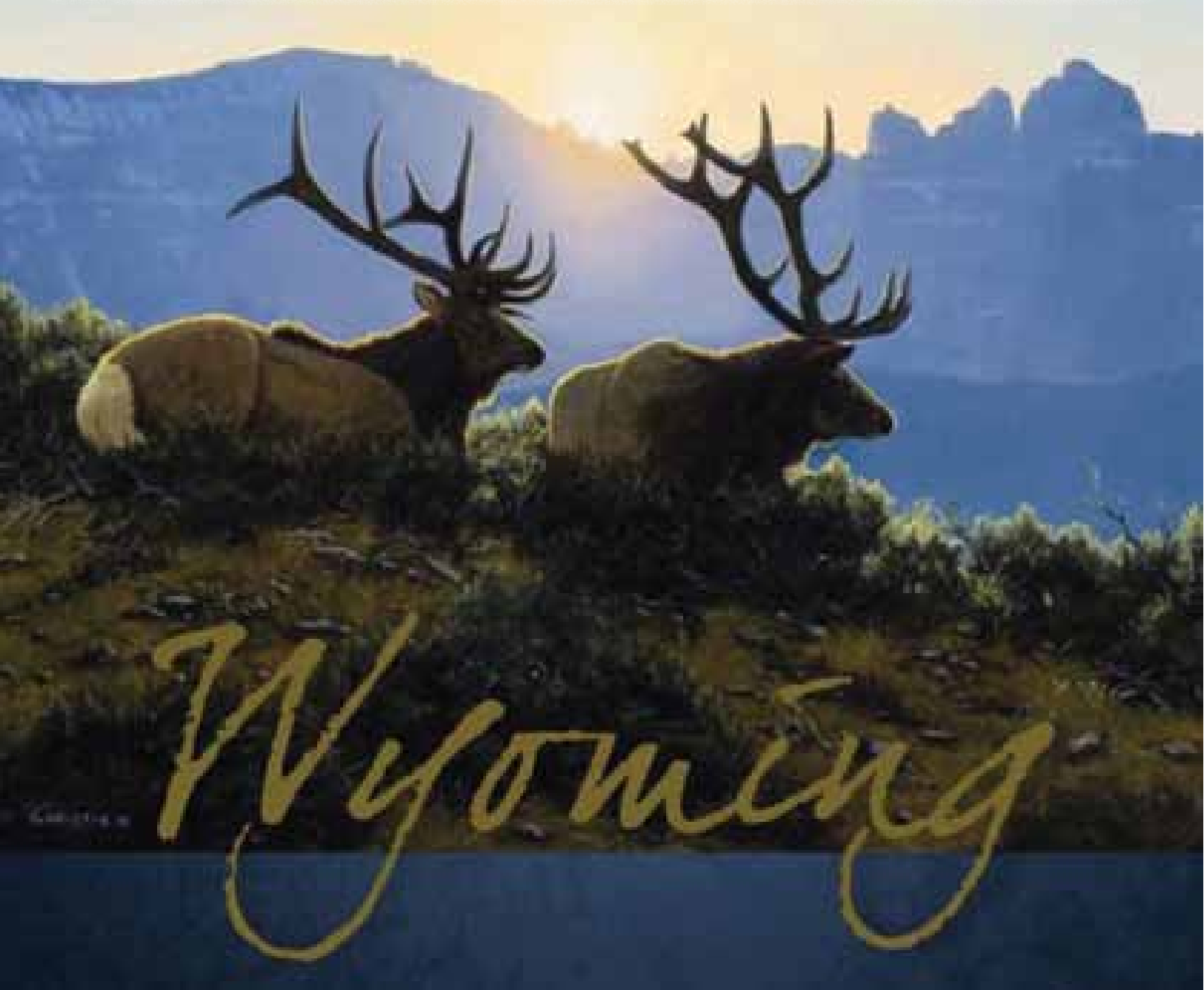
Clinical Practice Recommendations: DIABETES MELLITUS

2010 Revisions and Updates



Wyoming Clinical Practice Recommendations for Diabetes Mellitus

THIRD EDITION
2010

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AVAILABLE ONLINE AT:
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CLINICAL RECOMMENDATIONS COMMITTEE

Welcome to the third edition of the Wyoming Clinical Practice Recommendations for Diabetes Mellitus. These recommendations are intended for use by primary care professionals and are meant to be basic guidelines, not enforceable standards. The third edition is a printed supplement to the second edition of recommendations and is not a stand-alone document.

