Review of Treatment for Diabetes: GLP-1s

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Objectives

- Review criteria for diabetes mellitus type 1 and type 2
- Discuss pharmacological interventions for diabetes mellitus type 1 and type 2.
- Recognize when a child should be referred to endocrinology.

Type 1 vs Type 2 diabetes

- Type 1 diabetes (T1DM)
  - Autoimmune
  - Not enough insulin
  - Often not diagnosed until patient is in DKA (Diabetic Ketoacidosis)
  - Signs and symptoms
- Type 2 diabetes (T2DM)
  - Insulin resistance, body does not respond to insulin effectively
  - Can lead to decreased insulin production
  - Symptoms often less obvious, progress over time

TYPE 1 DIABETES

PROGRESSES IN 3 STAGES

Early-stage (or pre-insulin-dependent) type 1 diabetes is when the attack on beta cells has begun but the body can still make enough insulin to keep blood sugars in a relatively healthy range.

STAGE 1

Early-stage type 1 diabetes

- Beta cell attack begins
- Blood sugars are within a normal range
- **No visible signs or symptoms**

STAGE 2

Early-stage type 1 diabetes

- Beta cell attack continues
- Blood sugars are higher or lower than a normal range
- **No visible signs or symptoms**

STAGE 3*

Insulin-dependent type 1 diabetes

- Body no longer able to make enough or any insulin
- Blood sugars are much higher than normal range
- **Visible signs and symptoms appear, and insulin dependence begins**

*This stage is when type 1 diabetes is typically diagnosed

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Treatment for T1DM

- Insulin
  - basal: long acting
  - Bolus: short acting
- Insulin Pump therapy
- Continuous Glucose monitoring devices

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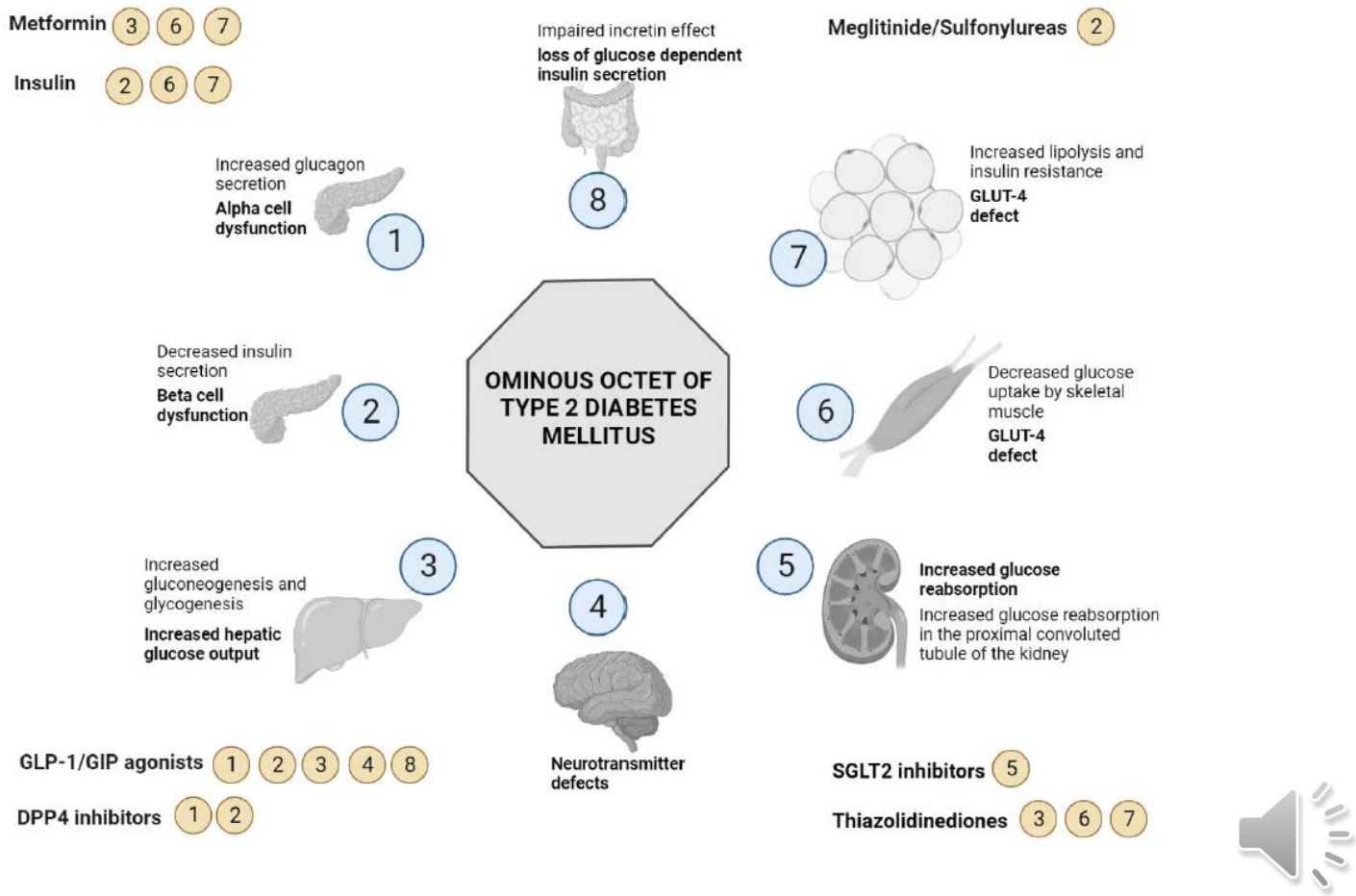
Ominous Octet of Type 2 Diabetes



