

RECOMMENDED FOLLOW UP

Adult in Health Care System		
1	Adult at risk, every 3 years (age >45)	Screen for diabetes (fasting plasma glucose [FPG] test)
2	Adult with fasting plasma glucose $\geq 110 < 126$	Lifestyle modification (exercise and diet to achieve weight loss)
Adult with Diabetes		
3	Initial visit following diagnosis	Patient education: comprehensive diabetes education and skills Influenza vaccination (in season)
4	Each routine primary care visit	Visual foot inspection if high risk for foot problems Tobacco assessment and counseling or referral for users Blood pressure measurements Review results of self-monitoring of blood glucose if monitored
5	Quarterly to annually	HbA _{1c} measurement and risk assessment
6	Annually	Dilated eye exam (every other year if no history of retinopathy or eye risk factors) Microalbuminuria / proteinuria screening and monitoring Lipid profile Visual inspection, foot risk assessment & education Influenza vaccination (in season)
7	When HbA _{1c} is not on target	Glycemic control management (diet, exercise and medication) Self-management, nutrition assessment and goal development
8	When change in vision, or eye risk factors	Referral to eye care provider for evaluation and treatment of retinopathy
9	Age 40 OR onset of cardiovascular disease risk factors	Consider aspirin prophylaxis
10	Confirmed microalbuminuria or SBP ≥ 140 or DBP ≥ 80	ACE inhibitor therapy if not contraindicated and if tolerated
11	Per national cholesterol guidelines (LDL-C ≥ 130)	Statin therapy

VA/DoD Clinical Practice Guideline for the Management of Diabetes Mellitus in Primary Care Pocket Guide

**RECOMMENDED FOLLOW UP
UPDATE 2003**

<ul style="list-style-type: none"> Consider aspirin therapy for patients with diabetes age > 40 OR evidence of cardiovascular disease risk factors If the patient is a candidate for an influenza vaccine, administer it in season Administer pneumonia vaccine, if indicated If the patient is using tobacco, refer to the VA/DoD Clinical Practice Guideline for the Management of Tobacco Use Cessation 	
IF	GO TO
If the individualized HbA _{1c} is not at target	Module G – Glycemic Control
If SBP ≥ 140 or DBP is ≥ 80 mmHg	VA/DoD Guideline for the Management of Hypertension
If a lipids evaluation was not done within one year or the patient has elevated cholesterol or lipids	VA/DoD Guideline for the Management of Dyslipidemia
If a renal evaluation was not done within one year or the patient has micro-/macroalbuminuria or elevated creatinine	Module R – Kidney Function
If an eye evaluation was not done within two years, the patient has symptoms, or a previous exam showed a high risk for visual loss or retinopathy	Module E – Eye Care
If a foot-risk assessment was not done within one year or the patient has risk factors or an active lesion	Module F – Foot Care
If the patient needs additional nutritional or lifestyle education	Module M – Self-Management and Education

VA access to full guideline: <http://www.oqp.med.va.gov/cpg/cpg.htm>

DoD access to full guideline: <http://www.gmo.amedd.army.mil>

Sponsored & produced by the VA Employee Education System in cooperation with the Offices of Quality & Performance and Patient Care Services and the Department of Defense

March 2003



DIAGNOSIS OF DIABETES MELLITUS

Status	Fasting Plasma Glucose (FPG) (Preferred) (a), (b)	Casual Plasma Glucose
Diabetes Mellitus	FPG \geq 126 mg/dL (7.0 mmol/L)	Casual plasma glucose \geq 200 mg/dL (11.1 mmol/L) plus symptoms of diabetes (c)
Impaired Glucose Tolerance	Impaired fasting glucose (IFG) FPG \geq 110, < 126 mg/dL	—
Normal	FPG < 110 mg/dL	—

- (a) Fasting is defined as no caloric intake for at least 8 hours.
- (b) FPG is the preferred test for diagnosis, but either of the two listed is acceptable. In the absence of unequivocal hyperglycemia with acute metabolic decompensation, one of these two tests should be used on a different day to confirm the diagnosis.
- (c) "Casual" means any time of day without regard to time since the last meal; classic symptoms include polyuria, polydipsia, and unexplained weight loss.

