This document describes screening, diagnosis, monitoring and treatment guidelines and therapeutic objectives for adults with diabetes; presents AACE algorithms; and provides detailed pharmacological information. It is designed to assist clinicians by providing a framework for managing diabetes in adults. It is not intended to replace a clinician's independent judgment or to establish a standard of care for all adults with diabetes. The document also establishes the protocols diabetes educators use to adjust diabetes medications with an order from an IU Health physician.
# Table of Contents

- **Adult Diabetes Practice Guidelines** ............................................. 4
- **Prediabetes Practice Guidelines** ............................................. 7
- **Metformin** .............................................................................. 9
- **GLP-1 Receptor Agonists** .................................................... 10
- **DPP4 Inhibitors** .................................................................... 11
- **Alpha-Glucosidase Inhibitors** ............................................. 12
- **SGLT-2 Inhibitors** .................................................................. 13
- **TZD** ....................................................................................... 14
- **Sulfonylureas** ....................................................................... 15
- **Glinides** ............................................................................... 16
- **Colesevelam** ......................................................................... 17
- **Bromocriptine** ...................................................................... 18
- **Pramlintide** ........................................................................... 19
- **Combination Drugs** .............................................................. 20
- **About Insulin** ......................................................................... 21
- **Insulin Types & Actions** ...................................................... 23
- **Intensive Insulin Management** .......................................... 24
- **Basal Insulin** .......................................................................... 25
- **Rapid-Acting Insulin** ............................................................ 26
- **Intermediate-Acting Basal Insulin** ....................................... 27
- **Split Mixed Dose Insulin** ...................................................... 28
- **Analog & Human Insulin Mixtures** ...................................... 29
- **Sources** .................................................................................. 30
- **Abbreviations** ....................................................................... 31
- **AACE Glycemic Control Algorithm** ...................................... 32
- **AACE Profiles of Antidiabetic Medications** ....................... 33
- **AACE Algorithm for Adding/Intensifying Insulin** .......... 34
- **Principles of the AACE Algorithm** ..................................... 35
## Adult Diabetes Practice Guidelines

### Screening — Asymptomatic Adults

**Prediabetes & Type 2**  
For overweight patients with (BMI ≥ 25) with one or more risk factors, test with an A1C, FBG or 2-hr OGT (75g glucose load). Without risk factors, begin testing at age 45 years. Repeat at 3-year intervals with more frequent test depending upon results and risk status.

**Risk Factors**
- Habitual physical inactivity
- First degree relative with diabetes
- Member of high-risk ethnic population — African-, Asian-, Native American; Latino; Pacific Islander
- History of gestational diabetes or delivery of baby > 9 lbs
- Hypertension (≥ 140/90 mmHg) or on therapy for hypertension
- HDL cholesterol ≤ 35 mg/dL &/or fasting triglycerides ≥ 250 mg/dL
- Polycystic ovarian syndrome (PCOS)
- Previously identified impaired fasting glucose (IFG) — FBG 100-125 mg/dL or impaired glucose tolerance (IGT) — 2-hr glucose 140-199 mg/dL
- A1C 5.7-6.4% for those without hemoglobin abnormalities
- Other clinical conditions associated with insulin resistance such as acanthosis nigricans or severe obesity
- History of cardiovascular disease
- Steroid therapy (not an ADA guideline)

**Type 1**  
Consider referring relatives of those with Type 1 diabetes for antibody testing for risk assessment in the setting of a clinical research study [www.diabetestrialnet.org](http://www.diabetestrialnet.org), 1-800-425-8361

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### Diagnosis

**Tests**
- FBG ≥ 126 mg/dL or
- Casual plasma glucose ≥ 200 mg/dL + symptoms or
- 2-hr pp glucose ≥ 200 mg/dL on 75g glucose load or
- A1C ≥6.5%

**Symptoms**

**Type 2**
- Gradual onset; often none
- Can include: UTI; yeast infection; blurred vision; dry, itchy skin; numbness or tingling in extremities; fatigue; polyuria; nocturia; polydipsia; polyphagia; unexplained weight loss

**Type 1**
- Acute onset: polyuria; nocturia; polydipsia; polyphagia; unexplained weight loss; dehydration; acidosis

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### Management

- Consider medications that promote weight loss ([GLP-1 RA, SGLT-2](https://www.diabetestrialnet.org))
- Diabetes education per National Standards for Diabetes Self-Management Education:
  - Describing the diabetes disease process and treatment options
  - Incorporating appropriate nutritional management
  - Incorporating physical activity into lifestyle
  - Utilizing medications (if applicable) for therapeutic effectiveness, consider effect on weight
  - Monitoring blood glucose, urine ketones (when appropriate) and using the results to improve control
  - Preventing, detecting, and treating acute complications
– Preventing (through risk reduction behavior), detecting and treating chronic complications
– Goal setting to promote health and problem solving for daily living
– Integrating psychosocial adjustment to daily life
– Promoting preconception care, management during pregnancy, and gestational diabetes management (if applicable).

### Care Guidelines

#### Weight

**CVD Screen**
Every visit

**Blood Pressure**
Goal: <140/80 mmHg

**Fasting Lipid Profile**
Goals: LDL <100 mg/dL or for CVD <70 mg/dL
Triglycerides <150 mg/dL
HDL >40 mg/dL (men), >50 mg/dL (women)

**AIC**
Goal: individualize; <7% for many non-pregnant adults

**Foot Exam**
Visual inspection each visit. Annual comprehensive exam, including assessment of foot pulses, testing for loss of protective sensation (10g monofilament plus any one of: vibration using 128Hz tuning fork, pinprick sensation, ankle reflexes, or vibration perception threshold). Examine more frequently if medically indicated.

Initial screening for peripheral arterial disease (PAD) including history of claudication and assessment of pedal pulses. Consider ankle-brachial index (ABI).

**Neuropathy Screen**
Annually, using clinical tests listed under foot exam. Screen for distal symmetric polyneuropathy (DPN) starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1.

**Nephropathy Screen**
Annual test to quantitate urine albumin excretion. Initiate at diagnosis of type 2 and at 5 years after diagnosis in type 1.
In patients on diuretics, ACE inhibitors or ARBs, monitor for increased serum creatinine or changes in potassium.

**Retinopathy Screen**
Annually if diabetic retinopathy is present, if planning pregnancy or are pregnant. If no evidence of retinopathy for one or more exams, then every 2 years may be considered. Initiate dilated and comprehensive eye examination at diagnosis of type 2 and within 5 years after diagnosis for type 1.

**Preconception Care**
Annually for all females with childbearing potential ensure use of effective contraception; discuss need for optimal preconceptional glycemic control. Review medications contraindicated in pregnancy prior to conception. ACE inhibitors, ARBs, statins, and most noninsulin therapies not recommended.

**Flu Shot**
Annually

**Pneumonia Shot**
Vaccinate all with diabetes ≥2 years of age. One time revaccinate individuals >65 years of age immunized >5 years ago. Other indications for revaccination include conditions such as chronic renal disease, nephrotic syndrome, and immunocompromised states.
**Hepatitis B Shot**
Administer to unvaccinated adults aged 19-59 years. Consider in those ≥60 years after assessing risk and likelihood of adequate immune response.

**Depression Screen**
Routinely assess.

<table>
<thead>
<tr>
<th>Therapeutic Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lifestyle Modification</strong></td>
</tr>
<tr>
<td><strong>Glycemic Goals</strong></td>
</tr>
<tr>
<td>- Pre-meal — 70-130 mg/dL.</td>
</tr>
<tr>
<td>- Peak postprandial — &lt;180 mg/dL.</td>
</tr>
<tr>
<td>- A1C — &lt;7%</td>
</tr>
<tr>
<td>- Hypoglycemia — inquire at each visit if on sulfonylureas or insulin; minimize severe episodes</td>
</tr>
</tbody>
</table>

| Reduce Cardiovascular (CVD) Risk |
| Treatment |
| CVD — Use ACE inhibitor, aspirin and statin therapy unless contraindicated. In patients with prior MI, continue B-blockers for at least 2 years after event. |
| Elevated BP — ACE inhibitors or ARBs. If needed to achieve BP targets, add thiazide diuretic if GFR ≥30 ml/min or a loop diuretic if GFR <30 ml/min. |
| Dyslipidemia — Statins to achieve LDL goal <70 mg/dL in patients with overt CVD; <100 mg/dL without overt CVD; or reduction of 30-40% from baseline if goal not achieved on maximal tolerated statin therapy. |
| Microalbuminuria — ACE inhibitors or ARBs. Treat even if BP is at goal. |
| Aspirin therapy — (75-162 mg/day) with history of CVD or at increased risk (most men >50 years old or women >60 years old with one or more major risk factors). Not recommended for those with low CVD risk. Contraindicated if <21 years. Use clopidogrel (75 mg/day) in patients with CVD and aspirin allergy. |
| Statin therapy (if not contraindicated) in patients: |
| - without CVD >40 years with one or more additional CVD risk factors |
| - without CVD <40 years of age if LDL >100 mg/dL or with multiple risk factors |
Prediabetes Practice Guidelines

Prediabetes is hyperglycemia not sufficient to meet the diagnostic criteria for diabetes, but too high to be considered normal. Impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are associated with obesity, hypertension and dyslipidemia with high triglycerides and/or low HDL cholesterol.

Having prediabetes substantially increases cardiovascular risk and the risk of future diabetes. Treatment through lifestyle intervention delays this progression and improves multiple risk factors.

