

GASTROINTESTINAL TRACT

Core Defect
Decreased incretin effect

ADIPOSE TISSUE

Core Defect
Increased lipolysis

PANCREATIC ALPHA CELL

Core Defect
Increased glucagon secretion

PANCREATIC BETA CELL

Core Defect
Decreased insulin secretion

KIDNEY

Core Defect
Increased glucose reabsorption

CORE DEFECTS IN T2 DIABETES¹

LIVER

Core Defect
Increased hepatic glucose production

MUSCLE

Core Defect
Decreased glucose uptake

BRAIN

Core Defect
Neurotransmitter dysfunction

TREATMENT OPTIONS FOR HYPERGLYCEMIA

| CLASS ^{2*} | PRIMARY PHYSIOLOGICAL ACTION(S) ² | CORE DEFECTS ¹ | | | | | | | | |
|--|--|---------------------------|-----------------------|-------|--------|----------------------|------------|----------------|-------|--|
| | | KIDNEY | PANCREATIC ALPHA CELL | LIVER | MUSCLE | PANCREATIC BETA CELL | G.I. TRACT | ADIPOSE TISSUE | BRAIN | |
| Biguanides | <ul style="list-style-type: none"> • ↓ Hepatic glucose production | | | | | | | | | |
| Sulfonylureas | <ul style="list-style-type: none"> • ↑ Insulin secretion | | | | | | | | | |
| Thiazolidinediones (TZDs) | <ul style="list-style-type: none"> • ↑ Insulin sensitivity | | | | | | | | | |
| DPP-4 Inhibitors (Dipeptidyl Peptidase-4 Inhibitors) | <ul style="list-style-type: none"> • ↑ Insulin secretion (glucose-dependent) • ↓ Glucagon secretion (glucose-dependent) | | | | | | | | | |
| SGLT2 Inhibitors (Sodium-Glucose Cotransporter-2 Inhibitors) | <ul style="list-style-type: none"> • Blocks glucose reabsorption by the kidney, increasing glucosuria | | | | | | | | | |
| GLP-1 Receptor Agonists (Glucagon-Like Peptide-1 Receptor Agonists) | <ul style="list-style-type: none"> • ↑ Insulin secretion (glucose-dependent) • ↓ Glucagon secretion (glucose-dependent) • Slows gastric emptying • ↑ Satiety | | | | | | | | | |
| Insulins | <ul style="list-style-type: none"> • ↑ Glucose disposal • ↓ Hepatic glucose production • Other | | | | | | | | | |

1. DeFronzo, RA. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes*. 2009;58:773-795.

2. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. *Diabetes Care*. 2015;38:140-149.

* This tool is intended to provide an overview of T2DM drugs and is not specific to only one product within the class. It is not intended to make any express or implied comparison among products. Classes shown are from the ADA Guidelines Chart and are not all T2DM classes available to treat hyperglycemia.

ALGORITHM FOR ADDING/INTENSIFYING INSULIN

START BASAL (Long-Acting Insulin)

A1C < 8%

A1C > 8%

TDD 0.1–0.2 U/kg

TDD 0.2–0.3 U/kg

Insulin titration every 2–3 days to reach glycemic goal:

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
 - FBG > 180 mg/dL: add 20% of TDD
 - FBG 140–180 mg/dL: add 10% of TDD
 - FBG 110–139 mg/dL: add 1 unit
- If hypoglycemia, reduce TDD by:
 - BG < 70 mg/dL: 10% – 20%
 - BG < 40 mg/dL: 20% – 40%

Consider discontinuing or reducing sulfonylurea after starting basal insulin (basal analogs preferred to NPH)

*Glycemic Goal:

- <7% for most patients with T2D; fasting and premeal BG < 110 mg/dL; absence of hypoglycemia
- A1C and FBG targets may be adjusted based on patient's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

INTENSIFY (Prandial Control)

Add GLP-1 RA
Or SGLT-2i
Or DPP-4i

Add Prandial Insulin

Basal Plus 1, Plus 2,
Plus 3

Basal Bolus

- Begin prandial insulin before largest meal
- If not at goal, progress to injections before 2 or 3 meals

- Start: 10% of basal dose or 5 units

- Begin prandial insulin before each meal
- 50% Basal / 50% Prandial TDD 0.3–0.5 U/kg

- Start: 50% of TDD in three doses before meals

Glycemic Control Not at Goal*

Insulin titration every 2–3 days to reach glycemic goal:

- Increase prandial dose by 10% or 1–2 units if 2-h postprandial or next premeal glucose consistently > 140 mg/dL
- If hypoglycemia, reduce TDD basal and/or prandial insulin by:
 - BG consistently < 70 mg/dL: 10% – 20%
 - Severe hypoglycemia (requiring assistance from another person) or BG < 40 mg/dL: 20% – 40%

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GLYCEMIC CONTROL ALGORITHM

LIFESTYLE THERAPY (Including Medically Assisted Weight Loss)

Entry A1C < 7.5%

Entry A1C ≥ 7.5%

Entry A1C > 9.0%

MONOTHERAPY*

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ⚠ TZD
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to Dual Therapy

DUAL THERAPY*

- ✓ GLP-1 RA
 - ✓ SGLT-2i
 - ✓ DPP-4i
 - ⚠ TZD
 - ⚠ Basal Insulin
 - ✓ Colesevelam
 - ✓ Bromocriptine QR
 - ✓ AGi
 - ⚠ SU/GLN
- MET**
or other 1st-line agent
- +

If not at goal in 3 months proceed to Triple Therapy

TRIPLE THERAPY*

- ✓ GLP-1 RA
 - ✓ SGLT-2i
 - ⚠ TZD
 - ⚠ Basal insulin
 - ✓ DPP-4i
 - ✓ Colesevelam
 - ✓ Bromocriptine QR
 - ✓ AGi
 - ⚠ SU/GLN
- MET**
or other 1st-line agent + 2nd-line agent
- +

If not at goal in 3 months proceed to or intensify insulin therapy

SYMPTOMS

NO YES

DUAL Therapy

OR

TRIPLE Therapy

INSULIN
±
Other Agents

ADD OR INTENSIFY INSULIN

Refer to Insulin Algorithm

LEGEND

- ✓ Few adverse events and/or possible benefits
- ⚠ Use with caution

* Order of medications represents a suggested hierarchy of usage; length of line reflects strength of recommendation

PROGRESSION OF DISEASE

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