

## **Diabetes- Summary-**

### **Diagnosis of Diabetes (DM):**

*Fasting* Glucose >125 mg/dl (twice, venous blood, in lab)

*Random* Glucose >200 mg/dl with symptoms (polyuria, polydipsia, polyphagia, unexplained weight loss, blurred vision)

*Oral Glucose Tolerance Test* (OGTT) – glucose over 200 mg/dl

A1C of 6.5 or greater

### **Pre-Diabetes:**

*Impaired Glucose Tolerance* (IGT): two hour glucose (after 75 gram glucose load) of 140-199 mg/dl

*Impaired Fasting Glucose* (IFG):100-125 mg/dl (twice, venous blood, in lab)

A1C 5.7-6.4

### **Screening:** (use fasting plasma glucose or OGTT)

Adults over age 45, BMI >25 kg/m<sup>2</sup>, first degree relative with DM, high risk ethnic population (African American, Hispanic, Asian, Native American, Pacific Islander), hypertension (HTN), HDL <35 mg/dl or Triglycerides (TRIG) >250 mg/dl, prior hx of Impaired Glucose Tolerance, Polycystic Ovarian Syndrome (PCOS), macrosomia (delivered a baby weighing over 9 lb), previous diagnosis of Gestational DM, physical inactivity, hx of Peripheral Vascular Disease (PVD), hx of Cardiovascular disease, acanthosis nigricans, Non Alcoholic Fatty Liver Disease, use of atypical antipsychotics

**Insulin Resistance Syndrome-** pre-diabetes, TRIG >150 mg/dl, HDL < 40 mg/dl men or <50 mg/dl women, BP >130/80 mmHg (either elevated), microalbuminuria, obesity

**Treatment Goals of Prediabetes-** BP <130/80, total cholesterol <200mg/dl, HDL > 40mg/dl, TRIG <150 mg/dl, LDL <100 mg/dl, Alb/ Cr (microalbumin) < 30 mg/g

**Treatment Goals of Diabetes** -A1C < 7% (more or less stringent glycemic goals may be appropriate for individual patients depending on duration of diabetes, age/life expectancy, comorbid conditions, known CVD, advanced microvascular complications or hypoglycemia unawareness), preprandial glucose <120mg/dl, bedtime glucose <140mg/dl, BP <130/80, total cholesterol <200mg/dl, HDL > 40mg/dl, TRIG <150 mg/dl, LDL <100 mg/dl, Alb/ Cr (microalbumin) < 30 mg/g

**Treatment (follow up)-** yearly dilated eye exams, yearly comprehensive foot exam, visual foot inspection each visit, daily foot exam by patient, yearly dental exam, tobacco cessation, preconception counseling, influenza and pneumococcal vaccines

**Treatment (follow up labs)-** A1C at least twice a year (preferably on a quarterly basis), microalbumin at least once a year (can do quarterly), lipids (at least twice a year but can obtain quarterly), comprehensive chemistry- every visit (at least quarterly).  
If starting or changing the dose of TZD- check lfts at baseline then periodically.

If starting or changing dose of metformin, check comprehensive chem at baseline and every visit

If starting ACE-I, ARB, or diuretic or changing dose, check renal function panel at baseline then at 1-2 weeks then every visit

If starting a lipid lowering agent (or changing dose)- LFTs at baseline then at 3 months then at least every 6 months

**Treatment- HTN\*** (ACE-I) or (ARB)- all hypertensive patients with diabetes should be on one of these unless there are contraindications

(BB)- atenolol or loproressor or carvedilol, (CCB)- non-DCCB-diltiazem or verapamil or DCCB-amlodipine or felodipine (Diuretic)-HCTZ

**Treatment-Lipids\*** Statin or Niacin (Niaspan®) or Fibrate (Lopid® or Fenoglide®) or add to statin ezetimibe (Zetia®)

**Treatment- Anti-platelet\*** - Daily enteric coated 81mg aspirin if known CVD, daily 81mg aspirin if cardiovascular 10 year risk is >10%. For patients with documented aspirin allergy, clopidogrel 75mg can be used.

