offered an examination and their decision to accept it or not needs to be respected.

Examination should be considered if there are symptoms in a woman's history to suggest any other underlying pathology or if clinically indicated. Some women may prefer to share a digital image rather than having an examination undertaken.

In addition, a genital examination should be undertaken if:

- symptoms do not improve
- symptoms worsen after an initial treatment period of at least three months
- symptoms change or worsen before this time

On examination, you may see:

- atrophy of the vulva and vagina
- thinning of vaginal epithelium with loss of rugae and elasticity
- paler vaginal epithelium due to reduced blood supply in this area
- petechial haemorrhages

Physical appearance does not usually correlate with severity of symptoms. In addition, a normal examination does not exclude the diagnosis of GSM.

Investigations

For the vast majority of women, investigations are not necessary.

If a woman is due (or overdue) for cervical screening, it should be used an opportunity for this to be done. The woman should be given information during the cervical screening appointment and extra lubrication should be used for the procedure if necessary. If speculum insertion is uncomfortable or painful, women should be advised to return for screening a few months after starting local oestrogen treatment.

Urine dipstix and microscopy should be considered for women who present with urinary symptoms.

If there is abnormal vaginal bleeding then appropriate, relevant investigation should be undertaken to exclude other causes.

For women who complain of a vaginal discharge, a vaginal swab should be considered to exclude any infections (including STIs if indicated in the history).

Referral

A presentation of postmenopausal bleeding or signs suggestive of malignancy on examination should prompt an urgent cancer pathway referral.

Most women can be treated for GSM successfully in the primary care setting. In situations where symptoms are resistant to the various treatment options available, a referral to a specialist is indicated.

Management

A number of different treatments are available for GSM. These include systemic hormone replacement therapy (HRT), vaginal oestrogen, other local hormonal preparations, and non-hormonal vaginal moisturisers and lubricants.

Principles of GSM management

The principles of management are to restore urogenital physiology and to alleviate symptoms. The correct treatment can relieve symptoms and considerably transform a woman's quality of life.¹⁰

As a lack of circulating, natural oestrogen is the primary cause of atrophic vaginitis, hormone replacement therapy and/or localised hormone treatment are the most logical choice of treatment and have been shown to be effective in the restoration of anatomy and the resolution of symptoms.

Systemic Hormone Replacement Therapy (HRT)

Systemic HRT can be very effective when given to women with other symptoms of the menopause (or perimenopause) in addition to symptoms of GSM. For the majority of women, taking HRT provides more benefits than risks.

It is essential that women receive the right dose and type of HRT. If women receive inadequate amounts of oestrogen, they are likely to experience symptoms and also have an increased risk of future diseases such as heart disease, diabetes, osteoporosis and dementia.

Testosterone is one of the sex hormones that women produce that is often overlooked. Women actually produce 3x as much testosterone than oestrogen before the menopause. Levels of testosterone gradually decline due to increasing age or reduce abruptly following oophorectomy.

Testosterone as a gel or cream can also be very effective to improve symptoms related to GSM. This can be prescribed off-licence for women who still experience symptoms of reduced sexual desire despite taking HRT. Testosterone can work well to improve symptoms of reduced libido, low mood, reduced motivation and poor stamina.

Reduced or lack of libido, despite taking HRT, is very common in menopausal women and NICE Guidelines state that testosterone supplementation can be considered for menopausal women with low sexual desire if HRT alone is not effective.⁴

Around 10–25% of women who take systemic HRT will have urogenital symptoms that persist. These women can be given vaginal local oestrogen in addition to taking HRT. It is important that all women taking HRT are asked about any GSM symptoms in their annual review.

Vaginal oestrogens and DHEA

The clinical response to treatment with topical oestrogen is usually rapid and sustained.¹⁵

Oestrogen replacement restores normal pH levels, and thickens and revascularises the vaginal epithelium.¹⁶ There is also a decreased incidence of urinary tract infections and urinary symptoms.^{17, 18, 19}

Women should be given treatment initially for three months and then be offered a review. After this time, treatment can then be put on a repeat prescription. It is preferable to start treatment early, rather than waiting for symptoms to worsen. If treatment is started earlier on, it helps restore the anatomy back to normal and prevents more severe changes occurring, such as labial resorption or clitoral atrophy.

It is not necessary to use progestogens or progesterone for endometrial protection when using vaginal oestrogen long term.²⁰

All women should receive information about their condition and their treatment, preferably in written format. Women should also be signposted to other useful sources of information – see Resources section at the end of this article.

Women should also be advised that the information packaged with vaginal hormone preparations is out of date and factually incorrect. This needs to be changed by the MHRA.