The Wyoming Diabetes Clinical Practice Recommendations Committee, in conjunction with the Wyoming Diabetes Prevention and Control Program, initially produced the recommendations as part of a statewide effort to improve the health care of people with diabetes. The Wyoming Diabetes Prevention and Control Program is coordinated by the Wyoming Department of Health and funded by a cooperative agreement from the Centers for Disease Control and Prevention.

These recommendations are offered in support of best practices consistent with current scientific knowledge. We encourage providers to modify these recommendations to meet the unique needs of each person with diabetes. These recommendations will be appropriate for treatment of most children and adults with diabetes most of the time, and the need for major modifications should not be common.

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II. Screening and Diagnosis

D. Diagnosis Criteria - Table 2

Diagnosing diabetes using A1c

A fourth measure for diagnosing diabetes is now available: A1c ≥ 6.5%.

The test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complication Trial (DCCT) assay.

III. Standards of Care for Diabetes in Adults

E2. Therapeutic Options: Oral Pharmacotherapy

TABLE 9a
Classifications of Non-Insulin Anti-Diabetic Agents

Drug Class	Generic Name	Brand Name	Dosing Range*	Dura-tion (hrs)	Average Cost (month)
Incretin-based agents: DPP IV Inhibitor	Saxagliptin	Onglyza	2.5-5.0 mg	Daily	$120-$140

* Although the maximum dose can often be safely exceeded, reaching the maximum dose usually indicates that it is time to move on to another type of therapy because dosing above the maximum dose usually does not produce any significant results, but does increase the cost of therapy.

DPP IV Inhibitor: Saxagliptin

Mode of Action: Onglyza is a DPP-IV inhibitor indicated as an adjunct oral therapy to diet and exercise to improve glycemic control with type 2 diabetes mellitus. Onglyza lowers blood sugar by helping the body increase the level of insulin after meals.

Profile: It is approved for use for patients who are on mono therapy and combination therapy using metformin, sulfonylureas, and thiazolidinediones. Caution must be used in the presence of hypoglycemia and use of sulfonylureas; dosings of sulfonylureas may need to be decreased.

Dosing: The recommended dose is a 2.5 mg or 5 mg tablet once daily taken regardless of meals.

Warnings: 2.5 mg daily is recommended for patients with moderate or severe renal impairment, or end-stage renal disease (CrCl ≤50 mL/min). Assess renal function prior to initiation of Onglyzia and periodically thereafter.

Moderate Inhibitors of CYP3A4/5: Diltiazem increased the exposure of saxagliptin. Similar increases in plasma concentrations of saxagliptin are anticipated in the presence of other moderate CYP3A4/5 inhibitors (e.g.,

amprenavir, aprepitant, erythromycin, fluconazolefosamprenavir, grapefruit juice, and verapamil); however, dosage adjustment of Onglyza is not recommended.

Strong Inhibitors of CYP3A4/5: Ketoconazole significantly increased saxagliptin exposure. Similar significant increases in plasma concentrations of saxagliptin are anticipated with other strong CYP3A4/5 inhibitors (e.g., atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin). The dose of Onglyza should be limited to 2.5 mg when coadministered with a strong CYP3A4/5 inhibitor.

Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Onglyza, like other anti-diabetic medications, should be used during pregnancy only if clearly needed.

Common side effects:

- Upper respiratory tract infection
- Urinary tract infection
- Headache

Contraindication: Onglyza should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis, as it would not be effective in these settings. Onglyza has not been studied in combination with insulin. No other contraindications are noted.

TABLE 9b
Classification of Incretin Mimetics-Injectable Non-Insulin Anti-Diabetes Agent

Drug Class	Generic Name	Brand Name	Dosing Range*	Dura-tion (hrs)	Average Cost (month)
Incretin-based Agents Incretin Mimetic	Exenatide	Byetta	5-10 mcg	Twice daily *(FDA approval pending for once weekly Bydureon)*	$200-$280
	Liraglutide	Victoza (rDNA origin)	0.6 - 1.2 mg or 1.2 - 1.8 mg	Once daily	$150

* Although the maximum dose can often be safely exceeded, reaching the maximum dose usually indicates that it is time to move on to another type of therapy because dosing above the maximum dose usually does not produce any significant results, but does increase the cost of therapy.

Incretin Mimetics: Liraglutide

Mode of Action: Victoza is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Profile: It is approved for use for patients who are on mono therapy and combination therapy using metformin, sulfonylureas, and thiazolidinediones. Caution must be used in the presence of hypoglycemia and use of sulfonylureas; dosings of sulfonylureas may need to be decreased.