### Diagnosis

#### Increased Risk of Diabetes
- Fasting blood glucose (FBG) between 100-125 mg/dL (IFG) or
- 2-hour plasma glucose in the 75g oral glucose tolerance test (OGTT) between 140-199 mg/dL (IGT) or
  - A1C 5.7 to 6.4% or
  - Metabolic syndrome diagnosed by the National Cholesterol Education Program (NCEP) criteria

#### Diagnostic Criteria for Metabolic Syndrome
- Presence of any three constitute diagnosis
  - Elevated waist circumference: ≥ 40 inches (102cm) men or ≥ 35 inches (88cm) women (population & country specific definitions available, see Sources: Harmonizing the Metabolic Syndrome)
  - Elevated triglycerides ≥ 150 mg/dL or drug treatment for elevated TG
  - Reduced HDL cholesterol < 40 mg/dL in men or < 50 mg/dL in women or drug treatment for reduced HDL
  - Elevated blood pressure ≥ 130 mmHg systolic &/or ≥ 85 mg/dL diastolic or drug treatment for hypertension
  - Elevated fasting blood glucose ≥ 100 mg/dL or drug treatment for elevated glucose

### Therapeutic Objectives

#### Prevention/ Delay of Type 2 Diabetes
- Refer to education/on-going support program targeting modest weight loss of 7% body weight and increased physical activity of moderate-intensity for at least 150 minutes/week.
- Follow-up counseling appears to be important for success.
- Monitor at least annually for the development of diabetes.
- Metformin therapy may be considered in those with IGT, IFG or an A1C between 5.7-6.4%, especially for those with BMI >35kg/m², age <60 years and women with prior GDM.

#### Medical Nutrition Therapy (MNT)
- Reduce calories, total fat, saturated fat and trans fat.
- Increase dietary fiber (14 g/1000 calories) and foods containing whole grains (1/2 of grain intake).
- Limit intake of sugar-sweetened beverages.

#### Reduce Cardiovascular Risk
- Hypertension
  - ACE inhibitors or ARBs preferred treatments
  - Blood pressure goal <140/<80 mmHg
- Aspirin therapy
  - Consider in those at increased CVD risk (most men > 50 or women >60 years old with one or more major risk factors, including family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria).
  - Use clopidogrel (75 mg/day) in patients with CVD and aspirin allergy
• Dyslipidemia
  – LDL cholesterol goal <100 mg/dL; in those with overt CVD, LDL cholesterol goal <70 mg/dL
  – Initiate statin therapy if LDL remains above goal; consider patient’s age and pregnancy possibilities

• Smoking
  – Advise all patients not to smoke
Metformin (MET): Metformin (Fortamet, Glucophage or Glucophage XR, Glumetza, Riomet liquid)

**Start MET**
- **Dose:** Taken with evening meal
  - Metformin 500, 850 or 1000 mg
  - Glucophage XR 500 or 750 mg
  - Fortamet ER 500 or 1000 mg
  - Glumetza 500 mg
  - Riomet liquid 500 mg (5 ml) or 850 mg (8.5 ml)

**Mechanism**
- Activates intracellular AMP-kinase
- Decreases hepatic glucose production

**Contraindications***
- Renal dysfunction (serum creatinine > 1.5 mg/dL in males, > 1.4 mg/dL in females)
- DKA

**Precautions**
- Pregnancy & lactation (may be appropriate in some circumstances)
- Hold on day of IV radiographic contrast procedures; restart in 48 hr or after serum creatinine is normal
- Interferes with vitamin B12 absorption
- Risk of lactic acidosis in patients with:
  - Liver dysfunction
  - Renal dysfunction
  - Alcohol abuse, binge drinking
  - Acute cardiovascular or pulmonary disease
  - In patients > 80 yr unless creatinine clearance > 60 ml/min
  - Patients with HF who require pharmacologic therapy

**Side Effects**
- GI symptoms – usually dose related & self-limited

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

**Blood glucose goals achieved:**
- Maintain regimen

**Dose Adjustments (in mg)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Start PM</th>
<th>Next Δ AM/PM</th>
<th>Next Δ AM/PM</th>
<th>Next Δ AM/PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin 500 mg</td>
<td>500</td>
<td>500/500</td>
<td>500/1000</td>
<td>1000/1000</td>
</tr>
<tr>
<td>Metformin 850 mg</td>
<td>850</td>
<td>850/850</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin 1000 mg</td>
<td>1000</td>
<td>1000/1000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riomet 5 ml</td>
<td>5</td>
<td>5/5</td>
<td>5/10</td>
<td>10/10</td>
</tr>
<tr>
<td>Riomet 8.5 ml</td>
<td>8.5</td>
<td>8.5/8.5</td>
<td>8.5/17</td>
<td></td>
</tr>
<tr>
<td>Metformin ER 500 mg</td>
<td>500</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin ER 750 mg</td>
<td>750</td>
<td>1500</td>
<td>2250</td>
<td></td>
</tr>
<tr>
<td>Fortamet ER 500 mg</td>
<td>500</td>
<td>1000</td>
<td>0/2000</td>
<td>0/2500</td>
</tr>
<tr>
<td>Fortamet ER 1000 mg</td>
<td>1000</td>
<td>0/2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glumetza 500 mg</td>
<td>1000</td>
<td>0/1500</td>
<td>0/2000</td>
<td></td>
</tr>
</tbody>
</table>

Δ May be increased every 1-2 weeks.
*OK to dose Metformin ER BID; promotes tolerance

**Follow-up in 1-2 weeks, phone or office visit**

**SMBG* 2 times/day**

**Recurrence hypoglycemia***:
- Maintain Metformin
- Decrease insulin by 10-25%
- Decrease dose of SU or GLN
*As monotherapy, these drugs are unlikely to cause hypoglycemia.

**Hyperglycemia:**
- Adjust dose

**Follow-up in 1-2 weeks, phone or office visit**

**GI distress, persistent:**
- Decrease/titrate dose
- Take with largest meal of day
- Consider Metformin ER, Fortamet ER or Glumetza
- Consider stopping & starting DPP4-i or GLP-1 RA

**Hyperglycemia:**
- Consider other treatment options

*SMBG* 2 times/day
- Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
GLP-1 Receptor Agonists (GLP-1 RA): Exenatide (Byetta), Exenatide ER (Bydureon) & Liraglutide (Victoza)

Start GLP-1 RA
- **Byetta**: 5 mcg BID
- **Bydureon**: 2 mg weekly
- **Victoza**: 0.6 mg daily

Mechanism
- Increases insulin (glucose dependent)
- Decreases glucagon (glucose dependent)
- Slow gastric emptying
- Increases satiety

Contraindications*
- Type 1 diabetes & DKA
- Pregnancy & lactation
- End-stage renal disease or severe renal impairment (creatinine clearance < 30 mL/min) except for Victoza. Use with caution in patients with renal transplants.
- Consider other therapies in patients with history of pancreatitis
- Severe GI disease including gastroparesis

Precautions
- **Boxed Warning**: Do not use Victoza/Bydureon if patient or family members have a history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2.
  - Risk of thyroid C-cell tumors with Victoza & Bydureon
- Associated with acute pancreatitis including fatal & non-fatal hemorrhagic or necrotizing pancreatitis after initiation & after dose increases. Observe closely for severe abdominal pain, sometimes radiating to the back with/without vomiting. Stop GLP-1 RA promptly.

Drug Interactions
- Oral contraceptives & antibiotics: absorption may be impacted. Take 1 hr before GLP-1 RA injection.
- Warfarin: increased INR sometimes associated with bleeding

Side Effects
- **Positive**: weight loss
- Nausea, vomiting &/or diarrhea resulting in dehydration; abdominal distension, abdominal pain, dyspepsia, constipation; headache, lack of strength;
- Altered renal function, increased serum creatinine, worsened chronic renal failure or acute renal function
- Injection site reactions

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

*See Sources for pancreatitis and pancreatic neoplasm citations.

**Hyperglycemia**: Maintain regime
- If on max effective doses of SU, GLN or basal insulin, consider basal insulin therapy
- Can use cautiously with basal + bolus insulin regimen.

Nausea:
- If Byetta dose is 10 mcg BID, ↓ dose to 5 mcg BID for 2 – 4 weeks; retry 10 mcg BID
- If Byetta dose is 5 mcg BID, consider alternative therapy
- Maintain Victoza dose at 0.6 or 1.2 mg for >1 week until nausea subsides

Recurrent hypoglycemia*:
- Decrease dose of SU, GLN or basal insulin
- Explore other causes for hypoglycemia (skipping meals, inadequate carbohydrate intake, etc.)
- Maintain other non-secretagogue meds

*As monotherapy, these drugs are unlikely to cause hypoglycemia.

Blood glucose goals achieved: Maintain regimen

Hyperglycemia: Adjust dose

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.

Dose Adjustments

<table>
<thead>
<tr>
<th>GLP-1 RA</th>
<th>Start</th>
<th>Next Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Byetta</strong></td>
<td>5 mcg</td>
<td>10 mcg after 1 month</td>
</tr>
<tr>
<td>(taken ≤60 min prior to AM &amp; PM meals)</td>
<td>BID</td>
<td></td>
</tr>
<tr>
<td><strong>Bydureon</strong></td>
<td>2 mg weekly</td>
<td></td>
</tr>
<tr>
<td><strong>Victoza</strong></td>
<td>0.6 mg daily x 1 week, then ↑ to 1.2 mg daily</td>
<td>1.8 mg daily</td>
</tr>
</tbody>
</table>

Follow-up in 1-2 weeks, phone or office visit, until blood glucose goals reached.