Foot Care

- Every patient with diabetes must have an annual documented foot risk assessment
- Every high-risk patient should have a visual inspection of his/her feet at each routine primary care visit

Eye Care

- Persons who have had no retinopathy on all previous examinations should be screened for retinopathy at least every other year
- Persons who have ocular risk factors, are on insulin, or have had retinopathy detected on a previous examination should have a yearly fundus examination

Definition of Chronic Kidney Disease Criteria

1. Kidney damage for \geq 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR), manifest by *either*:
 - Pathological abnormalities; OR
 - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR < 60 mL/min/1.73m² for \geq 3 months, with or without kidney damage

CHRONIC KIDNEY DISEASE (CKD): A CLINICAL ACTION PLAN

Stage	Description	GFR (mL/min/1.73m ²)	Action
	At increased risk	>90 (with CKD risk factors)	• Screen and CKD risk reduction
1	Kidney damage with normal or \uparrow GFR	\geq 90	• Diagnose and treat • Treat comorbid conditions • Slow progression • CVD risk reduction
2	Kidney damage with mild \downarrow GFR	60 – 89	• Estimate progression
3	Moderate GFR	30 – 59	• Evaluate and treat complications
4	Severe \downarrow GFR	15 – 29	• Prepare for kidney replacement therapy
5	Kidney failure	<15 (or dialysis)	• Replacement (if uremia present)

Dyslipidemia Treatment in Patients with Diabetes

	Baseline LDL-C [mg/dL]	
	\geq 100	\geq 130
Diabetes (with or without known CHD)	Diet & Exercise Consider drug therapy	Diet & Exercise Initiate drug therapy
LDL-C \leq 130 mg/dL and HDL-C < 40 mg/dL	Consider gemfibrozil	

Hypertriglyceridemia in Patients with Diabetes	
Diabetes with triglycerides (TG) 400-1000 mg/dL	Consider gemfibrozil if HDL-C < 40 mg/dL For high TG, use direct LDL-C measurement or non-HDL-C as lipid disorder to guide therapy

DETERMINATION OF TARGET HbA_{1c} LEVEL

Major Comorbidity ^(d) or Physiologic Age	Microvascular Complications		
	Absent or Mild ^(e)	Moderate ^(e)	Advanced ^(e)
Absent >15 years life expectancy	7% (<1% above upper normal range)	<8% (<2% above upper normal range)	<9% (<3% above upper normal range)
Present^(e) 5 – 15 years life expectancy	<8% (<2% above upper normal range)	<8% (<2% above upper normal range)	<9% (<3% above upper normal range)
Marked^(e) <5 years life expectancy	<9% (<3% above upper normal range)	<9% (<3% above upper normal range)	<9% (<3% above upper normal range)

- (a) Mild microvascular disease is defined by early background retinopathy, and/or microalbuminuria, and/or mild neuropathy.
- (b) Moderate microvascular disease is defined by pre-proliferative (without severe hemorrhage, intra-retinal microvascular anomalies [IRMA], or venous bleeding) retinopathy or persistent, fixed proteinuria (macroalbuminuria) and/or demonstrable peripheral neuropathy (sensory loss).
- (c) Advanced microvascular disease is defined by severe non-proliferative (with severe hemorrhage, IRMA, or venous bleeding) or proliferative retinopathy and/or renal insufficiency (serum creatinine level > 2.0 mg/dL) and/or insensate extremities or autonomic neuropathy (e.g., gastroparesis, impaired sweating, or orthostatic hypotension).
- (d) Major comorbidity includes, but is not limited to, any or several of the following conditions: cardiovascular disease, chronic obstructive pulmonary disease, chronic liver disease, stroke, and malignancy.
- (e) Moderate degree of major comorbid condition.
- (f) Severe degree or end-stage major comorbid condition.