Vaginal oestrogen can be absorbed from the vagina and surrounding area via a pessary, cream, gel or vaginal ring. There are two types of oestrogen used – oestradiol and oestriol.

The dose of vaginal oestrogen is very low; for example, using 10mcg oestrogen pessaries regularly for one year is an equivalent dose to just one 1mg of oestradiol HRT tablet.

Formulation	Administration	Frequency of administration	Advantages	Disadvantages
Pessaries containing oestradiol: Vagifem (10mcg) and Vagirux (10mcg)	Inserted into the vagina using an applicator.	Daily for first two weeks and then twice weekly. Can be used more frequently as dose is so low.	When used at nighttime, can stay in place for several hours. Vagirux more environmentally friendly as box contains one reusable applicator.	Vagifem less environmentally friendly. Low dose, so often needs to be used more frequently.
Pessary containing oestriol: Imvaggis (30mcg)	Inserted into the vagina using fingers.	Daily for first three weeks, then twice a week. Can be used more frequently as dose is so low.	No applicator.	Can result in a waxy discharge. Can damage latex condoms.
Pessary containing DHEA: Intrarosa* (active ingredient Prasterone, 6.5mg, converts intracellularly to androgens and oestrogens)	Inserted into the vagina with or without an applicator.	One pessary daily.	Easy to use.	Can damage latex in barrier contraceptives.
Creams: Ovestin (500mcg)	Inserted into the vagina with an applicator. Can also be applied to external genitalia.	Daily for two weeks then twice weekly. Can be used more frequently as dose is so low.	Useful for vulval itching or soreness.	Can be messy.
0.01% oestriol (500mcg)	Inserted into the vagina with an applicator.	Daily until symptoms improve and twice weekly thereafter.	Some women find it less irritating than Ovestin.	More dilute so large volume needed. Contains peanut oil, avoid if allergy.
Gel: Blissel (50mcg)	Inserted into the vagina with an applicator.	Daily for first three weeks and twice a week thereafter.	Lower dose option.	
Ring Estring (oestradiol), a soft flexible silicone ring	Inserted into the vagina by woman or by health professional if preferred.	Needs replacing every 90 days.	Doesn't require daily application and no discharge (as sometimes with pessaries or creams). Slightly stronger than Vagifem pessary. Can be removed for sex if preferred.	

Figure 2: Localised hormonal treatment options

*Intrarosa is a pessary treatment for vulval and vaginal atrophy in post-menopausal women having moderate to severe symptoms. Prasterone is the active ingredient which is identical to DHEA (dehydroepiandrosterone). This is administered locally in the vagina and is converted intracellularly to androgens and oestrogens. It has been demonstrated in clinical trials to improve dyspareunia, vaginal pH and vaginal epithelium.²¹ Intravaginal DHEA has been shown to be associated with improvements in symptoms without significant changes in serum oestrogen or androgen levels.²²

Further information on vaginal oestrogens

- Women should be reassured regarding the inaccuracy of the information in the product leaflet inside the vaginal hormonal preparations.
- If symptoms do not improve with vaginal oestrogen, consider increasing the dose, changing preparation (and consider DHEA) or using an additional treatment such as systemic HRT or two local treatments.
- The frequency of using these preparations can be increased in women who have persistent symptoms as the doses of these preparations are very low.
- Women using vaginal oestrogen – even in the long term – do not need to take progestogens or progesterone or have their endometrial thickness measured.
- Vaginal oestrogens can often improve urinary symptoms, including urinary infections.
- The beneficial effect of localised oestrogens can take a few months.
- For the majority of women, symptoms return after treatment is stopped. There is usually no need to stop treatment.
- Following the initial review after three months, local oestrogen can be put on a repeat prescription, as women need to use these preparations for ever.
- Consideration of local oestrogen therapy should be considered as part of the management of prolapse. It can also often alleviate symptoms of pressure from a prolapse.
- Urinary symptoms including recurrent UTIs can improve with vaginal oestrogen use.
- As there is some evidence of increase in level of serum oestradiol level in male partners of vaginal oestrogen users, it is advised to avoid sexual contact until at least a few hours after application.

Non-hormonal treatments

Vaginal moisturisers and lubricants should be considered for use in women with GSM, either on their own or alongside hormonal treatments. Vaginal moisturisers used on a regular basis offer relief from symptoms of vaginal dryness, whereas vaginal lubricants are intended for use with sexual or any penetrative activity, including pelvic examination and cervical screening.