Goals for management

- Achieve and maintain near normal glycemic control
- Improve insulin sensitivity and potentially improve insulin secretion
- Identify and treat comorbidities
- Prevent vascular complications
- Avoid unplanned pregnancies in young women

Treatment for T2DM

- Oral treatment
  - Metformin
  - Sulfonylureas
  - DPP4 inhibitors
  - SGLT2 inhibitors
- Injectables
  - GLP-1receptor agonists
  - Insulin therapy

Glucagon-like peptide 1 (GLP-1)

- Tells the pancreas to release insulin to keep blood glucose balanced
- Slows down food released from the stomach, decreasing movement of sugar into the blood stream
- Also tells the brain when to reduce food intake (feelings of fullness)

GLP-1 receptor agonists

- Mimic the action of GLP-1 in the body

- Dulaglutide (Trulicity)
- Exenatide (Byetta)
- Liraglutide (Saxenda, Victoza)
- Semaglutide (Ozempic, Wegovy, Rybelsus)

Trulicity

Reduces hepatic glucose production by decreasing glucagon secretion

Slows gastric emptying

Glucose-dependent insulin release

Approved for use in ages 10 years and older

Starting dose is 0.75 mg SQ once weekly

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Byetta

- No longer available due to increased risk of pancreatic cancer

Victoza

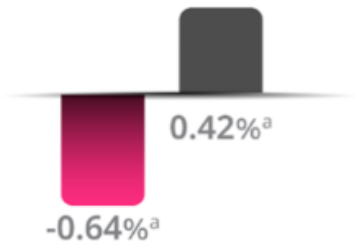
Special populations: Pediatric patients ≥10 years old

Victoza® was superior in reducing A1C from baseline versus placebo at 26 weeks[1]

See study design below

Average adjusted A1C reductions[a]
Victoza® + MET ± basal insulin
ELLIPSE

From mean baseline A1C:
7.7% to 7.9%



Approved for use in pediatric population 10 years of age and older

The change from baseline to end-of-treatment visit in A1C was analyzed using a pattern mixture model with multiple imputation. Missing observations (10.6% in Victoza®, 14.5% in placebo) were imputed from the placebo arm based on multiple (x10,000) imputations. The data for Week 26 were then analyzed with an ANCOVA model containing treatment, sex, and age group as fixed effects and baseline value as covariate.