Insulin					
Insulin (see Annotation J-3 Insulin Therapy)					
<ul style="list-style-type: none"> Efficacy: Dose can be adjusted to achieve a wide range of glucose lowering Requires intensive patient education Regular, neutral protamine Hagedorn insulin [NPH], and lente – inexpensive Insulin analogs – moderately expensive <p>Contraindications: Hypersensitivity to insulin Adverse Events: Hypoglycemia, hypersensitivity, injection site reactions, weight gain</p>					
Insulin	Onset (hours)	Peak (hours)	Duration (hours)	Compatible Mixed With	Appearance
RAPID-ACTING					
Regular (Novolin R®, Humulin R®)	0.5 – 1	2 – 5	6 – 10	NPH, lente, ultralente	Clear
Lispro (Humalog®)	0.25 – 0.5	0.5 – 2.5	3 – 6.5	Human NPH, human ultralente ^{c,d}	Clear
Aspart (Novolog®)	0.17 – 0.33	1 – 3	3 – 5	Human NPH ^{c,e}	Clear
INTERMEDIATE-ACTING					
NPH (Novolin N®, Humulin N®)	1 – 1.5	4 – 12	16 – 24	Regular	Cloudy
Lente (Novolin L®, Humulin L®)	1 – 2.5	7 – 15	16 – 24	Regular	Cloudy
LONG-ACTING					
Ultralente (Humulin U®)	4 – 6	8 – 20	24 – 28	Regular	Cloudy
Insulin glargine (Lantus®)	1.1	2 – 20	Up to 24	Not to be mixed with other insulins	Clear

Insulin (cont.)		
Insulin (see Annotation J-3 Insulin Therapy) cont.		
Insulin	Compatible Mixed With	Appearance
PRE-MIXED PRODUCTS		
70% NPH/ 30% Regular (Novolin 70/30, Humulin 70/30); 50% NPH/ 50% regular (Humulin 50/50)	Not to be mixed with other insulins	Cloudy
75% intermediate/25% lispro (Humalog mix 75/25)	Not to be mixed with other insulins	Cloudy

^a Adapted from AHFS Drug Information, American Society of Health-System Pharmacists, Inc., 2002
^b The time course of action is intended as a general guide as many factors may influence these parameters (e.g., type of preparation, dose, site of administration, and patient-related variables).
^c The effects of mixing insulin lispro or insulin aspart with insulins of animal source have not been studied. The only animal source insulin remaining on the market is purified pork as regular, NPH, and lente.
^d The effects of mixing insulin lispro with insulins produced by manufacturers other than Eli Lilly has not been studied.
^e The effects of mixing insulin aspart with insulins produced by manufacturers other than Novo Nordisk has not been studied.

DETERMINATION OF TARGET HbA_{1c} LEVEL

Major Comorbidity(d) or Physiologic Age	Microvascular Complications		
	Absent or Mild (a)	Moderate (b)	Advanced (c)
Absent >15 years life expectancy	7% (<1% above upper normal range)	<8% (<2% above upper normal range)	<9% (<3% above upper normal range)
Present (e) 5 – 15 years life expectancy	<8% (<2% above upper normal range)	<8% (<2% above upper normal range)	<9% (<3% above upper normal range)
Marked (f) <5 years life expectancy	<9% (<3% above upper normal range)	<9% (<3% above upper normal range)	<9% (<3% above upper normal range)