**Treatment-Lifestyle** - Exercise and diet modification

### **Oral Agents\***

**Sulfonylureas\*** glimepiride-Amaryl® 1-4mg daily, glipizide-Glucotrol® or Glucotrol XL® 5-20mg once daily or divided), glyburide –Diabeta®, Micronase®, or Glynase® 3-12 mg once a day or divided, can cause hypoglycemia, can be combined with metformin, alpha glucosidase inhibitors, TZD's and DPP-4 inhibitors.

**Meglitinides\*** –repaglinide-Prandin® or nateglinide –Starlix®, both TID with meals, can cause hypoglycemia, can be combined with metformin or TZD's.

**Biguanides\***- metformin-Glucophage® or Glucophage XR®- 500-2500 mg in divided doses, contraindicated with creatinine over 1.4 mg/dl (female) or over 1.5 mg/dl (male) or creatinine clearance <60 ml/min), contraindicated in unstable/uncompensated CHF, liver failure, ETOH abuse, hold day before contrast studies and restart 48-72 hours after contrast study (make sure creatinine is back to normal), hold in hospitalized patients, consider stopping if age >70 and certainly if age > 80, can cause GI side effects of abdominal pain and diarrhea, lactic acidosis, can be combined with sulfonylureas, TZD's, alpha glucosidase inhibitors, DPP-IV inhibitors and insulin.

**Thiazolidinediones (TZD)\*** pioglitazone –Actos® 15-45 mg once daily, contraindicated in CHF, CAD, and liver disease, discontinue if LFTs >3 times the upper limit of normal, can cause anemia, can cause weight gain and edema, use with caution if patient is on insulin due to synergistic effect in fluid retention, can be combined with metformin, sulfonylureas, alpha glucosidase inhibitors, DPP-4 inhibitors. Pioglitazone can be combined with insulin per PI. Should not be used in patients with history of bladder cancer.

**Alpha glucosidase inhibitors**\*- Acarbose-Precose®, or Miglitol-Glyset®-both are 50-100mg tid with meals, contraindicated in cirrhosis/liver dysfunction, chronic intestinal diseases, can be combined with metformin, sulfonylurea, TZD, or insulin.

**Sitagliptan (Januvia®)**\*-a DPP-4 inhibitor or gliptan which inhibits incretin breakdown (incretins potentiate release of insulin from the pancreas, decrease glucagon and hepatic glucose production, and slow gastric emptying). **Type 2 DM only.** Most effect is in lowering postprandial glucose. Available in 25 milligram, 50 milligram and 100 milligram tablets. End Stage Renal Disease (ESRD) or dialysis patients or CrCl <30mL/min use 25 milligrams once a day, CrCl 30mL/min to 50mL/min use 50 milligrams once a day and CrCl >50mL/min, use 100 milligrams once a day. Can be used with metformin, sulfonylureas, or TZD's. Use caution if using insulin. Can cause runny nose, sore throat, headache, or hypersensitivity reaction (including anaphylaxis, angioedema, and Stevens Johnson syndrome). Acute pancreatitis risk: counsel patients regarding symptoms of pancreatitis and stop the drug if pancreatitis occurs. Do not use in patients with a history of pancreatitis.

**Saxagliptin-Onglyza®**\*- a DPP-4 inhibitor or gliptan which inhibits incretin breakdown (see Sitagliptan above). Type 2 DM only. Available in 2.5mg and 5mg tablets taken once per day. 2.5mg tablet is for patients with CrCl <50mL/min and for patients on strong cytochrome P450 3A4/5 (CYP 3A4/5) inhibitors such as ketoconazole. Can be used with metformin, sulfonylureas, or TZD's. Use caution if using insulin. Can cause URI sxs, UTI, headache. Can reduce absolute lymphocyte count on average by 100-200 cells/microL.