Dosing: Administer once daily at any time of day, independent of meals. Inject subcutaneously in the abdomen, thigh or upper arm. The injection site and timing can be changed without

dose adjustment. Initiate at 0.6 mg per day for one week. This dose is intended to reduce gastrointestinal symptoms during initial titration, and is not effective for glycemic control. After one week, increase the dose to 1.2 mg. If the 1.2 mg dose does not result in acceptable glycemic control, the dose can be increased to 1.8 mg. When initiating Victoza, consider reducing the dose of concomitantly administered insulin secretagogues to reduce the risk of hypoglycemia.

Warnings - important limitations of use:

- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise.
- Has not been studied sufficiently in patients with a history of pancreatitis. Use caution.
- Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis.
- Has not been studied in combination with insulin.

Risk of thyroid C-cell tumors (See full prescribing information for complete boxed warning)
Liraglutide causes thyroid C-cell tumors at clinically relevant exposures in rodents. It is unknown whether Victoza causes thyroid C-cell tumors, including medullary thyroid carcinoma in humans, as human relevance could not be determined by clinical or nonclinical studies.

Contraindication: Victoza is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2.

V. Treatment of Comorbid Conditions

E. Bariatric Surgery - *New Section*

Bariatric surgery should be considered for individuals with type 2 diabetes with a BMI >35 kg/m^2; especially if comorbidities exist and are difficult to manage. Currently there is not enough evidence to recommend bariatric surgery for patients with type 2 diabetes and a BMI <35 kg/m^2.

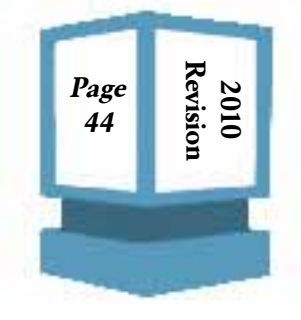
It is important for patients who have undergone bariatric surgery to have life-long medical and lifestyle support from the health care team. Screening for nutritional deficiencies, psychosocial adjustments, and assistance with physical activity are needed to help prevent recidivism.

VI. Complications, Prevention, Screening and Treatment

F. Hypoglycemia

Prevention of Hypoglycemia Unawareness

The ADA recommends that individuals with hypoglycemia unawareness or episodes of severe hypoglycemia be advised to raise their glycemic targets for at least several weeks to avoid further hypoglycemia. The goal is to reverse hypoglycemia unawareness and reduce the risk of future hypoglycemic episodes.



VII. Prevention and Lifestyle Measures

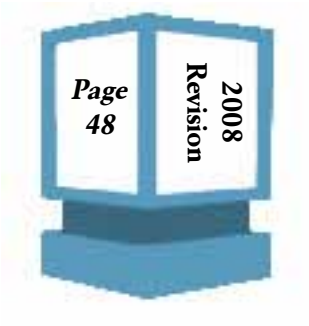
D. Physical Activity/Exercise

Frequency of Physical Activity

The ADA recommends a minimum of 150 minutes of physical activity a week. Resistance training is recommended three times a week for individuals with type 1 diabetes, type 2 diabetes or pre-diabetes in the absence of contraindications.

E. Medical Nutrition Therapy

Low-Carbohydrate Diets



The American Diabetes Association (ADA) made the following change concerning low-carbohydrate diets in the 2008 Clinical Practice Recommendations:

> "For weight loss, either low-carbohydrate or low-fat calorie-restricted diets may be effective in the short-term (up to one year)."

If low-carbohydrate diets are used, the ADA recommends monitoring lipid profiles and renal function. For patients with nephropathy, protein intake should also be monitored.

Additionally, the ADA states the recommended dietary allowance for digestible carbohydrate is 130 grams a day to meet required fuel needs for the central nervous system without reliance on glucose production from ingested protein or fat. The long term metabolic effects of very-low-carbohydrate diets (less than 130 grams a day) are unclear.

VIII. Pre-diabetes, Metabolic Syndrome and Prevention of Type 2 Diabetes

C. Recommendations to Prevent or Delay Type 2 Diabetes

Diagnosis of Pre-Diabetes

Pre-diabetes can now be designated by using A1c. Guidelines from the American Diabetes Association (ADA) use the range of A1c from 5.7 to 6.4 to designate pre-diabetes.