SMBG* BID

Follow-up in 3-7 days, phone or office visit

*For pancreatitis and pancreatic neoplasm citations.
DPP4 Inhibitors (DPP4-i): Sitagliptin (Januvia), Saxagliptin (Onglyza), Linagliptin (Tradjenta) & Alogliptin (Nesina)

Mechanism
- Increases GLP-1 & GIP concentration
- Increases insulin (glucose dependent)
- Decreases glucagon (glucose dependent)

Contraindications*
- Pregnancy & lactation
- Type 1 diabetes
- DKA
- Pancreatitis

Precautions*
- Assess renal function by measuring creatinine clearance prior to initiation. Reevaluate periodically.
- Nesina: assess liver enzymes prior to initiation. Reevaluate periodically.
- Nesina: D/C with clinically significant liver enzyme elevation; also if abnormal liver test persists or worsens.

Drug Interactions
- Onglyza - ketoconazole & CYP3A4/5 inhibitors
- Tradjenta - rifampin & CYP3A4/5 inhibitors

Side Effects
- Pancreatitis
- Upper respiratory infection
- Nasopharyngitis
- Headache
- Urinary tract infection
- Myalgia
- Urticaria
- Angioedema

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

Hyperglycemia:
- Consider other treatment

Blood glucose goals achieved:
- Maintain regimen

Follow-up in 2-4 weeks, phone or office visit

Recurrent hypoglycemia*:
- Maintain DPP4-i
- Decrease doses of SU, GLN or insulin

*SMBG* BID

Start DPP4-i; see adjustments for renal impairment below

<table>
<thead>
<tr>
<th></th>
<th>Januvia</th>
<th>Onglyza</th>
<th>Tradjenta</th>
<th>Nesina</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>25 mg</td>
<td></td>
</tr>
<tr>
<td>50 mg</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>12.5 mg</td>
<td></td>
</tr>
<tr>
<td>25 mg</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>6.25 mg</td>
<td></td>
</tr>
</tbody>
</table>

Dosage Adjustments for Renal Impairment

Moderate (creatinine clearance ≥30 - <60 ml/min)

<table>
<thead>
<tr>
<th></th>
<th>Januvia</th>
<th>Onglyza</th>
<th>Tradjenta</th>
<th>Nesina</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mg</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>12.5 mg</td>
<td></td>
</tr>
</tbody>
</table>

Severe (creatinine clearance <30 ml/min, ESRD or hemodialysis)

<table>
<thead>
<tr>
<th></th>
<th>Januvia</th>
<th>Onglyza</th>
<th>Tradjenta</th>
<th>Nesina</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 mg</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>6.25 mg</td>
<td></td>
</tr>
</tbody>
</table>

*As monotherapy, these drugs are unlikely to cause hypoglycemia.

Hyperglycemia:
- Consider other treatment

Blood glucose goals achieved:
- Maintain regimen

Follow-up in 2-4 weeks, phone or office visit

Recurrent hypoglycemia*:
- Maintain DPP4-i
- Decrease doses of SU, GLN or insulin

*SMBG* BID

*As monotherapy, these drugs are unlikely to cause hypoglycemia.

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.

*See Sources for pancreatitis citations.
Alpha-Glucosidase Inhibitors (AG-i): Acarbose (Precose) & Miglitol (Glyset)

**Start AG-i**
Dose: taken with 1st bite of main meal
- **Precose**: 25 mg TID
- **Glyset**: 25 mg TID

**SMBG* 1-2 times/day**

**Follow-up in 2-4 weeks, phone or office visit**

**Recurrent hypoglycemia*:**
- Maintain Precose or Glyset
- Decrease dose of SU, GLN or insulin
*As monotherapy, these drugs are unlikely to cause hypoglycemia.

**Hyperglycemia:** Adjust dose

**Blood glucose goals achieved:**
Maintain regimen

**Dose Adjustments (in mg)**

<table>
<thead>
<tr>
<th></th>
<th>Start</th>
<th>Next Δ</th>
<th>Next Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precose</td>
<td>25 TID</td>
<td>50 TID (max dose for those &lt;60 kg)</td>
<td>100 TID (max dose for those &gt;60 kg)</td>
</tr>
<tr>
<td>Glyset</td>
<td>25 TID</td>
<td>50 TID</td>
<td>100 TID</td>
</tr>
</tbody>
</table>

Δ May be increased every 4-8 weeks.
Follow-up in 2-4 weeks, phone or office visit, until blood glucose goals reached.

**Mechanism**
- Slows intestinal carbohydrate digestion/absorption

**Contraindications***
- Pregnancy & lactation
- Type 1 diabetes
- Chronic & acute gastrointestinal diseases
- Precose only
  - Cirrhosis
  - Serum creatinine >2.0 mg/dl
- Glyset only
  - Creatinine clearance <25 ml/min

**Precautions**
- Patients taking AG-i & secretagogues need glucose tablets or gel to treat hypoglycemia

**Side Effects**
- Abdominal pain, diarrhea, flatulence usually dose related & self-limited

**Drug Interactions**
- Precose
  - Digoxin may require dose increase

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.

**GI distress, persistent:**
- Decrease dose
- Consider alternate adjustment schedule:

<table>
<thead>
<tr>
<th>Week 1-2</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Supper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 3-4</td>
<td>25 mg</td>
<td>25 mg</td>
<td>25 mg</td>
</tr>
<tr>
<td>Week 5-12</td>
<td>25 mg</td>
<td>25 mg</td>
<td>25 mg</td>
</tr>
</tbody>
</table>

**Check ALT:**
- Precose only
  - At initiation
  - Every 3 months for 1st year if dose ≥50 mg TID

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Sodium Glucose Co-Transporter 2 (SGLT-2) Inhibitors: Canagliflozin (Invokana) & Farxiga (Dapagliflozin)

**Mechanism**
- Inhibits renal glucose reabsorption
- Lowers plasma glucose by increasing glucose excretion

**Contraindications***
- Type 1 diabetes
- Pregnancy & lactation
- Invokana eGFR <45 ml/min
- Farxiga eGFR <60 ml/min
- Dialysis

**Precautions:**
- Assess renal function before starting & during therapy
- Max dose Invokana is 100 mg/day if eGFR 45-60 ml/min.
- Hypotension: increased risk for patients with renal impairment, the elderly, patients with low systolic BP or those on diuretics.
- Hyperkalemia: monitor potassium levels especially if on ACE or ARB
- Increase in LDL; treat per standards of care
- Bladder cancer (Farxiga)

**Side Effects**
- Positive: weight loss; may improve BP
- Genital mycotic infections
- Urinary tract infections
- Increased urination (Invokana)
- Nasopharyngitis (Farxiga)

**Drug Interactions:**
- UGT inducers (Rifampin): Invokana exposure is reduced. Consider increasing dose from 100 to 300 mg.
- Digoxin: monitor levels

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

### Dose Adjustments (in mg)

<table>
<thead>
<tr>
<th></th>
<th>Start</th>
<th>Next Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invokana</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &gt;60 ml/min</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>eGFR 45-60 ml/min</td>
<td>100</td>
<td>---</td>
</tr>
<tr>
<td>Farxiga*</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

Δ May be increased every 1-2 months
*Do not use if eGFR <60 ml/min
Follow-up in 1-2 weeks, phone or office visit, until blood glucose goals reached

**Blood glucose goals achieved: Maintain regimen**

**Hyperglycemia:**
Adjust dose if eGFR >60 ml/min

**Recurrent hypoglycemia:**
Decrease dose of SU, GLN or insulin
*As monotherapy, these drugs are unlikely to cause hypoglycemia

**Follow-up in 1-2 weeks, phone or office visit**

**SMBG* 1-2 times/day**

**Hyperglycemia:**
Consider other treatment options

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Thiazolidinediones (TZD): Pioglitazone (Actos)

Start TZD
Dose: once daily without regard to meals
Pioglitazone 15 or 30 mg

SMBG* 1-2 times/day

Follow-up in 1-4 weeks, phone or office visit

Hypoglycemia*
- Maintain TZD, DPP4-i or GLP-1 RA
- Decrease SU or GLN
- Decrease insulin by 10-25%
*As monotherapy, this drug is unlikely to cause hypoglycemia.

Blood glucose goals achieved: Maintain regimen

Hyperglycemia: Adjust dose

Dose Adjustments (in mg)
Monotherapy or combined with MET or SU

<table>
<thead>
<tr>
<th>Start AM</th>
<th>Next Δ</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone 15 or 30</td>
<td>30 or 45</td>
<td>45</td>
</tr>
</tbody>
</table>

Δ May be increased every 8-12 weeks
Follow-up in 1-4 weeks, phone or office visit, until blood glucose goals reached.

