



**BHICCI**

# Diabetes Mellitus II CPG

## Candidates for Screening

**Integrated Complex Care Patients: Check Yearly**

**Prediabetes: Check Yearly**

**No Diabetes Mellitus (DM) Risk Factors: Check at Age 45, Repeat Every 3 Years**

**Patients with BMI  $\geq$  25 and Additional Risk Factors: Check Every 3 Years**

Additional Risk Factors:

- Physical inactivity
- First-degree relative with DM
- High-risk ethnicity (e.g. African American, Latino, Native American, Asian American, Pacific Islander)
- HDL  $<$  35 mg/dL or TG  $>$  250 mg/dL
- Hypertension
- History of Gestational Diabetes
- History of Cardiovascular Disease (CVD)
- Conditions associated with insulin resistance: acanthosis nigricans, polycystic ovary syndrome

## Diagnosis: Four Options

Fasting Plasma Glucose  $\geq$  126 mg/dL

- Fasting defined as no caloric intake  $\geq$  8 hours

Random Plasma Glucose  $\geq$  200 mg/dL

- In individuals with symptoms of hyperglycemia

2 Hour OGTT (75g) Plasma Glucose  $\geq$  200 mg/dL

- Requires a fasting glucose test, consuming a 75 gram glucose drink, then repeating the glucose test in 2 hours.

HgA1c  $\geq$  6.5%

- Point of Care/rapid HgA1c testing can be used to monitor diabetes but not to make initial diagnosis

**Prediabetes defined as:**

- Fasting Plasma Glucose 100-125 mg/dL
- 2 Hour OGTT (75g) Plasma Glucose 140-199 mg/dL
- HgA1c 5.7-6.4%

## Initial Labs

- Comprehensive Metabolic Panel
- Lipid Panel
- Random Urine Microalbumin to Creatinine Ratio

## Glycemic Targets in Patients with DM

**HgA1c  $<$  7%**

- Goal for most patients. More or less stringent targets may be appropriate for individual patients if achieved without significant hypoglycemia or adverse events

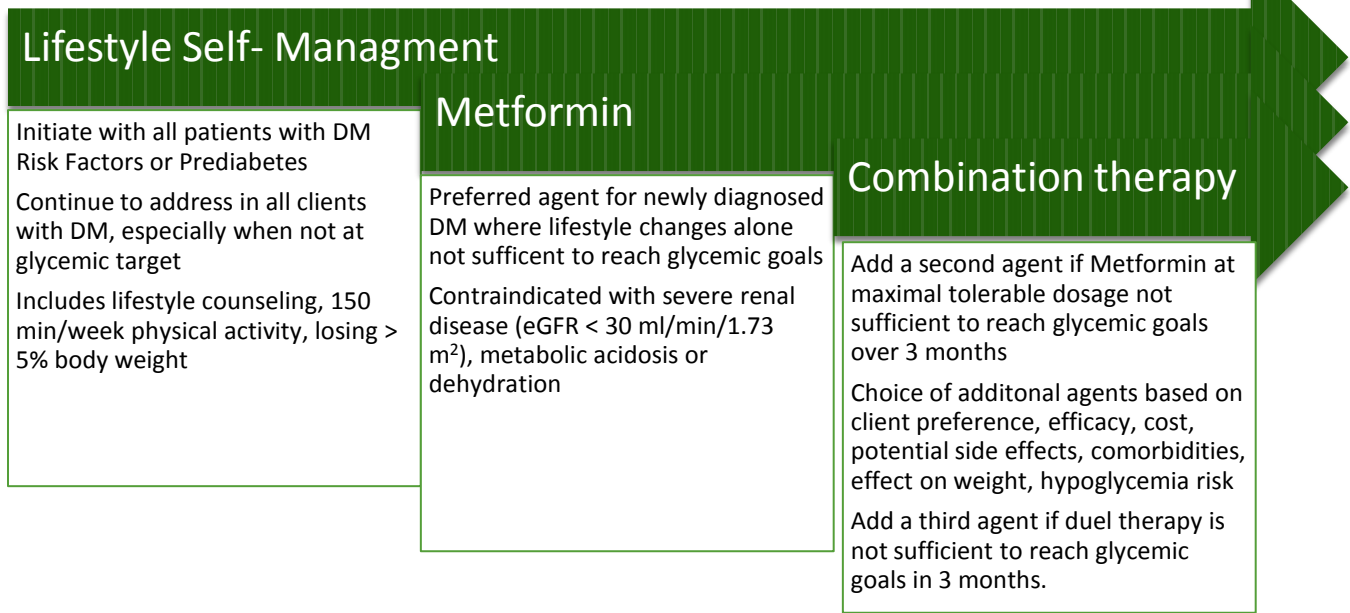
**HgA1c  $<$  6.5%**

- Short DM duration
- Long life expectancy
- DM II treated with lifestyle or metformin only
- No significant CVD/vascular complications

**HgA1c < 8%**

- Severe hypoglycemia history
- Limited life expectancy
- Advanced microvascular or macrovascular complications
- Extensive comorbidities

**Management of DM**



Each new class of noninsulin agents added to initial therapy lowers HgA1c around 0.9-1.1%.

