

## GLYCEMIC CONTROL OF DIABETES MELLITUS STANFORD COORDINATED CARE

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**PURPOSE:** To enhance collaborative patient care by referral of patients with a diagnosis of type 1 or type 2 diabetes (DM) to be co-managed by the clinical pharmacist, pharmacy resident or RN following this standardized protocol.

**ACKNOWLEDGEMENT:** This protocol is adapted from one developed at Santa Clara Valley Medical Center in San Jose, CA by Tyler Aguinaldo, MD, Director of Diabetes & Metabolism Center; Dorleen Von Raesfeld, MSN, RN, CDE, Assistant Nurse Manager and Susan Yu, Clinical Pharmacist, CDE, Chronic Care Management. We gratefully acknowledge their willingness to share this protocol.

### I. CONTENT:

#### A. INCLUSION CRITERIA

1. Adult 18 years and older.
2. Non-pregnant adult.
3. **Diagnosis of diabetes mellitus (DM), by American Diabetes Association (ADA) criteria:**
  - a. **A1C  $\geq$  6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.\***
  - OR**
  - b. **Fasting plasma glucose (FPG)  $\geq$  126 mg/dL (11.1 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.\***
  - OR**
  - c. **Two (2) hour plasma glucose  $\geq$  200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT). The test should be performed as described by World Health Organization, using a glucose load containing the equivalent of 75 grams of anhydrous glucose dissolved in water.\***
  - d. **Classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose  $\geq$  200 mg/dL (11.1 mmol/l). The classic symptoms of diabetes include polyuria, polydipsia, polyphagia and unexpected weight loss.**

**\*In the absence of unequivocal hyperglycemia, criteria a-c should be confirmed by repeat testing on a different day.**

4. **For suspected type 1 diabetes or LADA (Latent Autoimmune Diabetes of Adulthood), order anti-GAD antibody to confirm the diagnosis (unless diagnosis is already confirmed and/or patient has classic juvenile-onset type 1 diabetes).**  
**Factors that may raise suspicion for type 1 diabetes or LADA include:**
  - a. **Age of onset <35 years of age**
  - b. **BMI < 25 kg/m<sup>2</sup>**
  - c. **History of DKA**
  - d. **Personal or family history of auto-immune disease**
5. For patients with known type 1 diabetes or LADA, the patient may be managed per the glycemic protocols with MD approval upon initiation of the protocol.

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**B. EXCLUSION CRITERIA**

1. See specific protocol (A-M) for protocol-specific exclusion criteria

**C. ASSESSMENT**

1. SUBJECTIVE

- a. Review medication list (including Rx, OTC, and herbal supplements) and dietary compliance and adherence
- b. Assess the occurrence of any adverse reactions
- c. Set individualized A1C goal (usually less than 7.0%)
- d. Set individualized SMBG goal (usually 90-130 mg/dL fasting and pre-meal, less than 180 mg/dL postprandial)
- e. Self-monitoring blood glucose
- f. Management principles on complications and prevention
- g. Medical nutrition therapy
- h. Weight management
- i. Physical activity
- j. Set patient goals including self-management goals

2. OBJECTIVE

- a. Vital signs and blood glucose reading, BMI, etc.
- b. A1C (within 3 months)
- c. BMP (within 3 months)
- d. Hepatic function panel (within 1 year)
- e. Fasting lipid panel, (TC, TG, HDL-C, LDL-C) (within 1 year)
- f. TSH (within 1 year)
- g. Body mass index (kg/m<sup>2</sup>) (1 kg = 2.2 pounds; 1 inch = 0.0254 meters)
- h. Urine microalbumin (within 1 year)
- i. Serum beta-hydroxy-butyrate (if indicated per urgent hyperglycemia protocol)
- j. Anti-GAD antibody (one-time only, for suspected DM1/LADA)

**D. INSTRUCTIONS FOR PROTOCOLS**

1. Ascertain patient meets diagnostic criteria for diabetes, attempt to determine type 1 or type 2.
2. Obtain baseline evaluation parameters as above.
3. Interview and evaluate patient, review goals and reinforce lifestyle therapies at all visits.
4. Start Protocol.

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**PROTOCOL – NON-ACUTE PATHWAY**

<b>INCLUSION SUB-CRITERIA</b>	<ol style="list-style-type: none"><li>1. Fasting (self-monitoring blood glucose) SMBG <math>\leq</math> 250 mg/dL in <math>\geq</math> 80% of values</li><li>2. Random/post prandial SMBG <math>\leq</math> 350 mg/dL in <math>\geq</math> 80% of values</li></ol>
<b>EXCLUSION SUB- CRITERIA</b>	<ol style="list-style-type: none"><li>1. Evidence of ketosis, clinical (nausea/vomiting/confusion) or biochemical (urine/blood)</li><li>2. Severe symptoms of hyperglycemia (e.g. polyuria Q2hr or more frequent, polydipsia &gt; 3L/day, nocturia &gt;3x or acute visual change)</li></ol>
<b>ALGORITHM</b>	<ol style="list-style-type: none"><li>1. Obtain baseline evaluation parameters</li><li>2. Interview and evaluate patient – review goals and reinforce lifestyle therapies at all visits</li><li>3. Start at Protocol A (Metformin)</li><li>4. Proceed to/add Protocol B (glyburide/glipizide) if necessary</li><li>5. Proceed to/add Protocol C (pioglitazone) if necessary</li><li>6. Directly proceed to insulin protocols for all patients with type 1 diabetes or LADA</li><li>7. Consider proceeding directly to insulin protocols for the following situations:<ol style="list-style-type: none"><li>a. Fasting SMBG &gt; 250 mg/dL in &gt; 20% of values and/or random/post prandial SMBG &gt; 350 mg/dL in <math>\geq</math> 20% of values.</li><li>b. A1C &gt; 10%</li><li>c. Symptoms of hyperglycemia</li></ol></li></ol>

**PROTOCOL – ACUTE PATHWAY: HYPERGLYCEMIA**

<b>INCLUSION SUB-CRITERIA</b>	<ol style="list-style-type: none"><li>1. Fasting SMBG &gt; 250 mg/dL in &gt; 20% of values and/or random/post prandial SMBG &gt; 350 mg/dL in <math>\geq</math> 20% of values.</li></ol>
<b>ALGORITHM</b>	<ol style="list-style-type: none"><li>1. Obtain baseline evaluation parameters.</li><li>2. Proceed to Protocol H (Urgent Hyperglycemia Protocol) if clinic random/post prandial SMBG is &gt; 350 mg/dL or &gt; 250 mg/dL with symptoms of hyperglycemia (polyuria/polydipsia/nausea/blurred vision), ketosis (nausea/vomiting/confusion/dehydration), or other medical symptoms.</li><li>3. Interview and evaluate patient, review goals, and reinforce lifestyle therapies at all visits.</li><li>3. Regarding acute disease, contact primary care MD.</li><li>4. Consider same-day urgent/emergency level of care, if appropriate.</li><li>5. Consider proceeding directly to insulin protocols.</li></ol>