Structured Programs

Individuals at high risk for developing diabetes should be made aware of the benefits of participating in a structured program which emphasizes lifestyle changes including weight loss (7% of body weight), regular physical activity (at least 150 min/week), and nutritional strategies that include reducing calories and increasing dietary fiber from whole plant foods. Follow-up counseling can also be helpful for overall success.

Use of Metformin

At the present time, no pharmacologic intervention is proven to be effective in prevention of type 2 diabetes; however, individuals with both impaired fasting glucose and impaired glucose intolerance may benefit from metformin therapy.

Pre-diabetes Monitoring

Individuals with pre-diabetes should be monitored yearly for the development of diabetes.

IX. Diabetes During Pregnancy

B. Quick Reference Guide for the Care of Gestational Diabetes

Additions to Table 27

In addition to the blood glucose goals listed in the table, the following blood glucose goals are added:

- 2 hour post prandial: <120 mg/dL
- Night-time: >60 mg/dL

Differing Glycemic Control Guidelines in Pregnancy from Expert Panels

Several professional organizations, including the American Congress of Obstetricians and Gynecologists (ACOG), ADA, AACE and others, have released guidelines for glycemic control in pregnancy. Although the recommended targets are similar, they vary between groups. After reviewing currently available consensus statements (see references), the Wyoming Diabetes Clinical Recommendations Revision Committee recommends the AACE targets for glycemic control during pregnancy.

It is essential, however, that clinicians understand the need to individualize therapy. There may be situations where more aggressive targets are difficult to achieve, such as individuals with type 1 diabetes and hypoglycemic unawareness. The benefits of aggressive glycemic control on the outcome of pregnancy must be balanced with the potential increased risk of hypoglycemia.

References:

1. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Obstet Gynecol. 2005;105:675.
2. Metzger BE, Buchanan TA, Coustan DR, et al. Summary and Recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care. 2007;30:S251-S260.
3. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care. 2008 31:S12-S54.
4. AACE Diabetes Mellitus Guidelines. Endocr Pract. 2007;13(Suppl 1).
5. Kitzmiller JL, Block JM, Brown FM, et al. Managing Preexisting Diabetes for Pregnancy: Summary of evidence and consensus recommendations for care. Diabetes Care. 2008;31:1060-1079.

X. Diabetes Care in the Hospital

A. Guidelines for Hospitalization

Glycemic Goals For Hospitalized Patients

Inpatient diabetes management has been the focus of attention in the past few years and several highly-acclaimed studies have demonstrated important benefits in tighter glycemic control in hospital patients. These benefits are more apparent in acutely ill patients in the ICU settings, with less evidence for non-critically ill patients. In 2009, the American College of Endocrinology and the American Diabetes Association updated their consensus statement on inpatient diabetes and glycemic control.

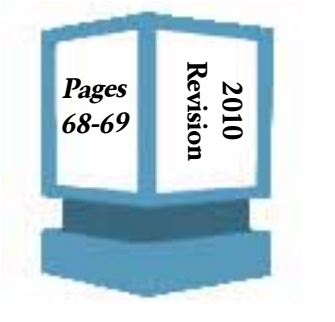
In the intensive care setting, insulin therapy is advised to treat persistent hyperglycemia, starting at a BG of no greater than 180 mg/dL with a recommended target range of 140 to 180 mg/dL. Lower glucose targets may be appropriate in selected patients.

For the majority of noncritically ill patients treated with insulin, the premeal BG target should be <140 mg/dL with random BG values <180 mg/dL, provided these targets can be safely achieved without hypoglycemia. More aggressive glycemic targets may be appropriate in stable patients with previous tight glycemic control. Less aggressive targets may be appropriate in terminally ill patients or those with severe comorbidities.

Values above 180 mg/dL are an indication to monitor glucose levels more frequently to determine the direction of any glucose trend and the need for more intensive intervention. Hypoglycemia (BG< 70 mg/dL) without a good explanation (i.e. a missed meal) merits further evaluation and modification of the regimen. Achieving these targets may require consultation with a diabetes specialist.

The occurrence of significant hyperglycemia in the hospital requires close follow-up after discharge. In those with previously diagnosed diabetes and an elevated A1c on hospital admission, revision of the pre-admission diabetes therapy is required to establish glycemic control. In those without previously diagnosed diabetes, the differentiation between hospital-related hyperglycemia and undiagnosed diabetes requires follow-up testing (Fasting BG, A1c, 2-hour OGTT) once metabolically stable.