(a) Mild microvascular disease is defined by early background retinopathy, and/or microalbuminuria, and/or mild neuropathy.
 (b) Moderate microvascular disease is defined by pre-proliferative (without severe hemorrhage, intraretinal microvascular anomalies [IRMA], or venous bleeding) retinopathy or persistent, fixed proteinuria (macroalbuminuria) and/or demonstrable peripheral neuropathy (sensory loss).
 (c) Advanced microvascular disease is defined by severe non-proliferative (with severe hemorrhage, IRMA, or venous bleeding) or proliferative retinopathy and/or renal insufficiency (serum creatinine level > 2.0 mg/dL) and/or insensate extremities or autonomic neuropathy (e.g., gastroparesis, impaired sweating, or orthostatic hypotension).
 (d) Major comorbidity includes, but is not limited to, any or several of the following conditions: cardiovascular disease, chronic obstructive pulmonary disease, chronic liver disease, stroke, and malignancy.
 (e) Moderate degree of major comorbid condition.
 (f) Severe degree or end-stage major comorbid condition.

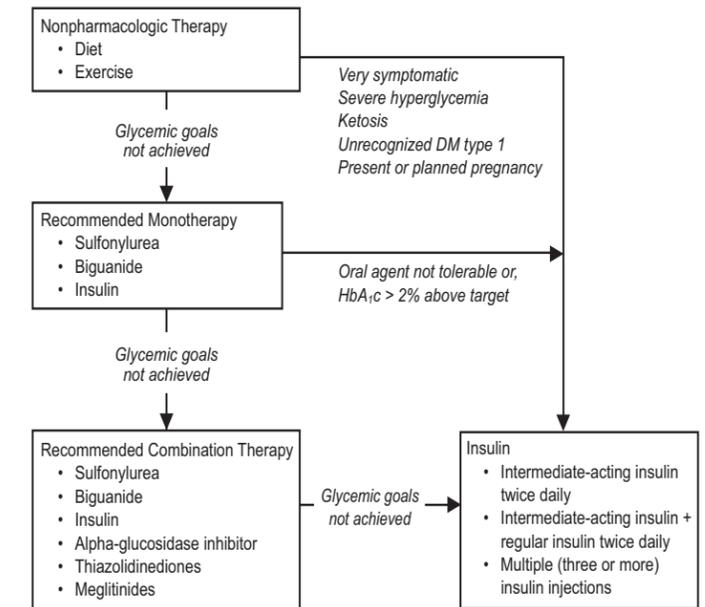
SEQUENTIAL TREATMENT FOR TYPE 2 DM

	Therapy	Drugs	Expected HbA _{1c} reduction Over a 2 – 3 month period of follow-up
1	Lifestyle modification, diet, and exercise	None	—
2	Lifestyle modification, diet and exercise and Monotherapy with oral agent or insulin	Sulfonylurea or biguanide	1 – 2%
3	Lifestyle modification, diet and exercise and Combination (add a second oral agent)	Sulfonylurea + biguanide	1 – 2%
		Sulfonylurea/biguanide + alpha-glucosidase inhibitor	0.5 – 1%
		Sulfonylurea/biguanide + thiazolidinedione	0.7 – 1.75%
4	Insulin with oral agent	Biguanide + insulin Thiazolidinedione + insulin Sulfonylurea + insulin	0.1 – 3%
5	Insulin	Insulin alone	0.2 – 2.6%
6	Referral	None	2%

Carefully selected individuals may benefit from three-drug oral hypoglycemic therapy. In general, such patients may benefit from referral to a diabetes care team.