**PROTOCOL – ACUTE PATHWAY: HYPOGLYCEMIA**

<b>INCLUSION SUB-CRITERIA</b>	<ol style="list-style-type: none"><li>1. Ascertain patient meets diabetes diagnostic criteria.</li><li>2. Fasting SMBG and/or random SMBG &lt; 80 mg/dL in <math>\geq</math> 20% of values.</li><li>3. Any severe hypoglycemia in the past 3 months as defined by a blood sugar less than 60 mg/dL causing disorientation OR any severe hypoglycemia requiring assistance of another person.</li></ol>
<b>ALGORITHM</b>	<ol style="list-style-type: none"><li>1. Obtain baseline evaluation parameters.</li><li>2. Proceed to Protocol I (Urgent Hypoglycemia Protocol) if clinic random/post prandial SMBG is &lt; 80 mg/dL.</li><li>2. Interview and evaluate patient, review goals, and reinforce lifestyle therapies at all visits.</li><li>3. Regarding acute disease, contact primary care MD.</li></ol>

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**PROTOCOL A - METFORMIN**

- INCLUSION CRITERIA**
1. Patients with type 2 diabetes
  2. HbA<sub>1c</sub> > 0.5% above individualized goal and/or SMBG > 20 mg/dL above individualized goals
  3. Therapy should be temporarily discontinued for 48 hours in patients undergoing radiologic studies involving intravenous contrast and for any surgical procedures
- EXCLUSION CRITERIA**
1. Patients with type 1 diabetes
  2. Clinically significant liver disease (ALT, AST >2.5 times ULN, and/or evidence of cirrhosis)
  3. Renal impairment: creatinine >1.4 mg/dL women, >1.5 mg/dL men or abnormal creatinine clearance (<70 ml/minute) from any cause
  4. Hypersensitivity to metformin
  5. Unstable or acute CHF
  6. Current heavy alcohol use (> 3 drinks/day)
  7. Acute or chronic metabolic acidosis with or without coma (including diabetic ketoacidosis)
  8. Risk for hypoxemia (e.g. heart failure, respiratory failure, acute MI, acute CHF & sepsis)
- CAUTIONS:**
1. Caution: if patient is on the following list of medications that may cause lactic acidosis, please contact MD prior to initiating metformin: abacavir, didanosine, emtricitabine, entecavir, lamivudine, tenofovir, zalcitabine, zidovudine.
  2. Caution: pre-menopausal/anovulatory females; may result in a resumption of ovulation, increasing risk of pregnancy. Discuss contraceptive measures. Inform MD if patient is or plans to become pregnant.
- ALGORITHM**
1. Start Metformin 500 mg once daily with largest meal **x 1 week** then increase to 500mg BID if tolerated.
  2. Discuss GI side effects and review for symptoms when increasing dosage.
  3. If not at SMBG goals after one to two weeks, increase dose, as follows: start metformin 500 mg BID for one to two weeks, then increase to 1000 mg QAM and 500 mg QPM with food for one week, then increase to 1000 mg BID with food (maximum recommended dose).
  4. If patient is on metformin 850mg BID and not at glycemic goal, increase to 1000mg BID.
  5. If still not at glycemic goal after two months, continue metformin therapy and go to Protocol B (glyburide/glipizide). If Protocol B (glyburide/glipizide) is contraindicated, or already on Protocol B (glyburide/glipizide), then add Protocol C (pioglitazone) **or consider Protocol D (Exenatide)**. If Protocol C (pioglitazone) or **Protocol D (Exenatide)** is contraindicated, or already on Protocol C (pioglitazone) or **Protocol D (Exenatide)**, continue to insulin protocols.
  6. Monitor ALT, AST at baseline (within one year) and periodically thereafter
  7. Monitor creatinine at baseline (within 6 months) and at least every 6 months thereafter.
  8. Discontinue metformin and notify MD if any of the following:
    - ALT or AST > 2.5 times ULN
    - Creatinine > 1.4 mg/dL women, > 1.5 mg/dL men or abnormal creatinine clearance (<70 mL/minute)
    - Ketosis
    - Severe diarrhea 5 times per day or > 400 mL/day
    - Development of any condition listed in contraindications
  4. Notify MD if any of following:
    - Flatulence, abdominal pain, nausea, bothersome to patient, at lowest starting dose
    - Radiologic contrast dye studies, withhold medication 24 hours prior to procedure
    - Initiation of a new medication
    - Any SMBG < 80 mg/dL ≥ 3 times a week
    - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of

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values, then proceed to Acute Pathway: Hyperglycemia Protocol.

- Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
- Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

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**PROTOCOL B – GLYBURIDE/GLIPIZIDE**

**INCLUSION  
CRITERIA**

1. Patients with type 2 diabetes
2. Creatinine < 2.0 mg/dL
3. HbA<sub>1c</sub> > 0.5% above individualized goal and/or SMBG > 20 mg/dL above individualized goals
4. Consider glipizide if elderly (≥ 65 years old) or creatinine 1.4 to 2.0 mg/dL

**EXCLUSION  
CRITERIA**

1. Patients with type 1 diabetes
2. Ketosis
3. Allergy to sulfonamides
4. Hypersensitivity to sulfonylureas
5. Pregnancy

**ALGORITHM**

1. If creatinine < 1.4 mg/dL start glyburide 5 mg QAM (if lean [BMI < 25kg/m<sup>2</sup>] or elderly [age > 65 years old] start at lower dose of 2.5 mg QAM).
2. Monitor creatinine at least every 6 months.
2. If not at SMBG goal after one to two weeks: When pre-dinner blood glucose is controlled but the fasting is still elevated, add pre-dinner dose of this agent: increase dose to 5 mg BID or 2.5 mg BID if initial starting dose was 2.5 mg.
3. If goals are not reached, increase dose each week with eventual goal of 10 mg QAM and 10 mg QPM.
4. Start glyburide 2.5 or 5 mg QAM, if not at SMBG goal after one to two weeks, then increase to 2.5 or 5 mg BID, if not at SMBG goal after one to two weeks, then increase to 7.5 or 10 mg QAM and 5 mg QPM, if not at SMBG goal after one to two weeks, then increase to 7.5 or 10 mg BID (maximum dose is 10 mg BID).
5. If creatinine from 1.4 to 2.0 mg/dL, start glipizide 5 mg QAM 30 minutes before meal. Geriatric (age > 65 years old) or patients with liver disease may need to start at lower dose of 2.5 mg daily. Titrate dose in 2.5 mg or 5 mg increments every several days (single or divided doses). Maximum dose of glipizide is 40 mg/day.
5. If still not at glycemic goal after two months, continue sulfonylurea therapy and add Protocol A (metformin). If Protocol A (metformin) is contraindicated, or already on Protocol A (metformin), then add Protocol C (pioglitazone) or consider Protocol D (Exenatide). If Protocol C (pioglitazone) or Protocol D (Exenatide) is contraindicated, or already on Protocol C (pioglitazone) or Protocol D (Exenatide), continue to insulin protocols.
6. If not at glycemic goal and taking ≥ 3 DM drugs, order c-peptide with correlating (non-fasting) blood glucose. If C-peptide < 1.5 when BG > 200 mg/dL, may discontinue sulfonylurea. Proceed to insulin protocols.
7. Decrease dose of sulfonylurea and notify MD if any of following:
  - Hypoglycemia (SMBG < 80mg/dL); severe hypoglycemia (SMBG < 60 mg/dL) or any hypoglycemic episode requiring assistance, nocturnal hypoglycemia, frequent (> 2 episodes/week) symptomatic hypoglycemia or prolonged (> 2 hours per episode) hypoglycemia.