YES, Sylk and Regelle are often available on prescription and are less likely to cause irritation, compared to some of the other over-the-counter preparations.²³

Although these preparations do not restore normal vaginal physiology, they are suitable for women who choose a non-hormonal solution for personal or medical reasons.¹⁵ They can be used in addition to local vaginal oestrogen preparations.

Women should be advised that oil-based lubricants can negatively impact condom integrity.²⁴

Vaginal moisturisers:

- are bio-adhesive and attach to mucin and epithelial cells on the vaginal wall, therefore retaining water
- can balance vaginal pH
- should be used regularly and can be used in the long term if they are beneficial
- often help with vulval sensitivity when used regularly
- can be used more or less frequently depending on the severity of the woman's dryness

- should be used regularly rather than using only for sexual intercourse
- can be used in combination with local oestrogen but preferably used at different times

Vaginal lubricants:

- come in a wide variety and are commercially available either as a water-, silicone-, mineral oil-, or plant oil-based product
- are applied to the vagina and vulva (and the partner's penis if required) prior to sex
- provide short-term relief for vaginal dryness and can prevent friction during sexual intercourse
- are particularly beneficial for women whose vaginal dryness is a concern only, or mainly, during sexual intercourse or for those who experience post-coital cystitis
- can also be used in combination with local oestrogen but preferably at different times, as some products may prevent the dispersion of the oestrogen pessary

Other treatments

There is increasing evidence to demonstrate the benefits of the oral medication, **ospemifene**, which is an oestrogen agonist/antagonist.²⁵ It does not appear to have any negative effects on the endometrium or be associated with an increased risk of thromboembolism. The commonest side effect is hot flushes, which are usually transient.

There have been numerous studies using **laser treatment** to increase thickness of the squamous epithelium and improve vascularity of the vagina. Advocates of the carbon dioxide laser²⁶ or the infrared/Erbium laser²⁷ propose this treatment for the improvement of sexual function, vaginal tightening, vaginal dryness and stress incontinence.

Although some early studies are promising, long term efficacy and safety of this procedure are still lacking. Laser treatment is not available on the NHS.

Advice to women

Perfumes, powders, soaps, deodorants, panty liners, spermicides and many brands of lubricants often contain irritant compounds and women should be advised about this. In addition, tight-fitting clothing and long-term use of sanitary pads or synthetic materials can worsen symptoms.

Women should be advised to avoid using intimate washes or intimate products and use a simple emollient to wash with, such as CetraBen.

Breast cancer and GSM

Breast cancer and GSM

Breast cancer is the second most common cause of cancer in women. In the UK, breast cancer survival has doubled over the past 40 years. Around 76% of women in UK survive breast cancer for 10 or more years.²⁸

As the vagina is highly regulated by oestrogen, cancer treatments that result in oestrogen depletion frequently cause unwanted effects on the vagina. This can result in vaginal dryness and discomfort, pain associated with intercourse, and increased susceptibility to infections – all of which may impair enjoyment of sexual intimacy.²⁹ Such symptoms can negatively affect other daily activities too, including sitting, walking, and wearing certain clothing or underwear.

Due to treatments such as surgery, chemotherapy, radiation, and hormonal therapy, women may experience an early menopause, and this can result in earlier and more severe GSM symptoms.³⁰

Non-hormonal approaches are usually the first-line choice for managing urogenital symptoms (or related urinary symptoms) experienced by women during or after treatment for an oestrogen-receptor-positive breast cancer.¹²

Oestrogen-receptor-positive breast cancer

Following an oestrogen-receptor-negative breast cancer, women can usually be given local vaginal oestrogen to improve their symptoms related to GSM.³¹

For the treatment of severe GSM symptoms, there are no specific data on the safety of local vaginal oestrogen after oestrogen-receptor-positive breast cancer. However, after regeneration and cornification of the vaginal skin, increased systemic levels of oestrogen are not seen and they remain below postmenopausal levels.²⁰ Such local oestrogen-only therapy, even long term – if associated with improved quality of life and sexual function – will seem a reasonable theoretical and unproven small risk to many informed breast cancer patients.²⁰

***Women with a history of any type of cancer – including oestrogen-receptor-positive cancer – should use vaginal oestrogen if required and if beneficial; they should continue using this in the long term.*³²**

The evidence does not show an increased risk of cancer recurrence among women using vaginal oestrogen who are undergoing treatment for, or have a history of, an oestrogen-receptor-positive cancer.^{32,33}

Aromatase inhibitors

There is controversial data (mainly due to small sample sizes) reporting on the safety and efficacy of using vaginal oestrogen to treat urogenital symptoms in patients taking aromatase inhibitors.³⁴

A recent meta-analysis, however, showed that vaginal oestrogen administration in postmenopausal women with a history of breast cancer is not associated with systemic absorption of sex hormones. This study therefore provides indirect evidence for the safety of their use in women taking aromatase inhibitors.³⁵

The use of vaginal oestrogens for women taking aromatase inhibitors is therefore not absolutely contraindicated and women may often benefit from their use when non-hormonal treatments have not provided adequate benefit.