Warning! Heart Failure
- Can cause or exacerbate congestive heart failure
- Contraindicated in patients with established NYHA Class III or IV heart failure
- Monitor for signs/symptoms of heart failure after initiation & dose increases; stop drug or reduce dose if heart failure develops

Mechanism
- Activates PPAR-γ transcription factor
- Increases insulin sensitivity

Contraindications*
- Type 1 diabetes
- Pregnancy or lactation
- ALT 3 times & serum total bilirubin 2 times reference range
- Active bladder cancer

Precautions
- Macular edema
- Ovulation in some premenopausal anovulatory women so increased risk for pregnancy
- Obtain liver function test before initiation
- Effectiveness decreased when used concomitantly with CYP2C8 inducers (e.g. Rifampin)
- Max recommended dose 15 mg when used concomitantly with strong CYP2C8 inhibitor (Gemfibrozil)
- Increased risk of fractures in females
- Use with caution in patients with elevated ALT or bilirubin
- Use with caution in patients with history of bladder cancer

Inform patients to:
- Stop drug & immediately report to MD unexplained symptoms of nausea, vomiting, abdominal pain, fatigue, anorexia, dark urine, rapid weight gain, edema, shortness of breath, hematuria, dysuria or urinary urgency

Side Effects
- Weight gain
- URI symptoms
- Sinusitis; pharyngitis
- Myalgia

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.
Sulfonylureas (SU): Glimepiride (Amaryl), Glipizide (Glucotrol), Glyburide (Micronase, Diabeta), Glyburide Micro (Glynase)

**Mechanism**
- Close \( \beta \)-cell \( K_{ATP} \) channels
- Increases insulin secretion (glucose dependent)

**Contraindications**
- Pregnancy** & lactation
- Type 1 diabetes
- DKA

**Precautions**
- Reduce doses
  - Geriatric patients, advance cautiously
  - Renal impairment
  - Hepatic impairment
- Sulfonamide allergy
- Associated with increased cardiovascular mortality
- Glucose-6-phosphate dehydrogenase deficiency

**Drug Interactions**
- Glipizide: administer at least 4 hr before Colesevelam

**Side Effects**
- Hypoglycemia
- Weight gain

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

****Only Glyburide has been shown to be safe (NEJM 2000, 343(16):1134-8).

**Start SU**
Dose: taken with 1st meal of day

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glimepiride</td>
<td>1-2 mg</td>
</tr>
<tr>
<td>Glipizide ER</td>
<td>5 mg</td>
</tr>
<tr>
<td>Glipizide</td>
<td>5 mg take 30 minutes before meals</td>
</tr>
<tr>
<td>Glyburide</td>
<td>2.5-5 mg</td>
</tr>
<tr>
<td>Glyburide Micro</td>
<td>1.5-3 mg</td>
</tr>
</tbody>
</table>

**SMBG** BID

Follow-up in 1-2 weeks, phone or office visit

Recurrent hypoglycemia:
- Decrease dose or stop
- Consider MET, GLP-1 RA, DPP4-i or GLN

Hyperglycemia: Adjust dose

Blood glucose goals achieved: Maintain regimen

**Dose Adjustments (in mg)**

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Start AM</th>
<th>Next Δ AM/PM</th>
<th>Next Δ AM/PM</th>
<th>Max Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glimepiride</td>
<td>1</td>
<td>2/-</td>
<td>4/-</td>
<td>8</td>
</tr>
<tr>
<td>Glipizide ER</td>
<td>5</td>
<td>5/-</td>
<td>10/-</td>
<td>20</td>
</tr>
<tr>
<td>Glipizide</td>
<td>5</td>
<td>5/5</td>
<td>10/10</td>
<td>40</td>
</tr>
<tr>
<td>Glyburide</td>
<td>2.5</td>
<td>5/-</td>
<td>5/5</td>
<td>50%</td>
</tr>
<tr>
<td>Glyburide Micro</td>
<td>1.5</td>
<td>3/-</td>
<td>3/3</td>
<td>12</td>
</tr>
</tbody>
</table>

Δ May be increased every 1-2 weeks. For persistent glucose >300 mg/dL, adjust dose weekly.

Follow-up in 1-2 weeks by phone or office visit until blood glucose goals reached.

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Glinides (GLN): Nateglinide (Starlix) & Repaglinide (Prandin)

**Mechanism**
- Close $\beta$-cell K$_{ATP}$ channels
- Increases insulin secretion (glucose dependent)

**Contraindications**
- Pregnancy & lactation
- Type 1 diabetes
- Do not use with Gemfibrozil

**Precautions**
- Hepatic insufficiency — advance dose cautiously with longer intervals between dose adjustments
- Starlix: use with caution for patients with severe renal disease; initiate 60 mg dose & carefully titrate
- Prandin: use with caution for patients with severe renal disease; initiate 0.5 mg dose & carefully titrate
- Certain drugs (NSAIDS, salicylates, sulfonamides, chloramphenicol, coumadin, probenecid, monoamine oxidase inhibitors, non-selective adrenergic blocking agents) and other antidiabetic agents may potentiate hypoglycemic action

**Side Effects**
- Hypoglycemia
- Weight gain

* Refer to product insert for comprehensive list of contraindications, precautions & side effects.

**Starlix**
Recommended starting & maintenance dose is 120 mg with meals; use 60 mg with meals if near A1C goal at initiation

- A1C <8% or no previous treatment with diabetes meds
  - Start: 0.5 mg with meals
  - Next Δ: 1 mg with meals

- A1C ≥ 8% or previous treatment with diabetes meds
  - Start: 1 mg with meals
  - Next Δ: 2 mg with meals

**Prandin**
- A1C <8% or no previous treatment with diabetes meds
  - Start: 0.5 mg with meals
  - Next Δ: 1 mg with meals

- A1C ≥ 8% or previous treatment with diabetes meds
  - Start: 1 mg with meals
  - Next Δ: 2 mg with meals

Δ May be increased at 1-week intervals doubling dose up to 4 mg.

Follow-up in 1-2 weeks by phone or office visit until blood glucose goals reached.

**Dose Adjustments**

**Hyperglycemia:**
Adjust dose

**Blood glucose goals achieved:**
Maintain regimen

**Hyperglycemia:**
Consider other treatment

**Recurrent hypoglycemia:**
- Decrease or stop drug
- If on Prandin, consider Starlix
- Consider MET, DPP4-i, GLP-1 RA

**SMBG**
BID

**Follow-up in 1-2 weeks,**
phone or office visit

* Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Colestevam HCl (COLSVL): Welchol

**Mechanism**
- Binds bile acids in intestinal tract increasing hepatic bile acid production
- Physiological action promoting glucose control is unknown

**Contraindications***
- Type 1 diabetes
- DKA
- TG >500 mg/dL
- History of hypertriglyceridemia-induced pancreatitis
- Gastroparesis, GI motility disorders, history of GI surgery or bowel obstruction

**Precautions:**
- Decreases absorption of fat-soluble vitamins A, D, E & K; advise patients to take vitamins at least 4-hr prior to Welchol
- Dysphagia & swallowing disorders
- Administer cyclosporine, sulfonylureas, levothyroxine, olmesartan medoxomil, oral contraceptives, metformin ER at least 4-hr prior to Welchol
- Causes TG increase; obtain baseline lipid profile & monitor
- Decrease in phenytoin levels if taking phenytoin
- Decrease in INR if on warfarin
- Not studied in combination with DDP4-i or GLP-1 RA

**Side Effects**
- Constipation
- Nausea
- Dyspepsia

*Refer to product insert for comprehensive list of contraindications, precautions & side effects.

**Start COLSVL**
Dose: take with a meal & liquid
- Welchol tabs
  - 6-625 mg tabs QD or 3-625 mg tabs BID
- Welchol oral suspension
  - 3.75 gm packet QD or 1.875 gm packet BID

**SMBG* 1-2 times/day**

**Follow-up in 2-4 weeks, phone or office visit**

**Recurrent hypoglycemia***:
- Decrease dose of SU, GLN or insulin
  *As monotherapy, this drug is unlikely to cause hypoglycemia.

**Blood glucose goals achieved:**
- Maintain regimen

**Hyperglycemia:**
- Adjust other diabetes meds or consider other treatment options

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Dopamine Receptor Agonist (BCR-QR): Cycloset (Bromocriptine)

Start BCR-QR
Dose: take with food & within 2 hours of waking
Cycloset 0.8 mg once daily

SMBG* 1-2 times/day

Follow-up in 1-2 weeks, phone or office visit

Recurrent hypoglycemia*:
Decrease dose of SU, GLN or insulin
*As monotherapy, this drug is unlikely to cause hypoglycemia.

Blood glucose goals achieved:
Maintain regimen

Hyperglycemia: Adjust dose

Dose Adjustments (in mg)
† by 0.8 mg weekly to max tolerated dose of 1.6–4.8 mg
Stop increase &/or reduce if side effects are intolerable
Follow-up in 1-2 weeks, phone or office visit, until blood glucose goals reached.

Hyperglycemia: Consider other treatment options

Mechanism
- Physiological action promoting glucose control is unknown

Contraindications*
- Type 1 diabetes
- Pregnancy & lactation
- Severe psychotic disorders
- Syncopal migraines

Precautions:
- Hypotension, including orthostatic; can occur at initiation of therapy & with dose increases
- May cause somnolence; patients experiencing should refrain from driving or operating heavy machinery

Side Effects
- Nausea, vomiting
- Fatigue
- Headache
- Dizziness

Drug Interactions:
- Avoid concomitant use with any other dopamine receptor agonists
- Avoid concomitant use with metoclopramide (Reglan) or sumatriptan
- Concomitant use with highly protein-bound therapies (salicylates, sulfonamides, chloramphenicol, probenecid) may alter their effectiveness & risk for side effects
- Avoid concomitant use with sympathomimetic drugs (phenylpropanolamine & isometheptene) > 10 days
- May increase ergot-related side effects & reduce effectives if administered within 6 hr of ergot-related drugs
- Use caution when administering with anti-hypertensive medications
- Use caution when administering with drugs that are strong inhibitors, inducers or substrates of CYP3A4 (azole antimycotics, HIV protease inhibitors)

* Refer to product insert for comprehensive list of contraindications, precautions & side effects.

* Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Pramlintide (PRAML): Symlin

**Mechanism**
- Increases satiety
- Slows gastric emptying
- Decreases glucagon (glucose dependent)

**Contraindications***
- Gastroparesis
- A1C > 9%
- Poor compliance with insulin regimen &/or prescribed SMBG
- Hypoglycemia unawareness or recent, recurrent episodes of hypoglycemia
- Using drugs that stimulate gastric motility

**Precautions**
- Monitor for hypoglycemia. May need further reduction of mealtime insulin dose.
- Do not mix with insulin or inject in proximity to insulin
- Do not administer in arm due to variable absorption
- Administer oral medications in which a rapid onset of action is desired 1 hr before or 2 hr after PRAML.