May use the following to decrease dose of sulfonylurea (SU):

  1. If hypoglycemia occurs from HS to AM, then halve PM dose of SU.
  2. If hypoglycemia occurs from noon to PM, then halve AM dose of SU.
  3. If hypoglycemia occurs throughout day, halve both the AM and PM doses of SU.
  4. If patient is on a total of ≤ 2.5 mg/day of SU and having hypoglycemia, discontinue SU entirely.
  5. For any episodes of severe hypoglycemia, contact MD; consider discontinuing SU entirely.
  6. For new hypoglycemia, check BMP if not done within the past month to assess for renal insufficiency. Notify MD if creatinine has increased > 50% above baseline.

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- Creatinine > 2.0 mg/dL
- Discontinue SU if patient develops allergic reaction to medication.
- Initiation of a new medication
- Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol.
- Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
- Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

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**PROTOCOL C – PIOGLITAZONE**

- INCLUSION CRITERIA**
1. Patients with type 2 diabetes
  2. HbA<sub>1c</sub> > 0.5% above individualized goal and/or SMBG > 20 mg/dL above individualized goals
- EXCLUSION CRITERIA**
1. Patients with type 1 diabetes
  2. Current ketosis
  3. Hypersensitivity to pioglitazone
  4. New York Heart Association Class III/IV heart failure
  5. Clinically significant liver disease (ALT, AST >2.5 times ULN, and/or evidence of cirrhosis)
  6. Pregnancy
  7. **Avoid use in patients with active bladder cancer**
- CAUTIONS**
1. Use with caution and monitor closely for adverse effects in the following patients:
    - a. NYHA Class I or II heart failure
    - b. Pre-existing macular edema or diabetic retinopathy
    - c. Pre-menopausal/anovulatory females; may result in a resumption of ovulation, increasing risk of pregnancy. Discuss contraceptive measures. Inform MD if patient is or plans to become pregnant
    - d. Pre-existing lower extremity edema
    - e. Fractures in women, particularly in lower limb and distal upper limb
    - f. **Consider risks vs. benefits prior to initiating therapy in patients with a history of bladder cancer**
- ALGORITHM**
1. Start Pioglitazone 15 mg daily.
  2. If not at SMBG goals after six to eight weeks, increase dose, with eventual goal of 45 mg daily.
  3. Monitor ALT and AST at baseline, 12 weeks after any dose adjustment, then yearly thereafter.
  4. If still not at glycemic goal after three months, continue TZD therapy and add Protocol A (metformin). If Protocol A (metformin) is contraindicated, or already on Protocol A (metformin), then add Protocol B (glyburide/glipizide). If Protocol B (glyburide/glipizide) is contraindicated or already on Protocol B (glyburide/glipizide), **consider Protocol D (exenatide)** or continue to insulin protocols.
  5. Notify MD if any of the following:
    - ALT or AST > 2.5 times ULN
    - Congestive heart failure, (New York Heart Association) NYHA class III or IV
    - Ketosis
    - Development of allergic reaction to medication
    - New and/or worsening edema
    - Initiation of a new medication
    - Any SMBG < 80 mg/dL ≥ 3 times a week
    - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol.
    - Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
    - Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

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**PROTOCOL D – EXENATIDE (BYETTA)**

- INCLUSION CRITERIA**
1. Patients with type 2 diabetes
  2. HbA<sub>1c</sub> > 0.5% above individualized goal and/or SMBG > 20 mg/dL above individualized goals
  3. BMI > 27.0 kg/m<sup>2</sup>.
  4. Glycemic targets not achieved, AND/OR have contraindications AND/OR side effects with at least two oral diabetes medication classes (metformin, TZD, SU).
- EXCLUSION CRITERIA**
1. Patients with type 1 diabetes
  2. Creatinine clearance <30 mL/minute
  3. Gastroparesis
  4. Pregnancy or lactation
  5. Hypersensitivity to exenatide
  6. Concomitant use of prandial insulin
  7. HbA<sub>1c</sub> > 10%
  8. History of pancreatitis
- ALGORITHM**
1. Start exenatide 5 mcg SC twice daily within 60 minutes prior to morning and evening meal (or prior to the 2 main meals of the day, approximately > 6 hours apart).
  2. After 1 month, dose may be increased to 10 mcg SC twice daily, if not at SMBG goals.
  3. If patient is on metformin and/or a TZD, simply add exenatide to the oral medication(s).
  4. If patient is on a sulfonylurea, initially halve the dose of the sulfonylurea when starting exenatide. You may eventually resume the prior dose of the sulfonylurea if not at SMBG goals.
  5. If patient is on basal insulin, initially reduce the dose by 20% when starting exenatide. You may eventually increase the dose of basal insulin if not at SMBG goals.
  6. Caution patients that the most common adverse reactions are gastrointestinal-related (usually nausea), but are generally mild and generally abate after days to weeks on the medication.
  7. GI symptoms can be minimized by injecting the medication immediately prior to the meal when starting the medication and/or when increasing the dose.
  8. Once GI symptoms resolve, instruct the patient to gradually delay the meal up to one hour after the injection to optimize the anorectic effects of the medication.
  9. If still not at glycemic goal after three months, continue exenatide therapy and add Protocol A (Metformin). If Protocol A (Metformin) is contraindicated, or already on Protocol A (Metformin), then add Protocol B (Glyburide/Glipizide). If Protocol B (Glyburide/Glipizide) is contraindicated or already on Protocol B (Glyburide/Glipizide), then add Protocol C (Pioglitazone). If Protocol C (Pioglitazone) is contraindicated or already on Protocol C (Pioglitazone), then continue to insulin protocols.
  10. Monitor creatinine at baseline (within 6 months) and at least every 6 months thereafter.
  11. Discontinue exenatide and notify MD if any of the following:
    - Creatinine clearance <30 mL/minute
    - Ketosis
    - Severe GI symptoms
    - Development of any condition listed in contraindications
  12. Notify MD if any of following:
    - Initiation of a new medication
    - Any SMBG < 80 mg/dL ≥ 3 times a week
    - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol and insulin protocols

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- Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
- Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

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**PROTOCOL E – DAILY INSULIN GLARGINE**

- INCLUSION SUB-CRITERIA** 1. HbA<sub>1c</sub> is greater than > 0.5 above individualized fasting goal and/or SMBG 20 mg/dL mg/dL above individualized goals
- ALGORITHM**
1. If transitioning from NPH BID to daily glargine, take 80% of total daily NPH dose as a new total daily dose (TDD) of glargine
  2. If BMI less than or equal to 25 kg/m<sup>2</sup>, start 10 units glargine 10 units SQ (QHS or QDAY). Continue oral glycemic medications.
  3. If BMI is greater than 25 kg/m<sup>2</sup>, start glargine 15 units SQ (QHS or QDAY). Continue oral glycemic medications.
  4. Monitor QAM fasting SMBG at least 6 times a week. Other monitoring as outlined in monitoring guidelines or as specified by the provider.
  5. Standardize carbohydrate intake to <30 gm at bedtime, if bedtime snack is absolutely necessary.
  6. Patient and provider to review SMBG values every 1-7 days either by phone or in person if patient is in acute pathway. Review every 1-12 weeks if patient is in non-acute pathway.
  7. If QAM SMBG < 80 mg/dL on ≥ 2 episodes per 7 days, decrease insulin by 10-20% of dose.
  8. If QAM SMBG > 80 mg/dL on ≥ 2 episodes per 7 days, follow titration schedule based on average QAM SMBG:
    - 80 - 130 mg/dL: no change in insulin dose
    - 131- 150 mg/dL: increase glargine by 2 units SQ
    - 151- 170 mg/dL: increase glargine by 4 units SQ
    - 171- 190 mg/dL: increase glargine by 6 units SQ
    - 191 mg/dL or greater: increase glargine by 8 units SQ
  9. If patient has type 2 diabetes, is agreeable and deemed capable to self-titrate basal insulin, give the following instructions:
    - a. Measure AM fasting BG daily for 3 days.
    - b. If the average AM fasting BG measures >130 mg/dL, then increase basal insulin dose by 2 units.
    - c. If the average AM fasting BG measures 90-130 mg/dL, then no change in basal insulin dose.
    - d. If the patient has any BG's <80 mg/dL or any symptoms of hypoglycemia, then decrease basal insulin dose by 2 units and care coordinator or pharmacist.
  10. Notify Pharmacist/CDE if any of following:
    - Any SMBG < 80 mg/dL ≥ 3 times a week
    - Initiation of a new medication
    - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol.
    - Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
    - Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)
  11. If glargine daily dose exceeds 30 units and still not reaching glycemic target, consider proceeding to an insulin regimen that includes a prandial insulin component
  12. If glargine daily dose > 100 units, split dose into BID schedule.