If initial HgA1c ≥ 9%, consider starting with dual therapy of metformin + a 2<sup>nd</sup> oral agent, GLP-1 RA or basal insulin. Adding basal insulin preferred if patient is having symptoms of hyperglycemia or if there are catabolic features (e.g. weight loss, ketosis)

If initial HgA1c ≥ 10% and or fasting blood glucose ≥ 300 mg/dL, consider starting with combination of metformin + basal insulin + mealtime Insulin or GLP-1-RA

In patients with long-standing suboptimally controlled type 2 diabetes and established atherosclerotic cardiovascular disease, empagliflozin or liraglutide should be considered as they have been shown to reduce cardiovascular and all-cause mortality when added to standard care. Ongoing studies are investigating the cardiovascular benefits of other agent sin these drug classes.

**Start with Monotherapy unless:**

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

**Monotherapy**

**Metformin**

**Lifestyle Management**

<b>EFFICACY*</b>	high
<b>HYPO RISK</b>	low risk
<b>WEIGHT</b>	neutral/loss
<b>SIDE EFFECTS</b>	GI/lactic acidosis
<b>COSTS*</b>	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

**Dual Therapy**

**Metformin +**

**Lifestyle Management**

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
<b>EFFICACY*</b>	high	high	intermediate	intermediate	high	highest
<b>HYPO RISK</b>	moderate risk	low risk	low risk	low risk	low risk	high risk
<b>WEIGHT</b>	gain	gain	neutral	loss	loss	gain
<b>SIDE EFFECTS</b>	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
<b>COSTS*</b>	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

**Triple Therapy**

**Metformin +**

**Lifestyle Management**

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin*	or GLP-1-RA	or Insulin*	or GLP-1-RA
or Insulin*	or Insulin*		or Insulin*		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

**Combination Injectable Therapy (See Figure 8.2)**

**Figure 8.1—Antihyperglycemic therapy in type 2 diabetes: general recommendations.** The order in the chart was determined by historical availability and the route of administration, with injectables to the right; it is not meant to denote any specific preference. Potential sequences of antihyperglycemic therapy for patients with type 2 diabetes are displayed, with the usual transition moving vertically from top to bottom (although horizontal movement within therapy stages is also possible, depending on the circumstances). DPP-4-i, DPP-4 inhibitor; fxs, fractures; GI, gastrointestinal; GLP-1 RA, GLP-1 receptor agonist; GU, genitourinary; HF, heart failure; Hypo, hypoglycemia; SGLT2-i, SGLT2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione. \*See ref. 21 for description of efficacy and cost categorization. †Usually a basal insulin (NPH, glargine, detemir, degludec). Adapted with permission from Inzucchi et al. (21).

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**Pharmacologic Options Available on IEHP Formulary**

Biguanide	
Mechanism	Decreases hepatic glucose production, increases peripheral glucose sensitivity
Covered options	Metformin (Glucophage)

Cautions	Contraindicated with eGFR < 30, metabolic acidosis or dehydration
<b>Sulfonylurea (SU)</b>	
Mechanism	Increases endogenous insulin secretion, effect not durable as disease progresses
Covered options	Glimepiride Glipizide Glipizide ER
Cautions	Hypoglycemia, weight gain. Glipizide and glimepiride preferred with renal disease
<b>Thiazolidinedione (TZD)</b>	
Mechanism	Insulin sensitizer
Covered options	Pioglitazone (Actos)
Cautions	Avoid with liver disease, congestive heart failure or history of bladder cancer
<b>Dipeptidyl Peptidase 4 Inhibitor (DPP-4 Inhibitor)</b>	
Mechanism	Enhances incretin activity which increases glucose dependent increase in insulin secretion
Covered options	Alogliptin (Nesina) ± Linagliptin (Tradjenta)¥ Sitagliptin (Januvia) ± Saxagliptin (Onglyza)¥ Jentadueto (linagliptin, metformin)¥ Janumet (sitagliptin, metformin) and Janumet XR (sitagliptin, metformin XR) ±
Cautions	Caution with eGFR < 50, avoid in patients at risk for pancreatitis
<b>Sodium-Glucose Cotransporter 2 Inhibitor (SGLT-2)</b>	
Mechanism	Inhibits SGLT-2 in kidney, results in glycosuria
Covered options	Canagliflozin (Invokana) ± Dapagliflozin (Farxiga)¥ Empagliflozin (Jardiance)¥ Invokamet (canagliflozin, metformin) ±
Cautions	Genitourinary infections, dehydration, risk of diabetic ketoacidosis
<b>Glucagon-like Peptide-1 Receptor Agonist (GLP-1-RA)</b>	

