NHS Greater Glasgow and Clyde

CLINICAL GUIDELINE

Hot Flushes Treatment - Pharmacological alternatives to Hormone Replacement Therapy (HRT), Gynaecology

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Title: Treating Hot flushes – Pharmacological alternatives to Hormone Replacement Therapy (HRT) (1116)

Objectives: To provide the audience with information on pharmacological alternatives to HRT for the control of vasomotor symptoms associated with the menopause.

Scope: Women wishing to explore pharmacological alternatives to HRT

Audience: All healthcare professionals within GGC who have a role in the care of women experiencing menopausal symptoms.

Body of Guideline:

There are many reasons why women prefer not to take hormone replacement therapy (HRT). This may because they wish to deal with symptoms without hormonal medication, or that they feel the symptoms are not severe enough to justify treatment. In some cases however, HRT is not recommended due to a history of a hormone dependent cancer. In these situations, there are some alternatives that can be tried to help reduce the symptoms and allow the woman to cope through the menopause transition.

The medications listed here are primarily for the treatment of vasomotor symptoms.

What non-hormonal medicines are used to reduce hot flushes?

The non-hormonal medicines used to reduce hot flushes in women include clonidine, venlafaxine (SNRI), selective serotonin reuptake inhibitors (SSRIs), gabapentin, or oxybutynin. The treatment option depends on the individual patient and their wishes.

Clonidine

Clonidine is an alpha-adrenergic agonist, used to treat high blood pressure and prevent migraine headache. It is also a non-hormonal medicine that has been shown to be effective in reducing menopausal hot flushes. It is currently the only licenced option for control of vasomotor symptoms.

What is the usual dosage?

Start the dose at 25micrograms (mcg) twice a day. This can be increased up to a maximum of 75 micrograms bd or 50mcgs tds. Doses greater than 75mcg bd have not shown any additional benefit in the control of hot flushes.

How long does it take to work?

If after two to four weeks at maximum dose, there is no noticeable benefit, treatment should be stopped by tapering the dose gradually to avoid rebound hypertension. The length of treatment depends on the response. Reviews should take place annually in Primary Care.

What are the side effects?

Clonidine can interact with other anti-hypertensives, and is not suitable for patient with baseline low blood pressure. Other side effects include constipation, dry mouth, drowsiness and difficulty in sleeping.

Venlafaxine (SNRI)

A serotonin and noradrenaline reuptake inhibitor (SNRI). It is has been shown to be effective in reducing menopausal hot flushes, with a decrease of up to 60% after 8 weeks of treatment with venlafaxine.

What is the usual dosage?

Venlafaxine should be started at 37.5mg Sustained Release (SR) tablets as a single daily dose. The dose can be increased every four to seven days to a maximum of 150mg SR daily, as doses above this level do not confer additional benefit.

Venlafaxine should be taken with food once a day, preferably at the same time each day. Some women prefer to take this at night if day time side effects are problematic. Food may lessen any feelings of nauea that the medicine may cause. Do not divide, crush, chew or place capsules in water.

How long does it take to work?

Symptom relief usually occurs within the first week. Review should take place by 3 months as to success and continuation of medication.

What are the side effects?

Side effects of venlafaxine include dry mouth, nausea, constipation, sleeplessness, sexual dysfunction and weight changes. Side effects are more common with higher doses.

Selective serotonin reuptake inhibitors (SSRIs)

SSRIs are used in the treatment of depression. They have also been found to be effective in reducing menopausal hot flushes. Fluoxetine, Citalopram, Paroxetine are commonly prescribed SSRIs for hot flushes.

What is the usual dosage?

Citalopram - start at 10mg daily for one week, and then increase to 20mg daily if needed. Citalopram may be taken with or without food, once a day, preferably at the same time each day.

Fluoxetine - started at 10mg daily for one week, and then increase to 20mg daily if needed. Fluoxetine may be taken with or without food, once a day, preferably at the same time each day.

Paroxetine - started at 10mg daily as this is the dose with best evidence for vaso-motor control. However, an increase to 20mg daily can be considered if low mood is associated with menopausal symptoms. Paroxetine should be taken with food once a day, preferably in the morning at the same time each day.