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### PROTOCOL F – DAILY GLARGINE + PRANDIAL INSULIN (INSULIN LISPRO, ASPART, GLULISINE) QAC

- INCLUSION SUB-CRITERIA**
1. HbA<sub>1c</sub> > 0.5% above individualized goal and/or SMBG > 20 mg/dL above individualized goal.
  2. Consider in patients who are currently taking basal insulin only with sub-optimal control.
  3. Consider in patients who demonstrate consistent SMBG at least 3 times per day.
  4. Consider in patient who currently take NPH insulin and have frequent ( $\geq 1x$  per week) early AM hypoglycemia that limits overall BS control.
- ALGORITHM**
1. If transitioning from Protocol E (Glargine at bedtime):
    - a. Take 100-120% of total current daily glargine dose as a new total daily dose (**TDD**) of insulin.
    - b. Split TDD into 50% glargine to be given at bedtime and 50% prandial insulin to be split into three doses to be given QAC.
    - c. Prandial insulin doses can be split evenly between the three meals if there is roughly an equivalent carbohydrate content for each meal.
    - d. Prandial insulin doses can be split unevenly between the three meals such that the higher doses are given at meals that contain the highest carbohydrate content.
    - e. If patient is taking fewer than 3 prandial injections/day, starting prandial dose per meal should be calculated as if the patient were taking 3 meals/day.
    - f. Patients on fixed-doses of scheduled prandial insulin should be referred to the diabetes educator for consistent carbohydrates.
    - g. If patient is interested and motivated to learn how to count carbohydrates and administer short-acting insulin based on a personalized carbohydrate ratio, refer to diabetes educator for 1:1 instruction.
  2. If transitioning from another insulin regimen that includes a prandial insulin component:
    - a. Take 100-120% of total current daily insulin as a new total daily dose (**TDD**) of insulin.
    - b. Follow steps b-g from above.
  3. If starting anew:
    - a. Calculate starting total daily dose (TDD) of insulin = 0.4 units/kg of body weight (for type 2), or 0.2 units/kg (for type 1 or insulin-sensitive patients)
    - b. Follow steps b-g from step 1 above.
  4. For some patients, you may consider starting once or twice daily doses of prandial insulin prior to the largest meal(s). Use the same doses for the prandial insulin as you would have delivered if the patient were on a TID prandial insulin regimen. (e.g. for a 75 kg patient, initial starting dose for patient with type 2 diabetes would be 30 units/day, split into 15 units glargine, 5 units prandial insulin QAC TID. For a patient who prefers a single dose of prandial insulin before dinner, start with 5 units QPM)
  5. Monitor blood glucose QAC and at bedtime daily. Also encourage occasional post-prandial SMBG (2 hours after meal), especially if overall control sub-optimal or erratic.
  6. If not counting carbohydrate, standardize carbohydrate intake for meals during day. Patient and provider to review SMBG values every 1-3 days either by phone or in person if patient is in acute pathway. Review every 3-7 days until adequate glycemic control has been reached.
  7. **For bedtime dose of insulin glargine:**
    - a. If QAM (fasting) SMBG < 90 mg/dL on  $\geq 2$  episodes per 7 days, decrease insulin glargine by 10-20% at bedtime
    - b. If QAM (fasting) SMBG > 90 mg/dL on  $\geq 2$  episodes per 7 days, follow titration schedule based on average QAM SMBG:
      - 90 - 130 mg/dL: no change in insulin dose
      - 131- 150 mg/dL: increase insulin glargine by 10% SQ HS
      - 151- 190 mg/dL: increase insulin glargine by 10-20% SQ HS

## GLYCEMIC CONTROL OF DIABETES MELLITUS STANFORD COORDINATED CARE

→ 191- 240 mg/dL: increase insulin glargine by 10-30% SQ HS

→ >240 mg/dL: increase insulin glargine by 10-40% SQ HS

**Note:** If HS -> AM BS trends show a consistent overnight drop in BS > 30 mg/dL, AND the patient is experiencing nocturnal and/or AM hypoglycemia, HS Lantus dose may be excessive and may need to be decreased. Consult with MD, as patient may benefit by more prandial insulin with dinner.

### 8. For prandial insulin doses:

- a. If pre-lunch SMBG < 90 mg/dL on  $\geq 2$  episodes per 7 days, decrease short-acting insulin dose by 10-20% at QAM
- b. If pre-lunch SMBG > 90 mg/dL on  $\geq 2$  episodes per 7 days, follow titration schedule based on average pre-lunch SMBG:
  - 90 - 130 mg/dL: no change in insulin dose
  - 131- 150 mg/dL: increase short-acting insulin dose by 10% SQ at breakfast
  - 151- 190 mg/dL: increase short-acting insulin dose by 10-20% SQ at breakfast
  - 191- 240 mg/dL: increase short-acting insulin dose by 10-30% SQ at breakfast
  - >240 mg/dL: increase short-acting insulin dose by 10-40% SQ at breakfast
- c. If pre-dinner SMBG < 90 mg/dL on  $\geq 2$  episodes per 7 days, decrease short-acting insulin dose by 10-20% at lunch.
- d. If pre-dinner SMBG > 90 mg/dL on  $\geq 2$  episodes per 7 days, follow titration schedule based on average pre-dinner SMBG:
  - 80 - 130 mg/dL: no change in insulin dose
  - 131- 150 mg/dL: increase short-acting insulin dose by 10% SQ at lunch
  - 151- 190 mg/dL: increase short-acting insulin dose by 10-20% SQ at lunch
  - 191- 240 mg/dL: increase short-acting insulin dose by 10-30% SQ at lunch
  - >240 mg/dL: increase short-acting insulin dose by 10-40% at lunch
- e. If HS SMBG < 80 mg/dL on  $\geq 2$  episodes per 7 days, decrease short-acting insulin dose by 10-20% at dinner.
- f. If HS SMBG > 90 mg/dL on  $\geq 2$  episodes per 7 days, follow titration schedule based on average HS SMBG:
  - 90 - 150 mg/dL: no change in insulin dose
  - 151- 190 mg/dL: increase short-acting insulin dose by 10% SQ at dinner
  - 191- 240 mg/dL: increase short-acting insulin dose by 10-20% SQ at dinner
  - >240 mg/dL: increase short-acting insulin dose by 10-30% SQ at dinner

### 11. For patients with no discernible pattern in their SMBG, making titration of insulin difficult, try the following trouble-shooting steps:

- a. First, assess the appropriateness of the evening basal insulin dose, by analyzing the overnight (HS->AM) SMBG trends.
  - If the overnight pattern is fairly "flat" (i.e. +/- 30 mg/dL), then the PM glargine insulin dose is likely appropriate.
  - If the overnight pattern trends down (i.e. SMBG drops >30 mg/dL overnight), then the PM glargine insulin dose is likely excessive; consider decreasing dose by 10-20%
  - If the overnight pattern trends up (i.e. SMBG increases >30 mg/dL overnight), then the PM glargine insulin dose is likely insufficient; consider increasing dose by 10-20%.

