

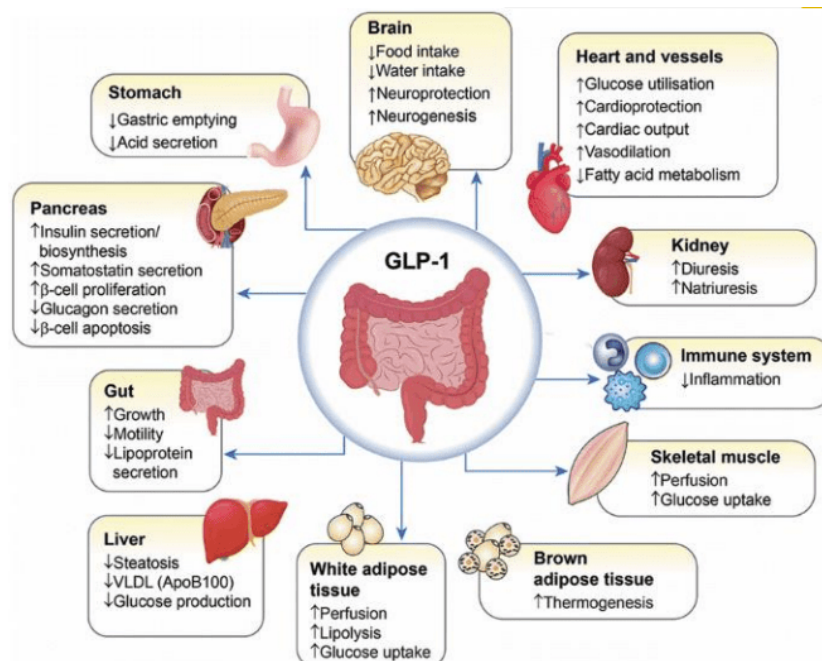


Clinical Pharmacology & Toxicology Pearl of the Week

~ Semaglutide for Weight Loss ~

Background

- ✓ Obesity 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 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.



Kalra S, Das AK, Sahay RK, Baruah MP, Tiwaskar M, Das S, Chatterjee S, Saboo B, Bantwal G, Bhattacharya S, Priya G. Consensus recommendations on GLP-1 RA use in the management of type 2 diabetes mellitus: South Asian task force. Diabetes Therapy. 2019 Oct;10:1645-717.

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

Wilding JP, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, McGowan BM, Rosenstock J, Tran MT, Wadden TA, Wharton S. Once weekly semaglutide in adults with overweight or obesity. *New England Journal of Medicine*. 2021 Feb 10.

Davies M, Færch L, Jeppesen OK, Pakseresht A, Pedersen SD, Perreault L, Rosenstock J, Shimomura I, Viljoen A, Wadden TA, Lingvay I. Semaglutide 2· 4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. *The Lancet*. 2021 Mar 13;397(10278):971-84.

Garvey WT, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, Jódar E, Kandler K, Rigas G, Wadden TA, Wharton S. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. *Nature Medicine*. 2022 Oct;28(10):2083-91.

Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes–state-of-the-art. *Molecular metabolism*. 2021 Apr 1;46:101102.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching “Toxicology” from the ARD home page.

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Created: April 12, 2023

Reviewed: March 11, 2025