In addition, the vaginal oestrogen preparation, Estring, has not been shown to cause persistent elevations in serum oestradiol levels and this might be a safer option for women who have had an oestrogen-receptor-positive breast cancer who are experiencing significant urogenital symptoms requiring localised oestrogen therapy.³⁴

Alternatively, some women may benefit from changing their aromatase inhibitor to tamoxifen and then considering use of vaginal oestrogen with tamoxifen, to improve their symptoms related to GSM.³⁶ The decision to do this needs to be made in conjunction with the patient's breast specialist.

DHEA pessaries

One randomised study has shown that DHEA pessaries can improve both the severity of vaginal symptoms of pain or dryness and also significantly improve sexual health measures (including arousal, lubrication and satisfaction) in women with a history of breast cancer.³⁷

Shared decision making with women with a history of breast cancer

***As the risks of vaginal oestrogen in women with a history of breast cancer are either absent or negligible, GPs and primary care healthcare professionals can usually prescribe vaginal oestrogen preparations to these women, after sharing the available evidence with them and discussing benefits as well as any potential risks.*³⁰**

The GMC Decision Making and Consent guidance is very clear that women can decide on treatment, even if risks are involved, as long as they understand the potential risks of that treatment.³⁸

There are some women with a previous history of an oestrogen-receptor-positive cancer who choose to take systemic HRT to improve their menopausal symptoms and also to improve their future cardiovascular, bone and brain health.³⁹ This decision should be undertaken jointly with the patient and most often a menopause specialist.

Review after starting treatment for all women with GSM

Women should be reviewed around three months after starting treatment. Compliance and any concerns about treatment should be addressed in their appointment. Consideration about systemic HRT should be given if the patient is not already taking HRT. If she is already taking HRT, the dose or type may need to be altered if the patient is still having menopausal symptoms (including symptoms related to GSM).

If a patient has not responded to initial localised treatment, the dose and type of treatment may need adjusting. It may be worth altering the frequency of vaginal oestrogen doses, changing the brand or formulation, and combining treatments, including adding non-hormonal lubricants and moisturisers.

If the above alterations bring no improvement to symptoms, an alternative diagnosis should be considered depending on the individual case and appropriate examination. Further investigation and referral should then be undertaken.

Any woman who experiences abnormal vaginal bleeding needs to be investigated and referred according to local guidelines.

After the three-month review, women should be reviewed annually. Their symptoms should be reassessed, and treatment may need to be changed if new symptoms occur or previous symptoms reoccur. Some women find a combination of treatments preferable; for example, using vaginal oestrogen tablets (Vagifem or Vagirux) in combination with an oestriol cream such as Ovestin, to use externally on the vulval area.

Some women use vaginal oestrogen preparations more frequently than the recommended dose to improve symptoms sufficiently, for example, using Vagifem alternate days instead of twice a week. It is safe to use the treatment in this way as the dose is very low.

Women should be reassured that it is safe for topical oestrogen to continue in the long term (medication should be on a repeat prescription). Women should continue to be reassured about the long-term safety of vaginal oestrogen preparations.

All women taking HRT should be asked about any possible symptoms related to GSM as part of routine questioning and localised treatment should be given, as appropriate, for these women.

It is imperative that women are able to access appropriate support and be given the most up-to-date and evidence-based information regarding their GSM treatment options, in order for them to make an informed choice.

Summary

The majority of postmenopausal women experience symptoms related to GSM.

Only a small minority of women with GSM receive treatment.

Too many women do not talk about their symptoms.

Treatment is safe, cost effective and usually works very well.

Oestrogen deficiency can also lead to urinary symptoms.

Vaginal oestrogens can be used safely in the long term.

A combination of different treatments can be given.

Women can receive systemic and local oestrogen concomitantly.

Some lubricants and moisturisers are available on prescription.

Women should be reassured regarding the inaccuracy of the information packaged with vaginal hormonal preparations.

Women with a history of breast cancer can usually be given vaginal oestrogen preparations.

Useful Resources for Women

'Me and My Menopausal Vagina' by Jane Lewis, PAL books (2018).

www.menopausedoctor.co.uk

<https://patient.info/womens-health/menopause/vaginal-dryness-atrophic-vaginitis>

<https://www.nhs.uk/conditions/vaginal-dryness/>

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