**Note:** In order to correctly analyze the HS->AM trends, make sure the patient is fasting during the night, not treating HS hyperglycemia with short-acting insulin AND the HS SMBG is at least 4 hours after the last dose of rapid-acting insulin.

- b. Second, once the basal insulin dose is deemed appropriate, assess the appropriateness of the prandial insulin doses, by analyzing the pre- and post-prandial SMBG trends. (Patient should check post-prandial BS 2 hours after eating, when the pre-prandial BS is at target, for most patients BS between 90-130mg/dL)

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- A post-prandial BS of <180 mg/dL suggests that the prandial insulin dose is likely appropriate.
- If the post-prandial BS is >180 mg/dL then the prandial insulin dose is likely insufficient; consider increasing dose by 10-20%

**Note:** In order to correctly analyze the post-prandial trends, make sure the patient is not treating pre-prandial hyperglycemia with a hyperglycemic correction scale, not snacking after the meal, AND waiting 90-120 minutes after eating to check the post-prandial BS.

- c. Third, most patients on this insulin regimen will require approximately 50-60% of the TDD of insulin as basal insulin and approximately 40-50% as short-acting insulin. If either type of insulin is > 60% of the TDD of insulin, contact MD.
  - d. Fourth, erratic SMBG may be due to inconsistent dietary patterns, inconsistent carbohydrate intake, and/or inconsistent carbohydrate counting (if applicable). Consider a referral to nutrition for a food diary evaluation, assessment of carbohydrate counting and utilization of carbohydrate:insulin ratios.
  - e. Fifth, if nocturnal hypoglycemia is suspected (unexplained AM hyperglycemia, report of nightmares, AM headaches), have patient check 2AM blood glucose.
12. Some patients may benefit from a customized hyperglycemic correction scale QAC and HS. See protocol I (Hyperglycemic Correction Protocol) for details
13. Notify MD if any of following:
- Initiation of a new medication
  - Any SMBG < 80 mg/dL  $\geq$  3 times a week
  - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol.
  - Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical (urine/blood)
  - Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

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### PROTOCOL G – HYPERGLYCEMIC CORRECTION PROTOCOL

- INCLUSION SUB-CRITERIA**
1. HbA<sub>1c</sub> > 0.5% and/or SMBG > 20 mg/dL above individualized goals.
  2. Consider in patients who are currently taking insulin with sub-optimal and/or erratic control.
  3. Consider in patients who demonstrate consistent SMBG at least 2 times per day.
- ALGORITHM**
1. Calculate the total daily dose (**TDD**) of insulin (total of long and rapid acting insulins)
  2. Using the “**Rule of 1800**”, estimate the patient’s “**insulin sensitivity**” using the following formula:
    - a. “**Insulin Sensitivity**” = 1800/TDD
    - b. e.g. if TDD is 60 units, the “insulin sensitivity” is 1800/60 = 30.
    - c. Therefore, 1 unit of rapid acting insulin will drop the BS by approximately 30 mg/dL.
  3. Provide a written “**AC Hyperglycemic Correction Scale**” using the patient’s estimated insulin sensitivity and the patient’s target BS.
    - a. e.g. if the insulin sensitivity is 25 mg/dL and the target BS is 150 mg/dL, a hyperglycemic correction scale would instruct the patient to take 1 unit of short (or rapid) acting insulin for every 25 mg/dL above the target of 150 mg/dL.
    - b. This scale could be simplified to 2 units for every 50 mg/dL above the target of 150 mg/dL:
      - For BS 80- 150 mg/dL: no correction
      - For BS 151- 200 mg/dL: add 2 units of **rapid** acting insulin
      - For BS 201- 250 mg/dL: add 4 units of rapid acting insulin
      - For BS 251- 300 mg/dL: add 6 units of short rapid acting insulin
      - For BS > 300 mg/dL: add 8 units of short rapid acting insulin
    - c. The calculated insulin dose could be given in addition to the scheduled rapid acting meal-time insulin dose, if applicable.
    - d. A similar scale could be used at bedtime, but consider a less aggressive scale and/or a less aggressive target BS to minimize the risk of early AM hypoglycemia.
    - e. Hyperglycemic correction scale templates are available for use.
    - f. As the TDD of insulin changes over time, the hyperglycemic correction scale may also need to be revised and updated using the most recent TDD to calculate insulin sensitivity.
  4. Consider providing a written “**HS Hyperglycemic Correction Scale**” for patients who are frequently hyperglycemic at bedtime and who do not have nocturnal or early AM hypoglycemia:
    - a. Initially, consider a higher threshold for HS hyperglycemic correction (e.g. HS BG > 200mg/dL)
    - b. Initially, consider using a less aggressive insulin sensitivity factor at bedtime (e.g., instead of an insulin sensitivity factor of 25, start with an insulin sensitivity factor of 50).
    - c. Consider adjusting the HS hyperglycemic correction scale to approach the insulin sensitivity factors and BG targets of the AC correction scale as clinically indicated.
  5. Rapid-acting insulin analogs such as Lispro, aspart or glulisine can be used for the protocol.
  6. Encourage patients to document how much total insulin is administered for any specific BS, including scheduled doses and doses administered using the hyperglycemic correction scale.
  7. Remind patient that insulin glargine is not to be mixed with any other insulin.
  8. Notify MD if any of following:
    - Initiation of a new medication
    - Any SMBG < 80 mg/dL ≥ 3 times a week
    - Fasting SMBG > 250 mg/dL or random/post prandial SMBG > 350 mg/dL in > 20% of values, then proceed to Acute Pathway: Hyperglycemia Protocol.

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- Any evidence of ketosis, clinically (nausea/vomiting/confusion) or biochemical  
Any symptom of severe hyperglycemia (polyuria Q2hr or more frequent, polydipsia > 3L/day, nocturia > 3x, or acute visual changes)

**PROTOCOL H – URGENT HYPERGLYCEMIA PROTOCOL**

INCLUSION 1. Random blood sugar >350 mg/dL OR

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SUB-CRITERIA 2. Blood sugar >250 mg/dL with symptoms of hyperglycemia (polyuria, polydipsia, weight loss, confusion) and/or ketosis (nausea, abdominal pain)

## ALGORITHM

Assessment:

1. Check vital signs: temperature, BP, HR, respiratory rate
2. Assess mental status: (Alert, drowsy, stuporous)
3. Assess for signs or symptoms of prolonged, severe hyperglycemia (weight loss, polyuria, polydipsia, polyphagia, dehydration, weakness, vomiting, abdominal pain, fruity odor on breath)
4. Assess for underlying stressor with focused history and physical exam (e.g chest pain, UTI, URI, medicine non-compliance, dietary indiscretion, prior history of DKA or hyperosmolar hyperglycemia)
5. Assess ability to take PO fluids
6. Assess reliability for follow-up with health care provider
7. Check urine ketones

I. Intervention for “stable” patients already taking insulin:

“Stable” defined as **ALL** of the following present:

Normal vital signs, normal mental status, able to take PO fluids well, asymptomatic, urine ketones absent or trace.