**Linagliptin -Tradjenta®**- a DPP-4 inhibitor or gliptan which inhibits incretin breakdown (see Sitagliptan above). Type 2 DM only. 5mg tablets taken once per day. Can be used with metformin, sulfonylureas or TZD's. Can cause URI sxs, headache, arthralgias. Not recommended for use with insulin.

**Fixed Combinations**\* Glucovance® (glyburide and metformin), Metaglip® (glipizide and metformin), Actoplusmet® (Actos® plus metformin), Duetact® (Actos® plus glimepiride). Janumet® (Januvia® plus metformin) Prandimet®(Prandin® plus metformin), Kombiglyze XR® (Onglyza® plus metformin), - any of these recommended only if patient already tolerating the two drugs in the combination and the combination product is cost neutral or cost saving.

### **Insulin**\*

Start with PM dose of glargine(Lantus®) or detemir(Levemir®)at 5-10 units or 0.1U/kg/day to 0.2U/kg/day given at bedtime, titrate up by 1-4 units every 2-3 days or so to keep fasting (morning) glucose <120 (See self adjustment sheet)

Once fasting glucose is controlled, consider adding rapid acting insulin (aspart – Novolog® or lispro –Humalog® or apidra- Glulisine®) to help with postprandial

glucoses (See sliding scale insulin sheet) If cost/formulary considerations are paramount, regular insulin can be used.

**Daily** insulin dose is 0.5 to 1.0 U/kg/day (higher depending on insulin resistance)

Glargine (Lantus®) or detemir (Levemir®) at bedtime is 50% of total daily dose and then split the rest with meals (tid) as short acting (aspart/lispro/gulisine)

NPH / Reg 1/3 of total daily dose in AM and 1/3 of total daily dose in PM

AM 2/3 NPH and 1/3 Reg

PM 1/2 NPH and 1/2 Reg

Example- total daily dose of 36 units (2/3 of 36 =24 and 1/3 =12)

AM 16 units NPH and 8 units Reg

PM 6 units NPH and 6 units Reg

**Pramlintide (Symlin®)\***- synthetic analog of amylin- approved for use as adjunctive treatment for Type 1 and Type 2 DM patients who inject insulin at mealtimes and have not achieved management goals. Side effects-nausea, vomiting, anorexia, headache. Synergistically with insulin (as prescribed) can cause hypoglycemia. Slows gastric emptying so should not be used with medications that slow gastric motility such as anticholinergics, contraindicated in patients with gastroparesis. SQ injection-TID with meals. Type 1 DM, start with 15 micrograms SQ before meals. If no significant nausea occurs over the first 3 days, increase by 15 microgram increments to a maximum of 60 micrograms TID. Type 2 DM, start with 60 micrograms TID before major meals with maximum dose 120 micrograms tid before meals. Reduce preprandial short acting insulin by 50% initially and titrate back up once maintenance dose of pramlintide is established.

**Exenatide (Byetta®)\***-an incretin mimic which stimulates (potentiates) release of insulin from pancreas, decreases glucagon and hepatic glucose production, slows gastric emptying, increases satiety. **Type 2 DM only**. Approved for use as adjunctive therapy for Type 2 DM who have not achieved management goals who are taking metformin, sulfonylurea, and / or TZD. Can cause hypoglycemia, nausea, vomiting, diarrhea. SQ injection given bid with meals. Start with 5 micrograms SQ bid before AM and PM meals. Increase to 10 micrograms after one month if necessary. If patient on sulfonylurea, consider decreasing dose of sulfonylurea or discontinuing altogether. Not recommended for patients with CrCl <30mL/min. Acute pancreatitis risk: counsel patients regarding symptoms of pancreatitis and stop the drug if pancreatitis occurs. Do not use in patients with a history of pancreatitis.

**Exenatide extended release (Bydureon®)\***- see Exenatide above. Patients with thyroid nodules should be evaluated as thyroid c-cell tumors have been noted in rats that were given Bydureon®. Bydureon® is contraindicated in patients with a personal or family history of Medullary Thyroid Cancer (MTC) and contraindicated in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Has not been studied in

combination with insulin and concurrent use with insulin is not recommended. Dosed as 2mg SQ injection once every 7 days at any time of day and with or without meals.