**VADoD Clinical Practice Guideline
 Management of Diabetes Mellitus in Primary Care
 Pocket Guide**

**MANAGEMENT OF GLYCEMIC CONTROL
 UPDATE 2003**



Oral Pharmacologic Agents				
Sulfonylureas				
<ul style="list-style-type: none"> Efficacy: estimate reduction in HbA_{1c} = 1.0 – 2.0 % 1st generation sulfonylureas are no longer commonly used No difference in long-term efficacy or failure rate has been demonstrated among the sulfonylureas The preferred agents have shorter half-lives and inactive metabolites 1st generation sulfonylureas are 100% renally eliminated. Chlorpropamide and tolazamide have active metabolites. Glipizide, glyburide, and glimepiride are renally eliminated by 80 – 85%, 50%, and 60%, respectively. All but glipizide have active metabolites. Inexpensive 				
Agents	Dose		Contraindications	Adverse Events
1st generation				
Chlorpropamide	100 – 500 mg qd		<ul style="list-style-type: none"> Hypersensitivity Pregnancy 	<ul style="list-style-type: none"> Hypoglycemia Hypersensitivity Weight gain
Tolazamide	1000 mg qd or in 2 divided doses			
Tolbutamide	250 – 2000 mg in 2 – 3 divided doses			
2nd generation				
Glimepiride	1 – 4 mg once daily			
Glipizide* Glipizide XL*	2.5 – 40 mg qd or in 2 divided doses 5 – 10 mg once daily	<ul style="list-style-type: none"> Taken 30 minutes before a meal Doses >15 mg should be divided into 2 doses 		
Glyburide*	1.25 – 20 mg once daily or in 2 divided doses			
Micronized glyburide*	0.75 – 12 mg once daily or in 2 divided doses	<ul style="list-style-type: none"> Doses >6 mg may provide a better response when divided If the response to a single daily dose of glyburide or glipizide does not achieve treatment goals, dividing the dose may be effective 		
Biguanide				
<ul style="list-style-type: none"> Efficacy: estimate reduction in HbA_{1c} = 1.0 – 2.0% The major blood glucose lowering effect is through decreasing hepatic glucose production with some decrease in peripheral insulin resistance May restore ovulation in premenopausal anovulatory females Monitor renal function prior to drug initiation and at least annually thereafter Inexpensive when using generic 				
Agents	Dose		Contraindications	Adverse Events
Metformin	Initial – 500 mg bid or 850 mg q am Maintenance – 850 mg bid with meals Maximum – 2550 mg/day in 3 divided doses	<ul style="list-style-type: none"> If on 500 mg bid, dosage increase may be made by 500 mg increments weekly up to 1000 mg bid If on 850 mg q am, dosage increase of 850 mg may be made every other week (given as 850 mg bid) The dose response curve usually plateaus after 2000 mg/day Take with food to avoid possible GI symptoms 	Contraindications <ul style="list-style-type: none"> Renal dysfunction (SCr >1.5 mg/dl for males or >1.4 mg/dl for females) CHF requiring pharmacologic management Acute or chronic metabolic acidosis Hold prior to IV dye procedures and for 48 hours after the procedure. Reinstigate only after renal function is found to be normal. Not Recommended <ul style="list-style-type: none"> Age ≥80 unless normal creatinine clearance, and the dose should not be escalated to the maximum in elderly patients due to increased susceptibility to lactic acidosis Hepatic disease or excessive ethanol intake Withhold in the presence of any condition associated with hypoxemia, dehydration or sepsis 	<ul style="list-style-type: none"> Potential for lactic acidosis when used in patients for whom the drug is contraindicated Transient dose-related GI symptoms (diarrhea, nausea, vomiting, bloating, flatulence, anorexia) Decrease in vitamin B12 levels
Metformin extended release	Initial – 500 mg qd with the evening meal	Dose may be increased by 500 mg per week to a maximum of 2000 mg once daily. If glycemic control is not achieved, consider dividing into 2 doses.		