How long does it take to work?

SSRIs may take six to eight weeks to have the full effects for depression, however, reduction in hot flushes is often seen within 2 weeks. If after four to six weeks there is no benefit, treatment should be stopped. Treatment should also be stopped if the woman develops significant side effects. When SSRIs are to be discontinued, gradually reduce the dose over two weeks to minimise side effects.

What are the side effects?

Side effects of SSRIs include nausea, drowsiness, tremor, weight changes, and sexual dysfunction. Side effects are more common with higher doses.

NOTE: Women taking Tamoxifen should not be prescribed Paroxetine or Fluoxetine as they interact with enzyme cytochrome P450 (CYN10) thereby rendering Tamoxifen less effective.

Gabapentin

Gabapentin is usually used to control epilepsy, neuropathic pain and migraine. It is also a non-hormonal medicine that has been shown to be effective in reducing menopausal hot flushes. Gabapentin appears to be comparable with low dose oestrogen in reducing the frequency and severity of hot flushes. It may also improve quality of sleep. At the dose of 900mg daily, it can lead to a reduction in hot flushes by about 50%.

What is the usual dosage?

The starting dose is 100mg three times a day. The dose can be increased as tolerated every 2-3 days to a maximum of 300mg three times daily.

If night sweats and sleep are troublesome, a single 300mg dose at night can be helpful.

How long does it take to work?

Use of 900mg daily has been found to be effective in reducing menopausal hot flushes for at least 12 weeks when compared to placebo treatment. If no improvement after 1 month of treatment at 900mg a day, consider alternative therapy. When stopping Gabapentin, care must be taken by titrating dose down over a few weeks.

What are the side effects?

Side effects include dry mouth, drowsiness, forgetfulness, light-headedness and dizziness.

Pregabalin

Pregablin is similar to Gabapentin with its effect on menopausal vaso-motor symptoms. Pregablin is more expensive than Gabpentin, with a potentially better side effect profile.

What is the usual dosage?

The starting dose is 25mg twice a day. The dose can be increased weekly until symptoms are controlled. The effective dose is 50-300mg daily in 2 divided doses.

If ineffective after 1 month of maximum therapy, stop by titrating dose down over a few weeks.

What are the side effects?

Side effects are similar to Gabapentin, but less marked and therefore better tolerated.

Cautions Gabapentin and Pregablin are Controlled Drugs and only one month of treatment will be dispensed at a time which may be a consideration for women if travelling out of the country Can affect ability to drive of use machinery due to central nervous system side effects.

Oxybutynin

Oxybutynin is an anticholinergic drug used in the treatment of overactive bladder. Decreased sweating is a common side effect of oxybutynin, which has led to its successful use in the treatment of generalized hyperhidrosis. It has also been found to be effective in the treatment of menopausal vasomotor symptoms when compared with placebo.

What is the usual dosage?

Immediate release tablets should be used, starting at 2.5mg twice per day, and increased to 5mg twice per day if required.

What are the side effects?

Treatment-related side-effects include dry mouth, difficulty urinating, and abdominal pain. Importantly, anticholinergic drugs can induce cognitive impairment.

Fezolinetant (Veoza)

Fezolinetant is a non-hormonal selective neurokinin 3 receptor antagonist. It works centrally to modulate neuronal activity in the thermoregulatory centre of the hypothalamus.

What is the usual dosage?

45mg once daily for moderate to severe hot flushes associated with the menopause.

Side effects and cautions

Side effects include abdominal pain, diarrhoea and insomnia. Rarely severe drug induced liver injury can occur and liver function should be obtained prior to commencing therapy and monthly for 3 months (see BNF for schedule).

This medication is not currently approved by SMC. Therefore, prescription is limited to initiation by tertiary menopause specialists only and requires additional approval prior to prescription. Please contact specialist pharmacist for advice on approval process. GGC Medicines: Non-Formulary Information

Changing Treatments

If switching from one treatment to another, there may need to be gradual tapering of the medicine.

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14. Fezolinetant | Drugs | BNF | NICE

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