Mechanism	Enhances incretin activity which increases glucose dependent increase in insulin secretion, slows gastric emptying and increases satiety.
Covered options	Albiglutide (Tanzeum)¥ Exenatide (Byetta)¥ Liraglutide (Victoza)¥ Dulaglutide (Trulicity)¥
Cautions	Caution with eGFR < 50. Nausea, vomiting, diarrhea in the first month. Avoid in patients with history of pancreatitis or family history of medullary thyroid cancer or Multiple Endocrine Neoplasia (MEN).
<b>Insulin</b>	
Mechanism	Corrects insulin deficiency, increases peripheral glucose uptake and decreases hepatic glucose output
Covered options	<p><b>Short-acting Insulin (Regular)</b></p> <ul style="list-style-type: none"> <li>• Insulin Regular (Humulin R) U-100 vial, U-500 vial</li> <li>• Insulin Regular (Novolin R) U-100 vial</li> </ul> <p><b>Rapid-acting Insulin</b></p> <ul style="list-style-type: none"> <li>• Glulisine (Apidra) U-100 vial, prefilled syringe** and pen*</li> <li>• Lispro (Humalog) U-100 vial, cartridge* and pen*</li> <li>• Aspart (Novolog) U-100 vial, penfill*, and pen*</li> </ul> <p><b>Intermediate-acting Insulin (NPH)</b></p> <ul style="list-style-type: none"> <li>• Isophane Insulin (Humulin N) U-100 vial and pen*</li> <li>• Isophane Insulin (Novolon N) U-100 vial</li> </ul> <p><b>Long-acting Insulin Treatments</b></p> <ul style="list-style-type: none"> <li>• Glargine Insulin (Lantus) U-100 vial and pen</li> </ul> <p><b>Combo Insulin (Mix)</b></p> <ul style="list-style-type: none"> <li>• Lispro protamine + Lispro (Humalog Mix 50-50) 100-U vial and pen *</li> <li>• Lispro protamine + Lispro (Humalog Mix 75-25) 100-U vial and pen*</li> <li>• Aspart protamine + Aspart (Novolog Mix 70-30) 100-U vial and pen*</li> <li>• Isophane Insulin + Regular Insulin (Humulin Mix 70/30) 100-U vial and pen*</li> <li>• Isophane Insulin + Regular Insulin (Novolin Mix 70/30) 100-U vial</li> </ul>
Cautions	Hypoglycemia, especially the shorter and rapid acting formulations. Weight gain.

± available with step therapy; ¥ available with PA, click “Medi-Cal PA Drug Criteria Summary Table” on the following IEHP webpage for specific requirements: <https://ww3.iehp.org/en/providers/pharmaceutical-services/clinical-information/pa-drug-treatment-criteria/>

\* only available on MCAL formulary

\*\* only available on MCR formulary

Preventing Complications of DM

<b>Hyperlipidemia</b>	<ul style="list-style-type: none"> <li>• See separate Clinical Practice Guideline</li> </ul>
<b>Hypertension</b>	<ul style="list-style-type: none"> <li>• See separate Clinical Practice Guideline</li> </ul>
<b>Aspirin 76-162 mg/day</b>	<ul style="list-style-type: none"> <li>• Consider aspirin therapy (75-162mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes who are at increased cardiovascular risk. This includes most men and women with diabetes aged <math>\geq 50</math> years who have at least one additional major risk factor (family history of premature atherosclerotic cardiovascular disease, hypertension, dyslipidemia, smoking or albuminuria) and are not at increased risk of bleeding.</li> </ul>
<b>Nephropathy Screening</b>	<ul style="list-style-type: none"> <li>• Annual random urine Microalbumin to Creatinine ratio and eGFR</li> </ul>
<b>Retinopathy Screening</b>	<ul style="list-style-type: none"> <li>• Biannual retinal scanning</li> </ul>
<b>Neuropathy Screening</b>	<ul style="list-style-type: none"> <li>• Annual foot exam including 10-g monofilament + pinprick, temperature or vibration sensation testing</li> </ul>

American Diabetes Association. Standards of medical care in diabetes—2017. Diabetes Care. 2017;40(suppl 1): S1-S132.