Alpha-glucosidase inhibitors				
<ul style="list-style-type: none"> Efficacy: estimate reduction in HbA_{1c} = 0.4 – 1.0% Delays the digestion of carbohydrates, thereby decreasing postprandial hyperglycemia Allows for flexible meal dosing Moderately expensive 				
Agents	Dose		Contraindications	Adverse Events
Acarbose Miglitol	Initiate – 25 mg tid Maintenance – 50 mg tid. Maximum – 100 mg tid	<ul style="list-style-type: none"> Or initiate gradually: 25 mg qd x 1-2 weeks followed by 25 mg bid for 1 – 2 weeks followed by 25 mg tid. Once a 25 mg tid dosing regimen is reached, further increases may be made at a 4 – 8 week intervals. Max dose for acarbose if weight <60 kg = 50 mg tid Dose is to be taken with the first bite of each main meal If the patient misses or adds a meal, he/she should omit or add the dose 	Contraindications <ul style="list-style-type: none"> Presence of intestinal complications (inflammatory bowel disease, colonic ulceration, intestinal obstructions, digestion or absorption disorders) Acarbose is contraindicated in patients with cirrhosis. Miglitol pharmacokinetics are not altered in cirrhosis and may be used. Not Recommended <ul style="list-style-type: none"> SCr > 2.0 mg/dl 	<ul style="list-style-type: none"> Transient dose-related GI symptoms (diarrhea, abdominal pain, flatulence) can limit compliance with therapy Acarbose, especially at doses greater than 50 mg tid, may cause serum AST/ALT elevation; monitor serum levels every 3 months during the first year of treatment
Thiazolidinediones				
<ul style="list-style-type: none"> Efficacy: estimate reduction in HbA_{1c} = 1.0 – 1.5% Enhances insulin sensitivity in skeletal muscle, hepatic, and adipose tissue without directly stimulating insulin secretion from the pancreas. Also has a small effect on inhibiting hepatic glucose Liver function and bilirubin should be tested every 2 months for 1 year, then periodically thereafter. If ALT is >3x upper limit of normal, recheck another level as soon as possible. If ALT remains >3x the upper limit, discontinue use May restore ovulation in premenopausal anovulatory females Very expensive 				
Agents	Dose		Contraindications	Adverse Events
Rosiglitazone Pioglitazone	4 – 8 mg qd or divided into 2 doses 15 – 45 mg qd	<ul style="list-style-type: none"> May be given without regard to meals, no dosage adjustment required for renal insufficiency, and the current sulfonylurea, metformin, or insulin dose should be continued when adding rosiglitazone or pioglitazone. When using with insulin, if plasma glucose levels decrease to less than 100-120 mg/dL, the dose of insulin should be decreased by 10-25%. Continue to monitor the patient for further adjustments Slow onset of action 	Not Recommended <ul style="list-style-type: none"> New York Heart Association Classes III and IV Do not initiate in patients with ALT >2.5x the upper limit of normal 	<ul style="list-style-type: none"> Edema Weight gain Decrease Hgb/HCT Hepatotoxicity (rare)
Meglitinides				
<ul style="list-style-type: none"> Efficacy: estimate reduction in HbA_{1c} = 0.6 – 1.9% Like sulfonylureas (SFU), it stimulates pancreatic secretion of insulin. It has a faster onset and shorter duration of action than SFUs, therefore postprandial glucose is affected to a greater extent than fasting blood glucose Allows for flexible meal dosing Do not use in patients who have failed sulfonylurea therapy Expensive 				
Agents	Dose		Contraindications	Adverse Events
Repaglinide Nateglinide	Initial – 0.5 mg in patients with HbA _{1c} <8%. 1 or 2 mg in patients previously treated with hypoglycemics or if HbA _{1c} >8% Maximum – 4 mg per meal 120 mg before each meal.	<ul style="list-style-type: none"> Take 1 – 30 minutes before a meal. If the patient misses or adds a meal, he/she should omit or add the dose 	Use With Caution <ul style="list-style-type: none"> Repaglinide <ul style="list-style-type: none"> Hepatic impairment Severe renal impairment Nateglinide <ul style="list-style-type: none"> Moderate-severe hepatic impairment 	<ul style="list-style-type: none"> Hypoglycemia Weight gain

*In general, the hypoglycemic effects of glyburide and glipizide tend to plateau at 10 mg and 20 mg, respectively.