Overall, the type and severity of adverse reactions in adolescents and children aged 10 years and above were comparable to those observed in the adult population.

In pediatric patients 10 years of age and older, the risk of hypoglycemia was higher with Victoza® regardless of insulin and/or metformin use.

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Ozempic

Ozempic® 0.25-mg or 0.5-mg dose
(2 mg/3 mL subcutaneous pen injector)

NDC: 0169-4181-13

Not approved for use in anyone under age 18 years

Ozempic® 1-mg dose
(4 mg/3 mL subcutaneous pen injector)

NDC: 0169-4130-13

Ozempic® 2-mg dose
(8 mg/3 mL subcutaneous pen injector)

NDC: 0169-4772-12

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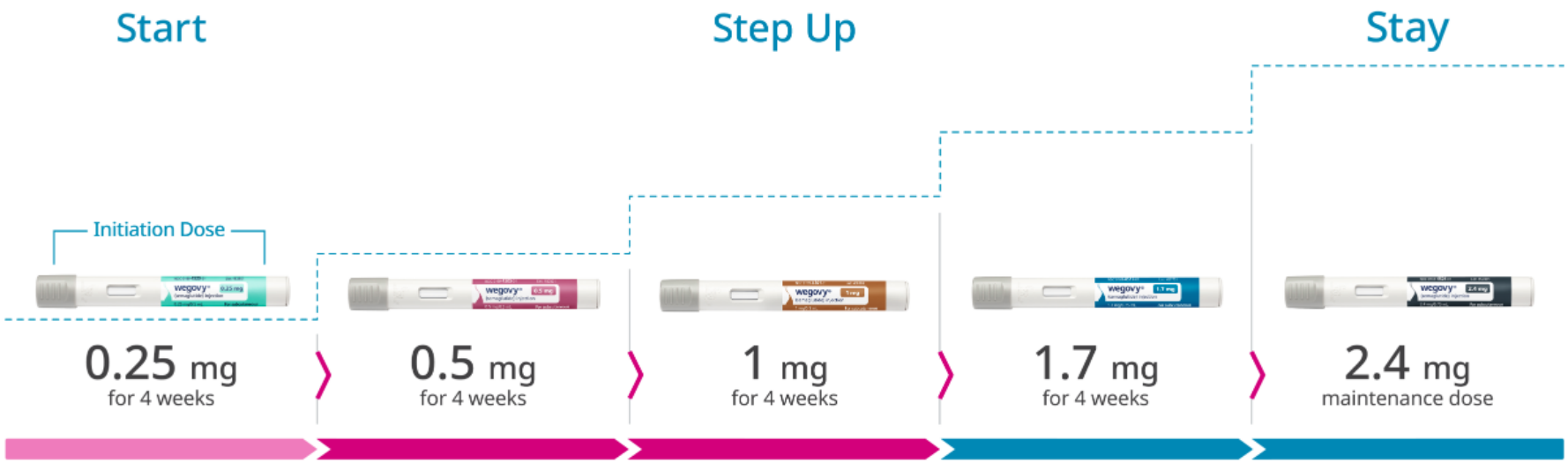
Wegovy

Dosing designed with your patients in mind

Gradual Wegovy® dose escalation gives patients time to adjust to treatment[1]

Adolescent dose-escalation schedule

Start your patients with once-weekly Wegovy® at 0.25 mg and escalate the dose every 4 weeks.



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What to do if adolescent patients...

Need additional time to adjust to Wegovy®[1]:

If patients do not tolerate a dose during dose escalation:

Consider delaying dose escalation for 4 weeks.

If adolescent patients do not tolerate the maintenance 2.4 mg dose:

The maintenance dose can be decreased to 1.7 mg once weekly. Discontinue Wegovy® if the patient cannot tolerate the 1.7 mg dose.

