# Clinical Pharmacology & Toxicology Pearl of the Week

~ Semaglutide for Weight Loss ~

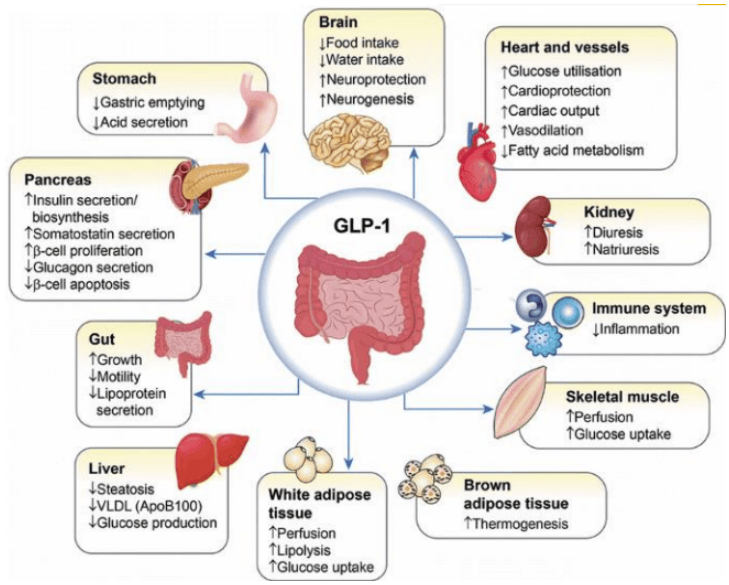
**Background**

- ✓ Obesity chronic disease is an increasingly challenging public health issue. The condition is associated with multiple adverse conditions including hypertension, type 2 diabetes, cardiovascular disease and nonalcoholic fatty liver disease.

- ✓ Clinical guidelines suggest adjunct of pharmacotherapy along with lifestyle interventions in patients with BMI of 30 or greater, or 27 or greater in persons with coexisting obesity related conditions.

- ✓ Semaglutide belongs to the class of medications called gut-derived glucagon-like-peptide-1 (GLP-1), which act on the incretin hormone system. These hormones are released after nutrient intake. The effect is to increase glucose-dependent insulin secretion, decrease inappropriate glucagon secretion, slow gastric emptying, and act on area of the brain that is involved in regulation of appetite.

- ✓ Behavioral intervention incorporating modifications in diet and physical activity remains the foundation of treatment for overweight and obesity.

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**Dosage**

- ✓ Dosage forms include oral and subcutaneous options, with studies in obesity being performed with the subcutaneous form. A slow up titration of the medication is advised to mitigate side effects. The first week through the fourth week is dosed at 0.25 mg once weekly, week 5 through week 8 at 0.5 mg once weekly, week 9 through week 12 at 1 mg once weekly, week 13 through week 16 at 1.7 mg once weekly, week 17 and thereafter (maintenance dosage): 2.4 mg once weekly.

**Evidence**

- ✓ The STEP 1 trial was a phase 3 trial that evaluated the use of a semaglutide dose of 2.4 mg once week in obese patients. The primary end point was percentage change in body weight over a 68-week period. It was found that at 68 weeks a -14.9% reduction in weight was found with semaglutide as compared to -2.4% with placebo. The change in body weight from baseline to week 68 was −15.3 kg in the semaglutide group as compared with −2.6 kg in the placebo group.

- ✓ The STEP 2 trial had 1210 patients with type 2 diabetes and obesity with the intervention being 1.2 mg versus 2.4 mg. Average bodyweight reductions were 9.64%, 6.99%, and 3.42% with semaglutide 2.4 mg, 1.0 mg, and placebo, respectively.

  The STEP 5 trial examined the efficacy and safety of semaglutide 2.4 versus placebo over a longer time period of 104 weeks in 304 participants. The mean change in body weight from baseline to week 104 was −15.2% in the semaglutide group versus −2.6% with placebo.

**Adverse Effects**

- ✓ The most common side effects of semaglutide are gastrointestinal in nature, namely nausea, diarrhea, vomiting and constipation. In STEP 5 GI side effects were found to happen in 82.2% of patients. However, for the most part, they were mild to moderate in nature and led to treatment discontinuation in only 3.9% of patients.

- ✓ In rodents, semaglutide causes dose dependent and treatment duration dependent thyroid C-cell tumors. It is currently unknown if the effect occurs in humans, but the medication is contraindicated in patients with a personal or family history of medullary thyroid cancer or in patients with Multiple Endocrine Neoplasia syndrome type 2.

**References**

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**The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Clinical Pharmacology consultations are also available through Netcare e-referral process and through Calgary Zone Specialist Link. Click HERE for more details.**

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