1. Estimate the average total daily dose of insulin (TDD)
2. Estimate the patient’s “insulin sensitivity” = 1500/TDD  
e.g. If TDD is 60 units, the “insulin sensitivity” is 1500/60 = 25.  
Therefore, 1 unit of rapid-acting insulin will drop the BS by approximately 25 mg/dL.
3. Administer a dose of rapid-acting insulin SQ that would decrease the BS to a goal of 150 mg/dL by using the following formula\*:  
\*((BS measured – BS goal)/insulin sensitivity)) = units of insulin  
e.g. If the measured BS is 450 mg/dL, goal BS is 150 mg/dL, and insulin sensitivity is 25, one would administer (450-150)/25 = 12 units
4. Patient re-checks BS in 2-4 hours (sooner if develops symptoms of hypoglycemia)
5. If BS is still >250mg/dL in 4 hours, administer a 2<sup>nd</sup> injection of insulin based on the current BS and the above formula.
6. Re-check BS in 2-4 hours.
7. If BS is still > 250mg/dL, call health-care provider (or page endocrine fellow on-call at 408-885-5000 if after-hours)
8. Instruct patient to continue to take his/her scheduled insulin regimen.

II. Intervention for “stable” patients **NOT** already taking insulin:

1. Assume an insulin sensitivity of 50 (i.e. 1 unit of insulin will drop BS approximately 50 mg/dL).
2. Administer a dose of rapid-acting insulin SQ that would decrease the BS to a goal of 150 mg/dL as per Algorithm I, step #3 above.  
e.g. If the measured BS is 450 mg/dL, goal BS is 150 mg/dL, and insulin sensitivity is 50, one would administer (450-150)/50 = 6 units
3. Follow steps 4-8 as per Algorithm I above.

III. Intervention for “stable” patients with urine ketones 1+ or greater:

1. Administer insulin as per Algorithm I or II above.
2. Check a stat panel 7, serum ketones.
3. Notify PCP (or endocrinology fellow on-call if no PCP) of pending results, patient’s clinical data, patient contact information and ask laboratory to page MD with results.
4. Follow steps 4-8 as per Protocol H above.

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IV. Intervention for “unstable” patients:

“Unstable” defined as having **ANY** of the following present:

Abnormal vital signs (HR>100, BP <90/50 or > 170/110, RR>24), any deterioration in mental status, symptoms of prolonged and/or severe hyperglycemia, inability to take adequate PO fluids, unreliable patient.

1. Notify PCP (or endocrinology fellow if no PCP)
2. Refer to urgent care/ER for immediate medical attention.
3. Phone follow-up within 24 hours (72 hours if weekend)
4. Arrange follow-up in diabetes clinic +/- diabetes education in 1-2 weeks.

\*\* Interventions for **ALL** hyperglycemic patients managed as out-patients:

1. Patient checks BS q 2-4 hours while BS remain > 250 mg/dL
2. For all patients with DM1, any DM with history of DKA, and any DM with at least 1+ urine ketones, instruct patient to check urine ketones q 2-4 hours while BS remain > 250 mg/dL.
3. Increase fluid intake (2-3 cups every hour)
4. Maintain some carbohydrate intake (at least 150 grams/day)
5. During acute illness, patient may be especially insulin-resistant. Rapid-acting insulin doses may need to be increased by 50-100%.
6. Maintain close contact by telephone with health-care provider.
7. Seek immediate medical attention if any of the following occur: persistent hyperglycemia >250mg/dL > 12 hours, persistent urine ketones > 12 hours, inability to maintain adequate PO intake, nausea, vomiting, abdominal pain, high fever (>101.5 F), any deterioration in mental status.
8. Educator to provide patient educational and resource materials.
9. Educator arranges follow-up with MD and/or diabetes education.

**PROTOCOL I – URGENT HYPOGLYCEMIA PROTOCOL**

- INCLUSION 1. Random blood glucose <80 mg/dL

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SUB-  
CRITERIA

ALGORITHM

I. Assessment:

1. Check vital signs: temperature, BP, HR, respiratory rate
2. Assess mental status: (Alert, drowsy, stuporous, uncooperative)
3. Assess for frequency and severity of hypoglycemia
4. Assess for cause of hypoglycemia (e.g. decreased carbohydrate intake, overdose of hypoglycemic agent, exercise, alcohol)
5. Assess for hypoglycemia unawareness (no or minimal adrenergic symptoms when blood glucoses < 60 mg/dL)
6. Assess reliability for follow-up with health care provider
7. Notify MD for all patients with blood glucose <80 mg/dL

II. Initial Intervention

A. If patient has loss of consciousness or seizures:

1. Activate EMS
2. Activate BLS, ACLS
3. Give glucagon 1mg IM x 1

B. If patient has altered mentation or uncooperative:

1. Consider EMS, security
2. Glucagon 1mg IM x 1

C. If patient is cooperative and glucose < 50mg/dL:

1. 30 gram fast-acting carbohydrate

D. If patient is cooperative and glucose 51-70mg/dL:

1. 15 gram fast-acting carbohydrate

E. If patient is cooperative and glucose 70-80mg/dL and a fast/rapid-acting insulin is "on board":

1. 15 gram fast-acting carbohydrate

F. If patient is cooperative and glucose 70-80 mg/dL and no fast/rapid-acting insulin is "on board"

1. No initial intervention required

III. Subsequent Management (15 minutes after initial intervention)

1. Repeat assessment as in section I above
2. Recheck blood glucose
3. If blood glucose is still <80 mg/dL, then repeat interventions as in section II above
4. If blood glucose is >80 mg/dL, but still has symptoms, discuss with MD
4. If blood glucose >80mg/dL, and feels well, then proceed to section IV

IV. Follow-up

1. Discuss with MD potential etiology of hypoglycemia
2. Discuss with MD suggestions for adjustments in medication regimen, education on adequate carbohydrate intake, exercise precautions, etc.
3. Provide a glucagon emergency kit, if appropriate
4. Discuss with patient management of hypoglycemia in the future including Rule of 15
5. Report to DMV if patient has a lapse of consciousness, if appropriate
6. Arrange appropriate follow-up

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**E. REPORTABLE CONDITIONS / INTERVENTIONS:**

1. Non-compliance for follow-up lab work
2. Any adverse side effects to medications listed above
3. Pregnancy
4. Ketonuria/Ketonemia

**F. REFERRAL TO A PHYSICIAN:**

1. Patient presents with severe hyperglycemia that may warrant initiation of I.V. insulin over oral agent therapy
2. Patient has ketouria/ketonemia
3. Frequent or difficult to manage hypoglycemia
4. Patient is pregnant