**Side Effects**
- Severe hypoglycemia
- Nausea, vomiting, indigestion, abdominal pain
- Anorexia
- Headache
- Fatigue, dizziness

*Refer to product insert for comprehensive list of contraindications, precautions & side effects

**Indication:**
Type 1: Adjunct to mealtime insulin if not achieving desired glucose control
Type 2: Adjunct to mealtime insulin if not achieving desired goals with or without other therapies

Start: PRAML; reduce rapid- or short-acting insulin by 50% including insulin mixtures used before meals
Type 1: 15 mcg before each meal containing ≥30 gm carbohydrate
Type 2: 60 mcg before each meal containing ≥30 gm carbohydrate
May start with one meal/day & add other meals every 3-7 days.

**Dose Adjustments (in mcg)**

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>15 mcg</td>
<td>60 mcg</td>
</tr>
<tr>
<td>Next Δ</td>
<td>30 mcg</td>
<td>120 mcg</td>
</tr>
<tr>
<td>Next Δ</td>
<td>45 mcg</td>
<td></td>
</tr>
<tr>
<td>Next Δ</td>
<td>60 mcg</td>
<td></td>
</tr>
</tbody>
</table>

Δ Increase PRAML dose if there is no nausea for 3-7 days to maximum dose tolerated.
Follow-up in 3-7 days.
Retitrate insulin to achieve target range blood glucose once at max or tolerated PRAML dose.

**Blood glucose goals achieved:**
- Maintain regimen

**SMBG***
- 6-8 times/day until titration complete

**Follow-up in 3-7 days, phone or office visit

**Recurrent or severe hypoglycemia:**
- Further decrease mealtime insulin

**Hyperglycemia:**
- Complete PRAML titration then adjust insulin

**Nausea:**
- Common in first weeks of treatment
- If significant nausea persists, decrease dose
- If unable to increase to max dose due to nausea, evaluate benefits & adjust insulin for hyperglycemia

**Hypo- or hyperglycemia or weight loss:**
- Adjust insulin
- With weight loss, may need to decrease basal insulin

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Drug Class</th>
<th>Available Doses</th>
</tr>
</thead>
</table>
| Actoplus Met (Pioglitazone & Metformin) | TZD & MET | 15 mg Pioglitazone/500 mg Metformin  
                                |            | 15 mg Pioglitazone/850 mg Metformin                |
| Actoplus Met XR (Pioglitazone & Metformin XR) | TZD & MET | 15 mg Pioglitazone/1000 mg Metformin  
                                       |            | 30 mg Pioglitazone/1000 mg Metformin               |
| Duetact (Pioglitazone & Glimepiride) | TZD & SU   | 30 mg Pioglitazone/2 mg Glimepiride  
                                       |            | 30 mg Pioglitazone/4 mg Glimepiride                |
| Glucovance (Glyburide & Metformin) | SU & MET   | 1.25 mg Glyburide/250 mg Metformin  
                                       |            | 2.5 mg Glyburide/500 mg Metformin                  |
| Janumet (Sitagliptin & Metformin) | DPP4-i & MET | 50 mg Sitagliptin/500 mg Metformin  
                                        |            | 50 mg Sitagliptin/1000 mg Metformin                |
| Jentadueto (Linaagliptin & Metformin) | DPP4-i & MET | 2.5 mg Linaagliptin/500 mg Metformin  
                                        |            | 2.5 mg Linaagliptin/850 mg Metformin               |
| Juvisync (Sitagliptin & Simvastatin) | DPP4-i & Statin | 50 mg Sitagliptin/10 mg Simvastatin  
                                         |            | 50 mg Sitagliptin/20 mg Simvastatin               |
| Kazano (Alogliptin & Metformin) | DPP4-i & MET | 12.5 mg Alogliptin/500 mg Metformin  
                                        |            | 12.5 mg Alogliptin/1000 mg Metformin              |
| Kombiglyze XR (Saxagliptin & Metformin XR) | DPP4-i & MET | 5 mg Saxagliptin/500 mg Metformin ER  
                                         |            | 5 mg Saxagliptin/1000 mg Metformin ER            |
| Metaglip (Glipizide & Metformin) | SU & MET   | 2.5 mg Glipizide/250 mg Metformin  
                                       |            | 2.5 mg Glipizide/500 mg Metformin                 |
| Oseni (Alogliptin & Pioglitazone) | DPP4-i & TZD | 12.5 mg Alogliptin/15 mg Pioglitazone  
                                      |            | 12.5 mg Alogliptin/30 mg Pioglitazone             |
| PrandiMet (Prandin & Metformin) | GLN & MET  | 1 mg Repaglinide/500 mg Metformin  
                                       |            | 2 mg Repaglinide/500 mg Metformin                  |
About Insulin

The pancreas secretes insulin in two ways:
- Burst of insulin released when blood glucose rises, usually after meals - bolus insulin
- Slow, steady release of insulin that maintains a background level in the blood - basal insulin

Today’s insulins are either ‘human’, produced using recombinant DNA technology, or ‘analog’ insulins, in which the amino acid sequence is changed to alter absorptive, metabolic and excretion characteristics. These modifications produce insulins 1) that are readily absorbed so act more quickly and 2) those that are released over an extended period time providing a basal coverage for a more prolonged period.

**Bolus Insulins** - taken before or with meals; used to control the increases in blood glucose levels that occur after meals. Also used to correct blood glucose elevations from causes other than food.
- Human
  - Humulin R (Regular), Novolin R (Regular)
  - Short-acting insulin
  - Inject 30 minutes prior to meal
- Analog
  - Humalog, NovoLog, Apidra
  - Rapid-acting insulins
  - Inject no more than 15 minutes before to immediately after a meal
  - Preferred due to better postprandial control and predictability

**Basal Insulins** - cover background insulin needs
- Human
  - Humulin N (NPH), Novolin N (NPH)
  - Intermediate-acting insulins
  - Cloudy suspension; must resuspend before use
  - Can be mixed with Regular or analog bolus insulins
  - More hypoglycemia
- Analog
  - Lantus (Glargine), Levemir (Detemir)
  - Long-acting insulins
  - Clear solution
  - Cannot be mixed
  - Preferred due to lack of pronounced activity peak, more predictable time-action profiles and lower risk of hypoglycemia

**Insulin Requirements**
- **Type 2**
  - Start with basal only at 0.1-0.3 units/kg/day. If A1C >8%, start at higher end of dose range.
    - Maintain MET, GLP-1 RA, DPP4-i, SU or GLN. Decrease dose or stop TZD and combinations.
  - Add bolus prandial insulin if basal dose is >0.5 units/kg/day
    - Maintain MET. Stop SU, GLN and their combinations.
  - 0.3-0.5 units/kg/day total daily dose (basal + bolus) per AACE algorithm. Obese patients may require higher doses.
- **Type 1**
  - Always need basal + bolus insulin
  - 0.5-1.0 units/kg/day total daily dose (basal + bolus); insulin requirements are variable
  - Daily insulin distribution approximately ⅕ to ⅓ total daily insulin requirement as basal (long-acting) insulin; ⅓ to ⅔ total daily insulin requirement given as bolus (rapid- or short-acting) insulin at meals.
  - Analog insulins preferred
• Blood glucose targets
  – Fasting and premeal: 70-130 mg/dL
  – Peak postprandial: <180 mg/dL
  – Individualize goals

**Blood Glucose Pattern Management**

• Always inquire about hypoglycemia
• Consider what may affect blood glucose readings, i.e., exercising or eating more or less than usual, changes in schedule, illness, injection sites, expired insulin or test strips, etc.
• Look for patterns of low or high glucoses based on individualized glycemic goals. Evaluate readings taken at the same time each day. Do not adjust unless there is a pattern.
• Adjust for low blood glucose pattern first. Never adjust for a pattern of highs if lows are present.
• Adjust only one type of insulin and one dose at a time.

**Dosing Adjustment for Renal Impairment**

Insulin requirements are reduced due to changes in insulin clearance or metabolism. No dosage adjustment recommendations are provided in manufacturer labeling. The following adjustments have been recommended by Aronoff, 2007.

• Creatinine clearance >50 mL/min: no adjustment necessary
• Creatinine clearance 10-50 mL/min: give 75% of recommended dose
• Creatinine clearance <10 mL/min: give 50% of recommended dose; monitor glucose closely

**Dialysis**

Insulin is not significantly removed by either peritoneal or hemodialysis; supplemental doses are not necessary.

