SERMs – their role in menopause management

SERMs is "shorthand" for a class of drug called selective oestrogen receptor modulators. They are a versatile group of drugs that can be used to treat/ prevent a number of conditions such as osteoporosis, infertility and hormone responsive cancers. Within the SERM class, different compounds have differing agonist or antagonist effects at the oestrogen receptor in different tissues, therefore they are "selective" (1, 2).

Different kinds of SERMS

- Naturally occurring SERMs include plant-derived oestrogens or **phyto-oestrogens** that are sometimes used to treat symptoms of menopause (see AMS Information Sheet *Complementary and Herbal Therapies for Hot Flushes*).
- **Clomiphene citrate** is an early SERM which is used to induce ovulation in women desiring pregnancy because it acts as an oestrogen antagonist at the pituitary and increases gonadotrophin drive to the ovary.
- **Tamoxifen** is another SERM which is taken to reduce the risk of recurrent breast cancer and to prevent the development of breast cancer in women at increased risk of breast cancer. It acts as an anti-oestrogen to reduce oestrogen stimulation in the breast but as an oestrogen agonist in other parts of the body. It improves bone density but increases the risk of endometrial cancer and also of deep vein thrombosis (DVT). In women who have had breast cancer this risk is outweighed by the benefits of reduction in risk of recurrent breast cancer.
- Newer SERMs are being developed with more favourable oestrogen receptor selectivity i.e. utilizing the positive effects of oestrogen such as preventing osteoporosis and treating genital atrophy (vaginal dryness), without stimulating breast cancer cells or inducing endometrial hyperplasia. These agents aim to minimise the negative effects of the older agents. Raloxifene is already available in both Australia and New Zealand. Bazedoxifene and ospemifene are available in the USA and in some parts of Europe. A combination product with conjugated equine oestrogens and bazedoxefine is available in Australia and New Zealand (3).

  Raloxifene

  - Raloxifene has been shown in clinical trials to increase bone density in the spine and hip and to reduce the risk of spinal fractures in women with osteoporosis (4).
  - Unlike tamoxifen, raloxifene is anti-oestrogenic in the uterus so it does not have an increased risk of endometrial cancer. It is unlikely to cause bleeding or spotting.
  - Raloxifene has been shown to reduce the risk of invasive breast cancer by 70% in women who are taking it for osteoporosis or who are at increased risk of developing breast cancer, with fewer side effects than tamoxifen.
  - Raloxifene lowers serum total and LDL cholesterol but does not affect HDL cholesterol or triglyceride levels.

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Risks and side-effects of raloxifene

- Raloxifene does not improve menopausal symptoms, and may in fact worsen them. Its use is therefore limited to postmenopausal women who do not have troublesome symptoms of menopause. Side-effects include hot flushes, leg cramps and swelling of the legs.
- Raloxifene does not reduce the risk of peripheral fractures.
- Like oral oestrogen, raloxifene slightly increases the risk of DVT, and has been shown to increase the risk of fatal stroke in women with coronary artery disease (CAD) or at high risk of CAD.

Other SERMS

Bazedoxifene

- Bazedoxifene is a third generation SERM and has oestrogen agonist effects on bone but appears to have no effect on the endometrium. Studies to date have not shown changes in breast density or breast tenderness. It is not available as a single agent in Australia and New Zealand.
- Bazedoxifene has been combined with conjugated equine oestrogens in what is referred to as a tissue selective oestrogen complex (TSEC) with the trade name Duavive™. It is used to prevent osteoporosis and treat menopausal symptoms without the need for a progestogen, in women with a uterus and at least 12 months since last menses. In clinical trials, Duavive was more effective than placebo but less effective when compared with menopausal hormone therapy (MHT) (conjugated equine oestrogen+ medroxyprogesterone acetate) for menopausal symptoms and bone density (5). However, Duavive was associated with less breast tenderness and less vaginal bleeding than the MHT. The most common side effects observed in the clinical trials of patients receiving Duavive v placebo were abdominal pain, nausea, diarrhoea, constipation, muscle spasms, vulvo-vaginal candidiasis and an increase in triglycerides (5).

Ospemifene

- Ospemifene is an oestrogen agonist in the vaginal epithelium and is used to treat dyspareunia. It is taken as a tablet once daily. The most common side effects include flushes, sweats and muscle cramps (6).

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References

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