**G. PATIENT EDUCATION / FOLLOW-UP:**

1. Evaluation of current lab data in accordance with ADA standards of care. This will include: HbA1c within last 3 months, serum creatinine (medication appropriate: e.g., glyburide, glipizide, and metformin), liver function test (medication appropriate: e.g., metformin and pioglitazone), annual urine creatinine and microalbumin, and TSH (type 1 diabetes).
2. Identify acute or other concerns, which need to be addressed by the referring provider.
3. Monitoring and Use of Results
  - a. Demonstrates how to care for the strips and supplies and verbalizes when to perform a quality control checking method of meter provided.
  - b. Verbalize the frequency of testing which is dictated by the patient's needs and goals.
  - c. Demonstrate the proper disposal of the lancets and implementation of universal precautions.
  - d. Verbalize meter company contact as initial source of troubleshooting meter problems.
4. Relationship among Nutrition, Exercise, Medication and Blood Glucose Levels
  - a. State the relationship of food and meals to oral agents and/or insulin, activity and blood glucose levels.
  - b. Identify the best time to exercise.
  - c. State that additional food/snack may be needed before, during, or after physical activity (provide a list of appropriate complex carbohydrate choice).
  - d. Describe the type and amount of food (extra may be necessary) to use to prevent hypoglycemia during and after exercise.
  - e. Identify times for snacks and the most appropriate choices.
  - f. Note with extended periods of exercise, hypoglycemia may result for up to 24 hours – teach patients to practice precautions.
  - g. Identify situations when exercise is not appropriate, e.g., sick days or DKA.
  - h. State the need to inform friends and/or others of possibility of hypoglycemia related to exercise, with instructions on how to prevent, recognize, and to treat.
  - i. State the need to consult with the health care team before beginning an exercise program if there are any existing medical problems that would potentially prohibit such activity.

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5. Prevention, Detection and Treatment of Acute Complications
  - a. Identify possible cause of hypoglycemia.
  - b. State how to prevent hypoglycemia.
  - c. List the possible symptoms of hypoglycemia and define mild, moderate (need assistance) and severe (unconscious or convulsing) hypoglycemia.
  - d. State how to treat hypoglycemia according to the “Rule of 15-15” (see Attachment D).
  - e. State the importance of always carrying a concentrated, quickly absorbed source of carbohydrate (i.e. glucose tabs).
  - f. State the need to wear or carry a medical alert identification.
  - g. State that drinking alcohol is a risk for hypoglycemia.
  - h. State and acknowledge that after moderate to severe hypoglycemia, operating machinery, heavy equipment or driving a motor vehicle can be impaired and a hazard risk. Always wait at least one hour and/or normal judgment status prior to attempt to such activity.
  - i. List the potential causes of hyperglycemia.
  - j. State how to prevent hyperglycemia.
  - k. States when and how to contact the educator or health care provider or other discipline if the blood glucose test are consistently higher or lower than the established individualized written goals provided.
  - l. Demonstrate and discuss urine ketone testing with the appropriate testing materials if the treatment calls for it (Type 1 DM or Type 2 with history DKA).
  - m. The need to contact provider within 1 hour or less if the urine ketone test is positive. May necessitate Emergency Department visit.
  - n. State the need to call for directions for insulin dose during time illness and/or stress.
  
6. Medications
  - a. When appropriate state that insulin and oral agents must be taken daily as prescribed. Indicate what time it must be taken and state what to expect if insulin or oral agents are omitted.
  - b. State what action insulin and/or oral agents have on the blood glucose level.
  - c. State the type, brand, amount, and time of insulin to be taken.
  - d. State the time of onset, peak, and duration of the insulin prescribed.
  - e. Demonstrate how to draw up and/or mix the correct amount of insulin.
  - f. Demonstrate how to use an insulin pen for injection.**
  - g. Demonstrate how to inject insulin correctly, into the abdomen area.
  - h. Describe the use and storage of insulin, needles, and syringes.
  - i. Describe the proper disposal of syringes and lancets.

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**G. DOCUMENTATION**

**1. Document the following in EPIC:**

- a. Patient goals and concerns
- b. Laboratory parameters assessment as defined in inclusion and exclusion criteria
- c. Allergy status
- d. Educational opportunities/reinforcement of care issues – patient education materials available on EPIC (Lane Library, Up-to-date, MyHealth, etc.)
- e. Action plan
- f. Any physician notification including reason and time
- g. Referral to diabetes educator and/or dietician

**A. II. CLINICAL REQUIREMENTS**

**A. REQUIREMENTS OF CLINICAL PHARMACIST**

- 1. EDUCATION / TRAINING: Graduated from an accredited School of Pharmacy. Current licensure by the California State Board of Pharmacy required and must have either a) a PharmD degree and completion of an ASHP accredited clinical residency program OR b) completed and passed a Board of Pharmaceutical Specialties (BPS) examination and have three years clinical experience in direct patient care. Specialty in ambulatory care pharmacy preferred. The clinical pharmacist must also sign the Collaborative Practice Agreement with the physician(s) at Stanford Coordinated Care prior to the start of practice.
- 2. EXPERIENCE: Minimum of three years of experience as a pharmacist, with familiarity in chronic care management.
- 3. INITIAL EVALUATION: In-service/orientation and competency validation to the protocol.
- 4. ON-GOING EVALUATION: Annual review of competency.

**B. REQUIREMENTS OF REGISTERED NURSE:**

- 1. EDUCATION / TRAINING: Current licensure in the state of California. Completion of an RN program from an accredited school of nursing.
- 2. EXPERIENCE: Minimum of one year of experience as a registered nurse, with familiarity in disease management or chronic care management.
- 3. INITIAL EVALUATION: In-service/orientation and competency validation to the protocol.
- 4. ON-GOING EVALUATION: Annual review of competency.

STANFORD HOSPITAL AND CLINICS

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ATTACHMENT A - APPENDIX A

**2013** QUICK REFERENCE GUIDE to the  
AMERICAN DIABETES ASSOCIATION'S STANDARDS OF CARE

## PHYSICAL ASSESSMENT

- Visits: every six months or appropriate to meet patient's needs and treatment goals.
- Blood Pressure: Every visit. Goal is less than 140/80 mm/Hg\*\*
- Weight: Every visit; establish growth chart for children. Weight loss is recommended for all overweight or obese individuals who have or at risk for diabetes. Bariatric surgery may be considered for adults with BMI  $\geq 35$  kg/m<sup>2</sup> and type 2 diabetes, especially if associated with comorbidities.
- Comprehensive Foot Exam (adults): At least yearly (more often in patients with high-risk foot conditions).
- Eye Exam: Yearly dilated and comprehensive eye exam for adults and children  $\geq 10$  with type 1 diabetes. The initial eye exam should be performed within 5 years after the onset of diabetes. Patients with type 2 diabetes should have an initial dilated and comprehensive eye exam shortly after the diagnosis of diabetes. High-quality fundus photographs can detect most clinically significant diabetic retinopathy.

## LABORATORY TESTS

- HbA1c: 2 times per year in patients who are meeting treatment goals. Perform A1C test quarterly in patient whose therapy has changed or who are not meeting glycemic goals. A reasonable goal is < 7% for many non-pregnant adults. Providers might suggest more stringent A1C goals (such as <6.5%) for selected individual patients or less stringent goals (such as <8%) for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with long-standing diabetes in whom the general goal is difficult to attain.
- Urine Protein (adults): Microalbumin measurement annually (in the absence of previously demonstrated microalbuminuria).
- Lipid Profile (adults): Annually. Target goals: LDL cholesterol <100 mg/dL, triglycerides <150 mg/dL, HDL > 40 mg/dL in men and > 50 mg/dL in women.

## SELF-MANAGEMENT TRAINING

- General Principles: Review goals at every visit. Medical Nutrition Therapy: Review goals at every visit.
- SMBG: Should be performed as appropriate to meet goals.
- Physical Activity: Adults with diabetes should be advised to perform at least 150 min/week of moderate-intensity aerobic physical activity (50-70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise.