## Insulin Types & Actions

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand Name</th>
<th>Onset (hr)</th>
<th>Peak Activity (hr)</th>
<th>Effective Duration (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAPID-ACTING Analogs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Apidra (Glulisine)</td>
<td>&lt;0.25</td>
<td>1-1.5</td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Humalog (Lispro)</td>
<td>&lt;0.3-0.5</td>
<td>0.5-2.5</td>
<td>3-6.5</td>
</tr>
<tr>
<td></td>
<td>NovoLog (Aspart)</td>
<td>&lt;0.25</td>
<td>0.5-1</td>
<td>3-5</td>
</tr>
<tr>
<td><strong>SHORT-ACTING Human Regular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humulin R</td>
<td>0.5-1</td>
<td>2-3</td>
<td>3-6</td>
</tr>
<tr>
<td></td>
<td>Novolin R</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>INTERMEDIATE-ACTING Human NPH</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Humulin N</td>
<td>2-4</td>
<td>4-10</td>
<td>10-16</td>
</tr>
<tr>
<td></td>
<td>Novolin N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LONG-ACTING Analogs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lantus (Glargine)</td>
<td>2-4</td>
<td>Relatively flat</td>
<td>20-24</td>
</tr>
<tr>
<td></td>
<td>Levemir (Detemir)</td>
<td>0.8-2</td>
<td>Relatively flat</td>
<td>Dose dependent: 12 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(dose</td>
<td></td>
<td>for 0.2 units/kg; 20-24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dependent)</td>
<td></td>
<td>hr for 0.4 units/kg</td>
</tr>
<tr>
<td><strong>INSULIN MIXTURES</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Analogs</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Humalog Mix 75/25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>75% insulin lispro protamine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>suspension + 25% insulin lispro</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>solution</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>NovoLog Mix 70/30</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>70% insulin aspart protamine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>suspension + 30% insulin aspart</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>solution</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Humalog 50/50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50% insulin lispro protamine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>suspension + 50% insulin lispro</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Similar to rapid-acting analog +</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>NPH</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Novolin or Humulin 70/30</td>
<td></td>
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<tr>
<td></td>
<td>70% insulin NPH suspension</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>+ 30% insulin Regular solution</td>
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<tr>
<td></td>
<td>Similar to short-acting human</td>
<td></td>
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<tr>
<td></td>
<td>Regular + NPH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humulin 50/50</td>
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<tr>
<td></td>
<td>50% insulin NPH suspension</td>
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<tr>
<td></td>
<td>+ 50% insulin Regular solution</td>
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</table>

Source: Practical Insulin, 3rd Edition: A Handbook for Prescribing Providers; American Diabetes Association

Intensive Insulin Management

Intensive insulin management is appropriate for most patients with type 1 diabetes and some with type 2. Intensive management uses insulin to carbohydrate ratio, insulin sensitivity factor and carbohydrate counting to allow flexibility in meal planning, close matching of mealtime insulin to the amount of food eaten and a systematic way to adjust for blood glucose values outside of target ranges.

Insulin to Carbohydrate Ratio (ICR)
An ICR predicts how many units of rapid-acting insulin are needed to cover a specific amount of carbohydrate. For example, a ratio of 1:10 means that a bolus of one unit of insulin will cover 10 grams of carbohydrate. ICR depends on a patient’s sensitivity to insulin, can vary by time of day and is affected by physical activity and stress.

Insulin Sensitivity Factor (ISF)
ISF is the expected drop in blood glucose for each one unit of rapid-acting insulin injected. ISF is used to calculate a bolus insulin correction dose needed to bring high blood glucoses into target range. The bolus is generally added to the mealtime insulin dose.

Formulas for ICR & ISF
500 Rule for ICR
- Divide 500 by the total daily dose (TDD) of insulin. The result is the number of carbohydrate grams covered by 1 unit of insulin.
  \[ \text{ICR} = \frac{500}{\text{TDD}} \]

1800 Rule for ISF (for use with rapid-acting analog insulins)
- Divide 1800 by the total daily dose (TDD) of insulin. The result is the expected drop in blood glucose from 1 unit of insulin.
  \[ \text{ISF} = \frac{1800}{\text{TDD}} \]
- To determine the rapid-acting insulin correction required to bring blood glucose to the goal range, subtract the goal BG from the actual BG and divide by the ISF.
  \[ \text{Correction dose (units of insulin)} = \frac{\text{actual BG} - \text{BG goal}}{\text{ISF}} \]

Sample Calculations
For these calculations, assume:
- TDD = 50 units
- Pre-meal BG = 185 mg/dL
- Target pre-meal BG = 120 mg/dL
- Meal contains 70 grams carbohydrate

ICR = 500/50 or 10; ICR = 1:10, 1 unit rapid-acting insulin for each 10 grams carbohydrate consumed
ISF = 1800/50 or 36 mg/dL, the expected BG drop for each unit of rapid-acting insulin
Correction dose = (185-120)/36 or 1.8 units of insulin (round to 2 units), the rapid-acting bolus needed to bring BG to goal range.

The appropriate rapid-acting insulin dose for this meal is 9 units; 7 units to cover the carbohydrate + 2 units to correct the pre-meal BG.
**Basal Insulin (Long-Acting): Glargine (Lantus) & Detemir (Levemir)**

**Indication:**
- FBG consistently > 130 mg/dL or A1C not at target

Start basal insulin

**Type 1**
- Variable basal requirements

**Type 2**
- Start once a day; give at same time each day generally evening
- Initial dosing guidelines:
  - Start 10 units/day or
  - Calculate dose based on weight
    - A1C ≤8% – 0.1-0.2 units/kg
    - A1C >8% – 0.2-0.3 units/kg
- For patients switching from NPH QD: initiate at current dose; stop NPH
- For patients using NPH BID: reduce TDD by 20%

**SMBG**

Type 2
- Lantus/Levemir only: 1-2 times/day
- If rapid-acting insulin, SU or GLN with Lantus/Levemir: 2-4 times/day

Type 1
- 4-6 times/day

**Phone follow-up within 3-7 days**

**Blood Glucose Pattern Adjustment**

<table>
<thead>
<tr>
<th>&lt;40 mg/dL</th>
<th>41-70 mg/dL</th>
<th>120-139 mg/dL</th>
<th>140-180 mg/dL</th>
<th>&gt;180 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting*</td>
<td>↓ dose 20-40%</td>
<td>↓ dose 10-20%</td>
<td>↑ 1 unit</td>
<td>↑ 2 units</td>
</tr>
</tbody>
</table>

Continue SMBG as above

Phone follow-up within 3-7 days

*Individualized glycemic goals may vary.

**Premeal or daytime hypo- or hyperglycemia:**
- Evaluate & adjust rapid-acting insulin, SU, GLN or SU MET combo before adjusting GLP-1 RA or DPP4-i
- If not on DPP4-i or GLP-1 RA, consider adding
- Phone follow-up within 3-7 days
- If basal insulin dose >0.5 units/kg, consider prandial insulin

**Type 1**
- Use with rapid-acting insulin
- May need Levemir twice/day

**Type 2**
- Stop NPH insulin mixtures & mixed dose regimens
- Use with MET, GLP-1 RA, DPP4-i, SU, GLN or rapid-acting insulin. Reduce dose or stop TZD.

**Precautions:**
- Do not dilute or mix with any other insulin or solution
- Do not use in insulin pump
- If on premixed insulin BID, reduce TDD by 20%. Divide this amount 50% Lantus/Levemir & 50% rapid-acting insulin
- Increased risk of hypoglycemia with insulin added to DPP4-i or GLP-1 RA
- Dosage reduction may be needed with hepatic or renal impairment
- Lantus – pregnancy risk factor C, risk cannot be ruled out

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.*
Rapid-Acting Insulin: Glulisine (Apidra), Lispro (Humalog) & Aspart (NovoLog)

**Indication**
- A1C above target on basal insulin & other non-insulin therapies
- BG 2-hr postprandial, premeal or bedtime > 180 mg/dL
- TDD basal insulin exceeds 0.5 units/kg, especially as it approaches 1.0 unit/kg

**Type 1**
- Always need basal + bolus

**Type 2**
- Continue basal insulin
- Initial dosing guidelines: TDD 0.3-0.5 units/kg
- Methods
  - Basal plus: add bolus before largest meal
  - Basal bolus: equal ‘fixed bolus’ doses with consistent carbohydrate
  - Intensive management: use ICR & ISF for mealtime insulin dosing

**Type 2**
- Stop SU & GLN
- Continue MET, DPP4-i
- Exercise caution with GLP-1 RA; not FDA approved with rapid insulins
- Reduce dose or stop TZD

**Precautions:**
- Dosage reduction may be needed with hepatic or renal impairment

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.

**SMBG**
- Type 2: 2-4 times/day
- Type 1: 4-6 times/day

Phone follow-up within 3-7 days

**Fasting hypoglycemia (<70 mg/dL):**
- Reduce basal insulin

**Post-prandial hypoglycemia (< 70 mg/dL):**
- Decrease bolus insulin before affected meal by 10%
- Phone follow-up within 3-7 days

**Postprandial hyperglycemia (2-hr post-prandial or next premeal glucose >180 mg/dL):**
- Assess treatment plan: review meal plan before insulin adjustment
- Increase insulin before affected meal by 10%
- Phone follow-up in 3-7 days
- Consider Symlin

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
**Intermediate-Acting Basal Insulin: NPH**

<table>
<thead>
<tr>
<th>Indication: FBG consistently &gt; 130 mg/dL or A1C not at target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start intermediate-acting insulin</td>
</tr>
<tr>
<td><strong>Type 2</strong></td>
</tr>
<tr>
<td>• Initial dosing guidelines:</td>
</tr>
<tr>
<td>- Start 10 units/day or</td>
</tr>
<tr>
<td>- Calculate dose based on weight</td>
</tr>
<tr>
<td>- A1C ≤8% – 0.1-0.2 units/kg</td>
</tr>
<tr>
<td>- A1C &gt;8% – 0.2-0.3 units/kg</td>
</tr>
<tr>
<td>• Usually started at bedtime</td>
</tr>
<tr>
<td>• Can be administered BID (divide dose 50% before breakfast, 50% before supper/bedtime)</td>
</tr>
<tr>
<td>• May use with bolus (rapid-acting or regular) insulin for meal coverage if dose exceeds 0.5-1 unit/kg</td>
</tr>
</tbody>
</table>

**Blood Glucose Pattern Adjustment**

<table>
<thead>
<tr>
<th>Blood Glucose Pattern</th>
<th>&lt;40 mg/dL</th>
<th>41-70 mg/dL</th>
<th>120-139 mg/dL</th>
<th>140-180 mg/dL</th>
<th>&gt;180 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fasting</strong>*</td>
<td>↓ PM dose by 20–40%</td>
<td>↓ PM dose by 10–20%</td>
<td>↑ PM dose by 1 unit</td>
<td>↑ PM dose by 2 units</td>
<td>↑ PM dose by 4 units</td>
</tr>
<tr>
<td><strong>Pre-supper or 2-hr after lunch</strong>*</td>
<td>↓ AM dose by 20–40%</td>
<td>↓ AM dose by 10–20%</td>
<td>↑ AM dose by 1 unit</td>
<td>↑ AM dose by 2 units</td>
<td>↑ AM dose by 4 units</td>
</tr>
</tbody>
</table>

*Continue SMBG as above
*Phone follow-up within 3-7 days.