AACE/ADA Consensus: Inpatient Hyperglycemia, Endocr Pract. 2009;15(No. 4)



Sample Intravenous Insulin Orders (Chart Pages 68-69)

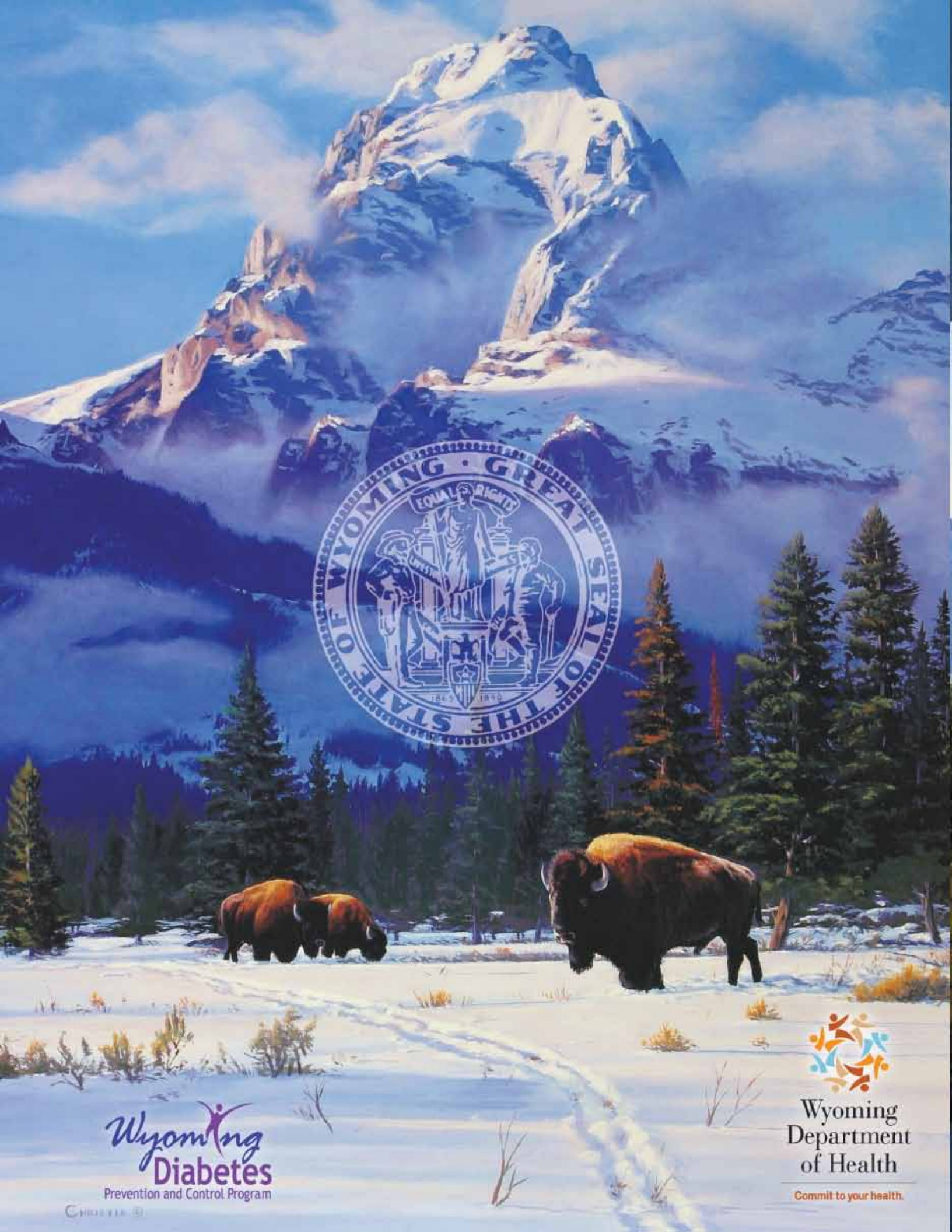
When preparing insulin for IV use, note the following:

1. Insulin adheres to IV bags and tubing
2. Therefore the insulin concentration should be no less than 10% (e.g. no less than 25 units in 250 cc)
3. Mix well, and
4. Discard the first 50 cc of the mixture through the IV tubing to ensure you are immediately delivering the full concentration of insulin you intend to deliver.

XII. Associated Disorders

B4. Psychosocial Assessment and Care - *New Section*

Patients with diabetes should receive regular assessment of psychological and social needs. The ongoing assessment can include attitudes about illness, expectations for medical management and outcomes, affect and mood, quality of life, resources (financial, social, and emotional), symptoms of depression, eating disorders, anxiety, and cognitive impairment.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