Drug Safety Update

NHS Lancashire and South Cumbria Integrated Care Board

Medicines Matters

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Incretin-based therapies (GLP-1 receptor agonists) and Hormone Replacement Therapy (HRT)

The British Menopause Society (BMS) has developed a useful "Tool for clinicians" which can be accessed here.

This seeks to clarify some of the considerations which should be taken when prescribing incretin-based therapies in women using HRT. It focuses on semaglutide and tirzepatide but the general principles apply broadly to products from these classes of incretin-based therapies.

General guidance from the British Menopause Society (BMS):

- **Incretin-based therapies delay gastric emptying** and therefore may **reduce the absorption of any oral component of HRT.**
- If treatment with incretin-based therapies is proposed in a woman using oral oestrogen-based HRT, consideration should be given to switching to transdermal-oestrogen based HRT.
- There is very little data on the interaction between incretin-based therapies and progestogens used in HRT; transdermal or vaginal routes are unlikely to interact, but incretin-based therapies delay gastric emptying and may therefore reduce absorption of oral progestogens.
- Switching to a non-oral progestogen (combined patch or levonorgestrel intrauterine device (LNG-IUD)) would be preferable in patients taking incretin-based therapies.
- Where oral progestogen is preferred by patients on HRT, there is no data to inform the dose adjustment required for endometrial protection in high-risk women, including those treated with incretin-based therapies. A potential approach is to temporarily increase the dose of oral progestogen for 4 weeks after commencing incretin-based therapies, and maintain a higher dose of progestogen with each dose increment on incretin-based therapy until a stable dose is achieved. This is based on extrapolation from combined oral contraceptive (COC) data and intuitive expert opinion. Uncertainty should be shared with the patient to aid informed decision making.
- In the presence of unscheduled bleeding in women using HRT and incretin-based therapies, national consensus guidance should be followed.

Recommendations for primary care prescribers:

Run a search for all women who are taking an oral oestrogen and/or oral progestogen (consider sending all of this cohort a text to advise that if they are using a GLP-1 agonist but have not informed the practice, that they should come for a HRT review) check their notes for GLP-1 letters and contact those who are using a GLP-1 to arrange a review. Searches can be accessed from your Medicines Optimisation Pharmacist/Pharmacy Technician.

At the review:

a. Inform the patient of the potential interaction and the impact this could have.

b. If the patient is using oral oestrogen-based HRT consider changing to a transdermal-oestrogen based HRT.

c. If the patient is using oral progestogen, consider switching to a non-oral method (LNG-IUD/combined patch) in line with BMS guidance.

d. If the patient insists on staying on an oral progestogen, increase the dose and share the uncertainty about what the correct dose increase might be and whether increasing the dose is enough to ensure safety.

e. Remind the patient to promptly report any unscheduled bleeding.

Care should be taken to assess for all factors affecting endometrial risk.

Additional information can be found from the Primary Care Women's Health Society website.