**Type 1***
- Best practice is basal + bolus insulin

**Type 2***
- Continue MET, DPP4-i or GLP-1 RA
- Decrease dose or stop SU & GLN as blood glucose improves

**Precautions:**
- Always roll vial or pen to mix suspension
- Can be mixed in a syringe with rapid-acting or regular insulin. If mixing, always draw clear insulin (regular or rapid-acting), then cloudy (NPH).
- Dosage reduction may be needed with hepatic or renal impairment
- Increased risk of hypoglycemia compared to long-acting basal insulin

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.

For persistent nocturnal hypoglycemia or fasting hyperglycemia:
Consider basal/bolus therapy with long- & rapid-acting insulin; lower risk of nocturnal hypoglycemia with long-acting insulins.

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Split Mixed Dose
Short-Acting Insulin: Regular + Intermediate-Acting Insulin: NPH

Indication:
FBG consistently > 130 mg/dL while receiving basal insulin, pre-meal or 2-hr postprandial BS >180 mg/dL or A1C not at target

Start short- & intermediate-acting insulin
Type 2
- TDD 0.3-0.5 units/kg/day, 50% NPH once/day or BID, 50% regular with meals
- If TDD is >1 unit/kg/day, consider adding MET or DPP4-i or their combinations

Type 1
- TDD 0.3-0.5 units/kg/day, ⅓ to ½ NPH BID, ½ to ⅔ regular with meals; adjust proportions as necessary

Blood Glucose Pattern Adjustment
NPH & Regular BID with Breakfast & Supper

<table>
<thead>
<tr>
<th>Fasting*</th>
<th>&lt; 40 mg/dL</th>
<th>41-70 mg/dL</th>
<th>120-139 mg/dL</th>
<th>140-180 mg/dL</th>
<th>&gt; 180 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM NPH dose by 20–40%</td>
<td>PM NPH dose by 10–20%</td>
<td>PM NPH dose by 1 unit</td>
<td>PM NPH dose by 2 units</td>
<td>PM NPH dose by 4 units</td>
<td></td>
</tr>
<tr>
<td>Pre-lunch or 2-hr after breakfast*</td>
<td>↓ AM Regular dose by 20–40%</td>
<td>↓ AM Regular dose by 10–20%</td>
<td>↑ AM Regular dose by 1 unit</td>
<td>↑ AM Regular dose by 2 units</td>
<td>↑ AM Regular dose by 4 units</td>
</tr>
<tr>
<td>Pre-supper or 2-hr after lunch* **</td>
<td>↓ AM NPH dose by 20–40%</td>
<td>↓ AM NPH dose by 10–20%</td>
<td>↑ AM NPH dose by 1 unit</td>
<td>↑ AM NPH dose by 2 units</td>
<td>↑ AM NPH dose by 4 units</td>
</tr>
<tr>
<td>Bedtime or 2-hr after supper*</td>
<td>↓ PM Regular dose by 20–40%</td>
<td>↓ PM Regular dose by 10–20%</td>
<td>↑ PM Regular dose by 1 unit</td>
<td>↑ PM Regular dose by 2 units</td>
<td>↑ PM Regular dose by 4 units</td>
</tr>
</tbody>
</table>

**Blood Glucose Pattern Adjustment for Regular with meals + NPH at bedtime or BID with breakfast & supper: adjust the insulin (Regular or NPH) which most directly influences the blood glucose out of range.

Continue SMBG as above
Phone follow-up within 3-7 days
*Individualized glycemic goals may vary.

For persistent hypo- or hyperglycemia:
Consider change to basal/bolus therapy with long- & rapid-acting insulin

Type 1 *
- Best practice is long-acting basal + rapid-acting bolus insulin

Type 2 *
- Continue MET, DPP4-i or GLP-1 RA
- Stop SU or GLN
- Reduce dose or stop TZD

Precautions:
- Always roll NPH vial or pen to mix suspension
- Can be mixed in syringe. Always draw clear (regular) insulin first, then cloudy (NPH).
- Regular insulin should be injected 30 minutes before a meal
- Regular insulin may be inappropriate in geriatric patients
- Dosage reduction may be needed with hepatic or renal impairment

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Analog & Human Insulin Mixtures: Humalog Mix 75/25 (Analog), NovoLog Mix 70/30 (Analog), Humulin & Novolin 70/30 (Human), Humulin 50/50 (Human)

Indication:
FBG consistently > 130 mg/dL, premeal or 2-hr post-prandial BG > 180 mg/dL or A1C not at target

Start insulin mixture
Type 1 or 2
- TDD 0.3–0.5 units/kg/day
Type 2
- If TDD is >1 unit/kg/day, consider adding MET or DPP4-i or their combinations to regimen.

SMBG* 2-4 times/day
Phone follow-up within 5-7 days

Blood Glucose Pattern Adjustment

<table>
<thead>
<tr>
<th>Fasting*</th>
<th>&lt; 40 mg/dL</th>
<th>41-70 mg/dL</th>
<th>120-139 mg/dL</th>
<th>140-180 mg/dL</th>
<th>&gt; 180 mg/dL</th>
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</thead>
<tbody>
<tr>
<td>PM dose by 20–40%</td>
<td>PM dose by 10–20%</td>
<td>PM dose by 1 unit</td>
<td>PM dose by 2 units</td>
<td>PM dose by 4 units</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Pre-lunch*</th>
<th>AM dose by 20–40%</th>
<th>AM dose by 10–20%</th>
<th>AM dose by 1 unit</th>
<th>AM dose by 2 units</th>
<th>AM dose by 4 units</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Pre-supper*</th>
<th>AM dose by 20–40%</th>
<th>AM dose by 10–20%</th>
<th>AM dose by 1 unit</th>
<th>AM dose by 2 units</th>
<th>AM dose by 4 units</th>
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</table>

<table>
<thead>
<tr>
<th>Bedtime*</th>
<th>PM dose by 20–40%</th>
<th>PM dose by 10–20%</th>
<th>PM dose by 1 unit</th>
<th>PM dose by 2 units</th>
<th>PM dose by 4 units</th>
</tr>
</thead>
</table>

Continue SMBG as above
Phone follow-up within 3-7 days

*Individualized glycemic goals may vary.

Able to consistently achieve pre-bedtime or FBG goals, but not both or pre-lunch or pre-supper goals, but not both:
Consider long-acting basal & rapid-acting bolus insulin or NPH & Regular

Type 1*
- Best practice is long-acting basal + rapid-acting bolus insulin

Type 2*
- Continue MET, DPP4-i or GLP-1 RA
- Stop SU or GLN
- Reduce dose or stop TZD

Precautions:
- Inject Humalog Mix 75/25 & NovoLog Mix 70/30 at start of meal
- Inject 50/50 & 70/30 30 minutes prior to meal
- Always roll vial or pen to mix suspension
- Dosage reduction may be needed with hepatic or renal impairment

*Refer to product insert for comprehensive list of contraindications, precautions and side effects.

*Alternating times; vary combinations of fasting, premeal, 2-hr post-prandial & bedtime tests depending on goals.
Sources

American Diabetes Association Clinical Practice Recommendations 2014, Diabetes Care, 2014; 37, Supplement 1: S1-S155.


Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention: National Heart, Lung and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity, Circulation, 2009; 120: 1640-1645.


Prescribing Information from Pharmaceutical Companies

Lexicomp Online, Lexicomp, 1100 Terex Road, Hudson, OH 44236, www.lexi.com

CITATIONS

Pancreatitis


Pancreatic Neoplasia

## Abbreviations

### MEDICATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AG-i</td>
<td>Alpha-Glucosidase Inhibitor</td>
</tr>
<tr>
<td>BCR-QR</td>
<td>Bromocriptine QR</td>
</tr>
<tr>
<td>COLSVL</td>
<td>Colesevelam</td>
</tr>
<tr>
<td>DPP4-i</td>
<td>Dipeptidyl Peptidase-4 Inhibitor</td>
</tr>
<tr>
<td>GLN</td>
<td>Glinides</td>
</tr>
<tr>
<td>GLP-1 RA</td>
<td>Glucagon-like Peptide-1 Receptor Agonist</td>
</tr>
<tr>
<td>MET</td>
<td>Metformin</td>
</tr>
<tr>
<td>PRAML</td>
<td>Pramlintide</td>
</tr>
<tr>
<td>SGLT-2</td>
<td>Sodium Glucose Co-Transporter 2</td>
</tr>
<tr>
<td>SU</td>
<td>Sulfonylurea</td>
</tr>
<tr>
<td>TZD</td>
<td>Thiazolidinediones</td>
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### ORGANIZATIONS