Miss dose(s) of Wegovy®[1]:

Patients miss 1 dose and the next dose is:

>2 days (48 hours): Instruct them to administer Wegovy® as soon as possible.
<2 days (48 hours): Inform them to NOT administer a dose of Wegovy®. Resume dosing on the regularly scheduled day of the week.

Patients miss 2 or more consecutive doses:

Inform them to resume dosing as scheduled. Or if needed, inform them to reinitiate Wegovy® and follow the dose-escalation schedule, which may reduce the occurrence of GI symptoms associated with reinitiation of treatment.

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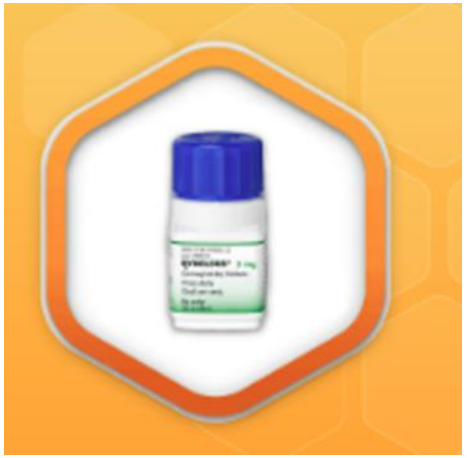
Rybelsus



DAY 1 WHEN PRESCRIBING RYBELSUS®

STARTER DOSE

Patients start RYBELSUS® on a 30-day sample of 3 mg once daily

3 mg (30 DAYS) **HELPS PATIENTS ADJUST TO THERAPY**

- Start RYBELSUS® with 3 mg once daily for 30 days
- This dose is intended for treatment initiation and is not effective for glycemic control

THERAPEUTIC DOSES

Patients should leave your office with a prescription for 7 mg

7 mg **OFFERS GLYCEMIC REDUCTION**

- Increase to 7 mg once daily after 30 days on the 3 mg dose

14 mg **ADDITIONAL GLYCEMIC REDUCTION**

- If additional glycemic reduction is needed, after at least 30 days on the 7 mg dose, the dose may be increased to 14 mg once daily

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Adverse effects

- GI side effects- nausea, vomiting, diarrhea, constipation, abdominal pain, pancreatitis
- Acute kidney injury
- Injection site reactions
- Headaches
- Nasopharyngitis
- Pancreatic and Thyroid Cancer*

Screening and when to refer

Table 2.5—Risk-based screening for type 2 diabetes or prediabetes in asymptomatic children and adolescents in a clinical setting

Screening should be considered in youth* who have overweight (≥85th percentile) or obesity (≥95th percentile) A and who have one or more additional risk factors based on the strength of their association with diabetes:

- Maternal history of diabetes or GDM during the child's gestation A
- Family history of type 2 diabetes in first- or second-degree relative A
- Race and ethnicity (e.g., Native American, African American, Latino, Asian American, Pacific Islander) A
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight) B

GDM, gestational diabetes mellitus. *After the onset of puberty or after 10 years of age, whichever occurs earlier. If tests are normal, repeat testing at a minimum of 3-year intervals (or more frequently if BMI is increasing or risk factor profile is deteriorating) is recommended. Reports of type 2 diabetes before age 10 years exist, and this can be considered with numerous risk factors.

Table 2.2—Criteria defining prediabetes in nonpregnant individuals
A1C 5.7–6.4% (39–47 mmol/mol)
OR
FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG during 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)

For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range. FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; 2-h PG, 2-h plasma glucose.

Prediabetes is a “warning sign” that the individual is headed toward developing T2DM.

Table 2.1—Criteria for the diagnosis of diabetes in nonpregnant individuals
A1C ≥6.5% (≥48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
FPG ≥126 mg/dL (≥7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (≥11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (≥11.1 mmol/L). Random is any time of the day without regard to time since previous meal.

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results obtained at the same time (e.g., A1C and FPG) or at two different time points.

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