## **PREDIABETES TREATMENT GUIDELINES**

Lifestyle changes to include exercise, weight loss, diet change and classes in prediabetes management. The lipid and blood pressure goals are as stated above. There is not an FDA approved medication for the treatment of prediabetes. Off-label use of metformin has been shown to decrease advancement to diabetes but the most effective treatment modalities are weight loss and exercise.

## **DIABETES TREATMENT GUIDELINES**

In general, start with metformin 500mg bid (see contraindications and monitoring information above) and increase to 1000mg bid with meals. **(PLEASE NOTE: If a patient has fasting blood sugars over 250, random blood sugars over 300, A1C over 10, OR ketonuria and is newly diagnosed or the patient has been off of his/her medications for diabetes, the patient will need insulin right up front). The oral medications will not be effective enough to bring down the blood sugars and the patient may need insulin for 1 to 3 months while the islet cells recover. Start with Lantus® or Levemir® as outlined under Insulin above and start at 10-40 units QHS depending on the blood glucose level and use the Lantus®/Levemir® self-adjustment outline to have the patient increase the dose by 2-4 units every two days until the fasting blood glucose is less than 120 mg/dl**). If the patient does not tolerate metformin (always make sure the patient takes the medication AFTER eating), consider using metformin XR and most of the time the patient will not have the GI side effects.

For cost considerations, after metformin has been titrated as above, add insulin OR a sulfonylurea such as Glipizide or Glyburide . Basal insulin (Lantus® or Levemir®) is used as in the paragraph above and as in notes under Insulin above. Consider adding insulin when there is hyperglycemia despite maximal oral medications, acute injury, stress, infection, surgery or pregnancy. There is no upper limit on Lantus® or Levemir®. Some patients with extreme insulin resistance need well over 100 units of Lantus®! Lantus® or Levemir® is preferred over NPH as NPH is bid. If postprandial blood glucose is elevated after controlling the fasting morning blood sugar, add aspart/lispro/glulisin using a sliding scale (use sliding scale sheet). . Aspart/lispro/glulisine are preferred over regular insulin as these cover the meal (quick onset but lasts for 2 to 3 hours). However, if cost/formulary considerations are paramount, regular insulin can be used.

Consider using TZD's, alpha glucosidase inhibitors, meglitinides, DPP-4 inhibitors, GLP-1 agonists, or amylin for those patients intolerant of metformin or sulfonylureas or for those patients with contraindications to metformin or sulfonylureas. Treatment should be individualized based on duration of diabetes, age/life expectancy, comorbid

conditions, known CVD, advanced microvascular complications or hypoglycemia unawareness.

**Please Note: follow newly diagnosed diabetics and diabetics who are uncontrolled closely and frequently (weekly or more often if severe elevations of blood glucose).**

\* For all medications, please consult Up-To-Date, a PDR, or other comprehensive drug reference for interactions and full list of indications and contraindications. Check hospital formulary status and use formulary drugs whenever possible and as indicated.

**WHASC Diabetes Educators:** (292-7594) and (292-2818) (292-0352)

**SAMMC Diabetes Self-Management Education:** 916-0794  
916-5974, 916-0794, 916-3123, pager 513-6030 (CDE is Certified Diabetic Educator)

**For Diabetes Referrals: Type DIAB**

Diabetes Education SAMMC is for either SAMMC or WHASC based on zip code of patient  
Diabetes Management BAMC for SAMMC  
Diabetes Management WHMC for WHASC  
Diabetes Prevention BAMC  
Diabetes Prevention SAMMC for WHASC

See ADA Clinical Practice Recommendations-Diabetes Care, Vol 35, supplement 1, Jan 2012, VA/DOD DM CPG- Aug 2010, ACE DM guidelines, Management of Hyperglycemia in Type 2 Diabetes: A Patient Centered Approach-Diabetes Care, 19 Apr 2012.