## SPECIAL SITUATIONS

- Hypoglycemia: Recurrent hypoglycemia calls for reassessment of treatment plan. Additional action suggested might include enhanced diabetes self-management education, co-management with a diabetes team, referral to an endocrinologist, change in pharmacological therapy, initiation or increased SMBG, or more frequent contact with the patient.
- Preconception Counseling: Begin counseling at puberty; enhance counseling with adolescence; consult with high-risk perinatal programs with appropriate.
- Pregnancy Management: Intensify glycemic control; consult with high-risk perinatal programs when appropriate.
- Smoking Cessation: Emphasize and assist as much as possible.
- Aspirin Therapy: Use aspirin (75 - 162 mg/day) therapy as secondary prevention in those patients with a history of CVD. Consider for primary prevention in those type 1 or type 2 patients at increased cardiovascular risk (e.g., family history of CVD, smoking, hyperlipidemia, hypertension, and albuminuria).

\*\* These guidelines have been condensed from the American Diabetes Association's Standards of Medical Care in Diabetes. They do not reflect all the actions that should be provided by health professionals in the medical management of diabetes. Full text of the Association's Clinical Practice Recommendations, including the Standards of Medical Care, is available at [www.diabetes.org](http://www.diabetes.org).

## ATTACHMENT B

### For Hypoglycemia “The Rule of 15/15”

The “Rule of 15/15” is an easy way to remember to treat low blood glucose: check your blood glucose, take 15 grams of fast acting carbohydrate, wait 15 minutes, then recheck again, if your blood glucose is not up to 100 mg/dl, then repeat the treatment.

#### STEP-BY-STEP TREATMENT

**1. Check your blood glucose, if possible**

- A. If between 70 – 100 mg/dl with symptoms, treat- step 3
- B. If less than 70 mg/dl, with or without symptoms, treat - step 3

**2. If in doubt and cannot test blood glucose, treat – step 3**

**3. Treatment:**

- A. Take 15 grams of fast acting carbohydrate
  - Glucose Tablets 3 – 4
- B. If unable to chew these, then select one of these:
  - Or Glucose Gel – 1 tube
  - Regular soda – 4 oz.
  - Fruit juice – 4 oz.

**4. *WAIT 15 Minutes.*** Recheck your blood glucose. If you still feel symptoms of low blood sugar and/or your blood glucose is 70mg/dl, then repeat the treatment.

**5. If the symptoms of low blood glucose are gone,** but it is more than 1 hour away from your mealtime, eat a snack of 1 starch and 1 protein.

- Sandwich ½
- Or cheese 1 oz. and crackers (6)
- Or peanut butter 1 Tbsp. and crackers (6)
- Or non-fat milk 4 oz. and graham crackers (2)

ATTACHMENT C

**Drug interactions with Glyburide/Glipizide**

Precipitant drug/food	Object drug	Comments
Bosentan	Glyburide	Bosentan and glyburide are contraindicated. Concurrent use of bosentan and glyburide may result in risk of liver enzyme elevations.
Fluoroquinolones	Glyburide/glipizide	Concurrent use of fluoroquinolones and glyburide/glipizide may result in changes in blood glucose and increase risk of hypoglycemia or hyperglycemia.
Acarbose	Glyburide/glipizide	Concurrent use of acarbose and glyburide/glipizide may result in increased risk of hypoglycemia.
EtOH	Glyburide/glipizide	Concurrent use of ethanol and glyburide/glipizide may result in hypoglycemia.
Food	Glipizide	Concurrent use of glipizide and food may result in delayed insulin release.
Beta-Blockers	Glyburide/glipizide	Concurrent use of beta-blockers and antidiabetic agents may result in an increased risk of hypoglycemia. Beta-blockers may mask the symptoms of hypoglycemia in some patients.
NSAIDs	Glyburide/glipizide	Hypoglycemic action of sulfonylurea may be potentiated
Highly protein bound drugs (e.g., salicylates, sulfonamides, chloramphenicol, probenecid, monoamine oxidase inhibitors)	Glyburide/glipizide	Hypoglycemic action of sulfonylurea may be potentiated

**Drug interactions with Metformin**

Precipitant drug/food	Object drug	Comments
Iodinated Contrast Material	Metformin	Iodinated contrast materials are contraindicated with metformin. May result in lactic acidosis and acute renal failure. In patients, whom such a study is planned, temporarily discontinue metformin prior to, and 48 hours subsequent to, the procedure and reinstitute only after renal function has been reevaluated and found to be normal.
Cimetidine	Metformin	Concurrent use of metformin and cimetidine may result in an increase of 60% peak metformin plasma concentration and 40% increase in AUC.
Cationic Drugs (e.g., amiloride, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, or vancomycin)	Metformin	Cationic drugs that are eliminated by renal tubular secretion theoretically have the potential for interaction with metformin by competing for common renal tubular transport systems.
EtOH	Metformin	Concurrent use of metformin and ethanol may result in an increased risk of lactic acidosis.
Drugs that may cause lactic acidosis: abacavir, didanosine, emtricitabine, entecavir, lamivudine, tenofovir, zalcitabine, zidovudine	Metformin	Concurrent use may increase risk of lactic acidosis.

**Drug interactions with Pioglitazone**

Precipitant drug/food	Object drug	Comments
Oral contraceptives	Pioglitazone	Concurrent use of pioglitazone and contraceptives may result in loss of contraceptive efficacy
Gemfibrozil	Pioglitazone	Concurrent use of pioglitazone and gemfibrozil may increase AUC of pioglitazone 3fold, resulting in risk of hypoglycemia.
Rifampin	Pioglitazone	Concurrent use of pioglitazone and rifampin may result in 54% decrease in pioglitazone AUC.

**Drug interactions with Insulin (NPH, Regular, 70/30, Glargine, and Lispro)**

Precipitant drug/food	Object drug	Comments
Corticosteroids, isoniazid, niacin, estrogens, oral contraceptives, phenothiazines, and thyroid replacement therapy	Insulin	Insulin requirements may need to be increased in the presence of these agents due to their hyperglycemic activity
Oral hypoglycemic agents, salicylates, sulfa antibiotics, MAO inhibitors, ACE inhibitors, inhibitors of pancreatic function (eg., octreotide), EtOH, and fluoroquinolones,	Insulin	Insulin requirements may need to be decreased in the presence of these agents due to hypoglycemic activity

**Drug interactions with Exenatide**

Precipitant drug/food	Object drug	Comments
Acetaminophen	Exenatide	Reduced acetaminophen bioavailability may be due to slower gastric emptying. Administer acetaminophen 1 hour before exenatide.
Lovastatin	Exenatide	Reduced acetaminophen bioavailability may be due to slower gastric emptying. Higher doses of lovastatin may be required.
Warfarin	Exenatide	Increase in INR has been reported in post-marketing surveillance. Monitor INR and signs and symptoms of bleeding.
Sulfonylurea	Exenatide	Concurrent use increases risk of hypoglycemia. Reduction in the dose of sulfonylurea may be considered.

**Drug interactions with Pramlintide**

Precipitant drug/food	Object drug	Comments
Insulin	Pramlintide	Concurrent use increases risk of insulin-induced severe hypoglycemia, particularly in Type 1 DM. Recommend frequent SMBG and initial 50% reduction of prandial insulin.
Anticholinergics-atropine	Pramlintide	Avoid concurrent use. Not studied in clinical trials
$\alpha$ -glucosidase inhibitors	Pramlintide	Avoid concurrent use. Not studied in clinical trials