<table>
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<tr>
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<th>Abbreviation</th>
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<tr>
<td>American Association of Clinical Endocrinologists</td>
<td>AACE</td>
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<tr>
<td>American Diabetes Association</td>
<td>ADA</td>
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<tr>
<td>National Cholesterol Education Program</td>
<td>NCEP</td>
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### GENERAL

<table>
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<tr>
<th>Symbol</th>
<th>Description</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ</td>
<td>Change</td>
<td>ICR</td>
</tr>
<tr>
<td>ACE</td>
<td>Angiotensin converting enzyme</td>
<td>IGT</td>
</tr>
<tr>
<td>ARB</td>
<td>Angiotensin-receptor blocker</td>
<td>ISF</td>
</tr>
<tr>
<td>BG</td>
<td>Blood glucose</td>
<td>kg</td>
</tr>
<tr>
<td>BID</td>
<td>Two times/day</td>
<td>LDL</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
<td>mcg</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
<td>MI</td>
</tr>
<tr>
<td>CDE</td>
<td>Certified diabetes educator</td>
<td>MNT</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive heart failure</td>
<td>mg</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
<td>ml</td>
</tr>
<tr>
<td>DKA</td>
<td>Diabetic ketoacidosis</td>
<td>NAFLD</td>
</tr>
<tr>
<td>dl</td>
<td>Deciliter</td>
<td>OGGT</td>
</tr>
<tr>
<td>FBG</td>
<td>Fasting blood glucose</td>
<td>pp</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational diabetes mellitus</td>
<td>PPG</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
<td>QD</td>
</tr>
<tr>
<td>GL Sx</td>
<td>Gastrointestinal symptoms</td>
<td>SMBG</td>
</tr>
<tr>
<td>GU</td>
<td>Genitourinary</td>
<td>TDD</td>
</tr>
<tr>
<td>HDL</td>
<td>High density lipoprotein</td>
<td>TID</td>
</tr>
<tr>
<td>ICR</td>
<td>Insulin to carbohydrate ratio</td>
<td>TG</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired fasting glucose</td>
<td>UTI</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired fasting glucose</td>
<td>UTI</td>
</tr>
<tr>
<td>IFG</td>
<td>Impaired fasting glucose</td>
<td>UTI</td>
</tr>
</tbody>
</table>
AACE Diabetes Management Algorithm

Glycemic Control Algorithm

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

ENTRY A1c < 7.5%
ENTRY A1c ≥ 7.5%
ENTRY A1c > 9.0%

MONOTHERAPY*
- Metformin
- GLP-1 RA
- DPP4-i
- AG-I
- SGLT-2
- TZD
- SU/GLN

If A1c > 6.5% in 3 months add second drug (Dual Therapy)

DUAL THERAPY*
- GLP-1 RA
- DPP4-i
- TZD
- SGLT-2
- Basal Insulin
- Colesevelam
- Bromocriptine QR
- AG-I
- SU/GLN

If not at goal in 3 months proceed to triple therapy

TRIPLE THERAPY*
- GLP-1 RA
- TZD
- SGLT-2
- Basal insulin
- DPP4-i
- Colesevelam
- Bromocriptine QR
- AG-I
- SU/GLN

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

LEGEND
- Few adverse events or possible benefits
- Use with caution

P R O G R E S S I O N  O F  D I S E A S E

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### Profiles of Antidiabetic Medications

<table>
<thead>
<tr>
<th></th>
<th>MET</th>
<th>DPP-4i</th>
<th>GLP-1 RA</th>
<th>TZD</th>
<th>AGI</th>
<th>COLSVL</th>
<th>BCR-QR</th>
<th>SU GLN</th>
<th>INSULIN</th>
<th>SGLT-2</th>
<th>PRAML</th>
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<td><strong>HYPO</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate/Severe</td>
<td>Moderate to Severe</td>
<td>Neutral</td>
<td>Neutral</td>
</tr>
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<td><strong>WEIGHT</strong></td>
<td>Slight Loss</td>
<td>Neutral</td>
<td>Loss</td>
<td>Gain</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Gain</td>
<td>Gain</td>
<td>Loss</td>
<td>Loss</td>
</tr>
<tr>
<td><strong>RENAL/GU</strong></td>
<td>Contraindicated Stage 3B,4,5</td>
<td>Dose Adjustment May be Necessary (Except Linagliptin)</td>
<td>Exenatide Contraindicated CrCl &lt; 30</td>
<td>May Worsen Fluid Retention</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>More Hypo Risk</td>
<td>More Hypo Risk &amp; Fluid Retention</td>
<td>Infections</td>
<td>Neutral</td>
</tr>
<tr>
<td><strong>GI Sx</strong></td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>CHF</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>CVD</strong></td>
<td>Benefit</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Safe</td>
<td>?</td>
<td>Neutral</td>
<td>Neutral</td>
<td></td>
</tr>
<tr>
<td><strong>BONE</strong></td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Moderate Bone Loss</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>Neutral</td>
<td>? Bone Loss</td>
</tr>
</tbody>
</table>

- **Few adverse events or possible benefits**
- **Use with caution**
- **Likelihood of adverse effects**

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**AACE Adding/Intensifying Insulin Algorithm**

**Algorithm for Adding/Intensifying Insulin**

**Start Basal** (long-acting insulin)
- **A1c < 8%**
  - TDD: 0.1–0.2 U/kg
- **A1c > 8%**
  - 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 4 U
  - FBG 140–180 mg/dL: add 2 U
  - FBG 110–139 mg/dL: add 1 U
- If hypoglycemia, reduce TDD by:
  - BG < 70 mg/dL: 10% – 20%
  - BG < 40 mg/dL: 20% – 40%

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

**Glycemic Goal:**
- For most patients with T2D, an A1c < 7%, fasting and premeal BG < 110 mg/dL in the 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 DPP-4i**
- **Add Prandial Insulin**
  - TDD: 0.3–0.5 U/kg
    - 50% Basal Analog
    - 50% Prandial Analog
    - Less desirable: NPH and regular insulin or premixed insulin

**Insulin titration every 2–3 days to reach glycemic goal:**
- Increase basal TDD as follows:
  - Fixed regimen: Increase TDD by 2 U
  - Adjustable regimen:
    - FBG > 180 mg/dL: add 4 U
    - FBG 140–180 mg/dL: add 2 U
    - FBG 100–139 mg/dL: add 1 U
  - Increase prandial dose by 10% for any meal if the 2-hr postprandial or next premeal glucose is > 180 mg/dL
  - Premixed: Increase TDD by 10% if fasting/premeal BG > 180 mg/dL
  - If fasting AM hypoglycemia, reduce basal insulin
  - If nighttime hypoglycemia, reduce basal and/or pre-supper or pre-evening snack short/rapid-acting insulin
  - If between meal daytime hypoglycemia, reduce previous premeal short/rapid-acting insulin

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Lifestyle optimization is essential for all patients with diabetes. This is multifaceted, ongoing, and engages the entire diabetes team. However, such efforts should not delay needed pharmacotherapy, which can be initiated simultaneously and adjusted based on the response to lifestyle efforts. The need for medical therapy should not be interpreted as a failure of lifestyle management, but as an adjunct to it.

The A1c target must be individualized, based on numerous factors, such as age, co-morbid conditions, duration of diabetes, risk of hypoglycemia, patient motivation, adherence, life expectancy, etc. An A1c of 6.5% or less is still considered optimal if it can be achieved in a safe and affordable manner, but higher targets may be appropriate and may change in a given individual over time.

Glycemic control targets include fasting and postprandial glucose as determined by self blood glucose monitoring.

The choice of therapies must be individualized based on attributes of the patient (as above) and the medications themselves (see Profiles of Anti-Diabetic Medications). Attributes of medications that affect their choice include: risk of inducing hypoglycemia, risk of weight gain, ease of use, cost, and safety impact of kidney, heart, or liver disease. This algorithm includes every FDA-approved class of medications for diabetes. This algorithm also stratifies choice of therapies based on initial A1c.

Minimizing risk of hypoglycemia is a priority. It is a matter of safety, adherence, and cost.

Minimizing risk of weight gain is a priority. It too is a matter of safety, adherence, and cost.

The algorithm provides guidance to what therapies to initiate and add, but respects individual circumstances that would make different choices.

Therapies with complementary mechanisms of action must typically be used in combinations for optimum glycemic control.

Effectiveness of therapy must be evaluated frequently until stable (e.g. every 3 months) using multiple criteria including A1c, SMBG records including both fasting and post-prandial data, documented and suspected hypoglycemia, and monitoring for other potential adverse events (weight gain, fluid retention, hepatic, renal, or cardiac disease), and monitoring of co-morbidities, relevant laboratory data, concomitant drug administration, diabetic complications, and psycho-social factors affecting patient care.

Safety and efficacy should be given higher priorities than initial acquisition cost of medications per se since cost of medications is only a small part of the total cost of care of diabetes. In determining the cost of a medication, consideration should be given to monitoring requirements, risk of hypoglycemia and weight gain, etc.

The algorithm should be as simple as possible to gain physician acceptance and improve its utility and usability in clinical practice.

The algorithm should serve to help educate the clinician as well as to guide therapy at the point of care.

The algorithm should conform, as nearly as possible, to a consensus for current standard of practice of care by expert endocrinologists who specialize in the management of patients with type 2 diabetes and have the broadest experience in outpatient clinical practice.

The algorithm should be as specific as possible, and provide guidance to the physician with prioritization and a rationale for selection of any particular regimen.

Rapid-acting insulin analogs are superior to Regular because they are more predictable.

Long-acting insulin analogs are superior to NPH insulin because they provide a fairly flat response for approximately 24 hours and provide better reproducibility and consistency both between subjects and within subjects, with a corresponding reduction in the risk of hypoglycemia.