Wegovy (semaglutide)

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Introduction

- **Brand name:** Wegovy
- **Generic name:** Semaglutide
- **Pharmacologic class:** Glucagon-like peptide-1 (GLP-1) receptor agonist
- **Strength and Formulation:** 0.25mg/0.5mL, 0.5mg/0.5mL, 1mg/0.5mL, 1.7mg/0.75mL, 2.4mg/0.75mL; per pen-injector; soln for SC inj
- **Manufacturer:** Novo Nordisk
- **How supplied:** Single-dose prefilled pens—4
- **Legal Classification:** Rx

Indication

- As an adjunct to a reduced calorie diet and increased physical activity for **chronic weight management** in adults with an initial BMI of ≥30kg/m^2 (obese) or ≥27kg/m^2 (overweight) in the presence of at least 1 weight-related comorbid condition (eg, hypertension, type 2 diabetes mellitus, dyslipidemia).

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Limitations of Use

- Do not use with other semaglutide-containing products or with any other GLP-1 receptor agonists.
- Safety and efficacy have not been established with other products intended for weight loss (eg, prescription drugs, OTC drugs, herbal preparations).
- Not studied in patients with history of pancreatitis.

Dosage and Administration

- Administer Wegovy once weekly, on the same day each week, with or without meals.
  - Administer by subcutaneous (SC) injection in the abdomen, thigh, or upper arm. Injection site can be changed without dose adjustment.
- Initially with a dose of 0.25mg SC once-weekly.

Dose Escalation Schedule		
Weeks	**Weekly Dose**	
1 through 4	0.25mg	Dose escalation
5 through 8	0.5mg	
9 through 12	1mg	
13 through 16	1.7mg	
17 and onward	2.4mg	Maintenance dose

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Dosage and Administration

- Consider delaying dose escalation for 4 weeks if increased dose is not tolerated.
- If maintenance dose (2.4mg) is not tolerated, temporarily decrease to 1.7mg once weekly for maximum of 4 weeks.
  - After 4 weeks, increase to 2.4mg once weekly.
  - If not tolerated, discontinue Wegovy.

Considerations for Specific Populations

- **Pregnancy:** Potential risks to fetus from exposure during pregnancy.
  - *Pregnancy exposure registry: 800-727-6500*
- **Nursing mothers:** No data on presence of semaglutide in human milk, but was detected in milk of lactating rats at levels 3-12 fold lower than maternal plasma.
- **Pediatrics**: Not established.
- **Geriatrics**: No overall differences in safety or effectiveness observed from younger patients.
- **Renal impairment**: No dose adjustment necessary.
- **Hepatic impairment**: No dose adjustment necessary.

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Contraindications

- History (personal or family) or medullary thyroid carcinoma.
- Multiple endocrine neoplasia syndrome type 2.

Boxed Warning

- Risk of thyroid C-cell tumors
  - In rodents, semaglutide causes thyroid C- cell tumors at clinically relevant exposures.
  - Unknown whether Wegovy causes thyroid C-cell tumors in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Warnings and Precautions

- Risk of thyroid C-cell tumors; inform patient of risk.
- Monitor for acute pancreatitis: discontinue if suspected, and do not restart if confirmed.
- History of pancreatitis.
- Acute gallbladder disease.
- Monitor renal function when initiating or escalating doses, or in renal impairment.
- History of diabetic retinopathy: monitor for progression.
- History of suicidal attempts or ideation: avoid.
  - Monitor for emergence or worsening depression, suicidal thoughts or behavior; discontinue if occurs.

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Warnings and Precautions

- Monitor blood glucose prior to and during treatment in patients with type 2 diabetes (T2DM).
- Monitor heart rate periodically; discontinue if sustained increases.
- History of anaphylaxis or angioedema with other GLP-1 receptor agonists.
- Discontinue if hypersensitivity reactions occur.
- Women and men of reproductive potential should discontinue ≥2 months prior to planned pregnancy.

Drug Interactions

- Increased risk of hypoglycemia with concomitant insulin secretagogues (eg, sulfonylureas) or insulin.
  - May need to lower doses of these.
- May affect absorption of other oral drugs and cause delayed gastric emptying.

Adverse Reactions

- **Most common (≥5%)**: Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with T2DM, flatulence, gastroenteritis, gastroesophageal reflux disease.
- **Others**: Acute kidney injury, retinal disorders, lab abnormalities (eg, increased lipase or amylase), hypersensitivity reactions.

Mechanism of Action

- **Semaglutide** acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.
- GLP-1 is a physiological regulator of appetite and caloric intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation.

Pharmacokinetics

- Semaglutide is extensively bound to plasma albumin (>99%).
- Elimination half-life: ~1 week; present in the circulation for about 5-7 weeks after the last dose of 2.4mg.
- Metabolism: Proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.
- Excretion: Primary routes are via the urine and feces.

Clinical Trials

- Approval was based on data from three 68-week, randomized, double-blind, placebo-controlled trials and one 68-week, randomized, double-blind, placebo withdrawal trial (ClinicalTrials.gov Identifier: NCT03548935, NCT03552757, NCT03611582, NCT03548987), which evaluated the safety and efficacy of Wegovy for chronic weight management (weight loss and management) in conjunction with a reduced calorie deficit.

Clinical Trial

Patient Demographics				
	Study 1	Study 2	Study 3	Study 4
Clinical Trial Identifier	NCT03548935	NCT03552757	NCT03611582	NCT03548987
Patients (n.)	1961	807	611	902
Mean age (yrs)	46 (18-86)	55 (19-84)	46	46
Women (%)	74.1	50.9	81.0	79
White (%)	75.1	62.1	76.1	83.7
Asian (%)	13.3	26.2	19.0	2.4
Black (%)	5.7	8.3	1.8	13
Hispanic (%)	12.0	12.8	19.8	7.8
Mean baseline body weight (kg)	105.3	99.8	105.8	96.1
Mean baseline BMI (kg/m^2)	37.9	35.7	38.0	34.4

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Clinical Trial

- Primary efficacy parameter
  - Studies 1, 2, 3: mean percent change in body weight and percentage of patients achieving ≥5% weight loss from baseline to week 68.
  - Study 4: mean percent change in body weight from randomization (week 20) to week 68.
- After 68 weeks, treatment with Wegovy resulted in statistically significant reduction in body weight compared with placebo in all 4 trials.

Clinical Trial

Primary Efficacy (Study 1, 2, 3)						
	Study 1		Study 2		Study 3	
	Placebo	Wegovy	Placebo	Wegovy	Placebo	Wegovy
Body Weight at baseline (kg)	105.2	105.4	100.5	99.9	103.7	106.9
% of patients losing ≥5% body weight	31.1	83.5	30.2	67.4	47.8	84.8
% change from baseline (LSMean)	-2.4	-14.9	-3.4	-9.6	-5.7	-16.0
% difference from placebo (LSMean) (95% CI)		-12.4 (-13.3, -11.6)		-6.2 (-7.3, -5.2)		-10.3 (-11.8, -8.7)

Primary Efficacy (Study 4)		
	Placebo	Wegovy
Body Weight at baseline (kg)	107.2	
% change from Week 20 at Week 68	6.9	-7.9

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Clinical Trial

- Reduction in body weight was observed with Wegovy irrespective of age, sex, race, ethnicity, BMI at baseline, body weight (kg) at baseline, and level of renal function impairment.

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/wegovy/