1. When switching to insulin glargine U300 from twice daily insulin NPH, the daily dose of the new basal insulin should be _________.
   a) 50% of the daily insulin NPH dose
   b) 80% of the daily insulin NPH dose
   c) The same as the daily insulin NPH dose
   d) 120% of the daily insulin NPH dose
   e) 150% of the daily insulin NPH dose

**Rationale:** When initiating insulin glargine U300 in patients with T2DM who are already being treated with NPH insulin, the US Food and Drug Administration recommends an initial dose reduction to 80% of the daily NPH insulin dose. This recommendation reflects the increased focus on avoiding hypoglycemia, the most common adverse reaction to insulin replacement therapy.

2. Compared with insulin glargine U100, insulin degludec U100 has _________.
   a) Shown a shorter duration of effect in clinical trials for T2DM
   b) Generally shown lower rates of overall and nocturnal hypoglycemia in clinical trials
   c) Shown greater pharmacodynamic variability in its antihyperglycemic effect over a 24-hour period
   d) Produced less weight gain in trials for T2DM
   e) None of the above

**Rationale:** Compared with insulin glargine U100, the ultra-long-acting basal insulin degludec U100 has demonstrated reduced daily pharmacodynamic variability in its glucose-lowering effect, which has been shown to persist for more than 40 hours in clinical trials. These properties likely contribute to the observed lower rates of overall and nocturnal hypoglycemia with insulin degludec compared with insulin glargine, whereas no advantage has been noted for changes in body weight.

3. Compared with adding prandial insulin, adding a GLP-1 receptor agonist to a basal insulin regimen for a patient with T2DM who has an A1c value of 7.7% is likely to produce each of the following clinical outcomes EXCEPT_________.
   a) Reductions in body weight
   b) Increased risk of treatment-related nausea
   c) Fewer episodes of hypoglycemia
   d) Decreased fasting blood glucose levels without markedly affecting postprandial hyperglycemia
**Rationale:** Studies examining GLP-1 receptor agonists vs various prandial insulin regimens in patients with T2DM have generally shown similar A1c reductions and good control of prandial hyperglycemic excursions, with the additional benefit of reduced in body weight in trial cohorts treated with the incretin-based agents (Diamant M, et al. *Diabetes Care*. 2014;37:2763-2773; Mathieu C, et al. *Diabetes Obes Metab*. 2014;16:636-644; Rosenstock J, et al. *Diabetes Care*. 2014;37:2317-2325). Moreover, because the antihyperglycemic effects of GLP-1 receptor agonists are glucose-dependent, the activity of these agents decreases in the presence of low blood sugar, thereby reducing the risk of hypoglycemia vs treatment with prandial insulin.

4. Which of the following GLP-1 receptor agonists has been combined with a basal insulin analog in a fixed-dose, 2-drug formulation that has been recommended for approval by a US Food and Drug Administration advisory committee for the treatment of patients with T2DM?

   a) Albiglutide
   b) Exenatide once weekly
   c) Dulaglutide
   d) Liraglutide

**Rationale:** In mid-2016, 2 fixed-dose combinations of a GLP-1 receptor agonist and a basal insulin analog were recommended for approval by an FDA advisory committee. Liraglutide plus insulin degludec (IDegLira) received a 16-0 vote in favor of approval, and lixisenatide plus insulin glargine (iGlarLixi) received a 12-2 positive vote.

5. A 55-year-old woman with T2DM (current A1c, 7.1%) who recently lost 10% of her body weight comes to an appointment complaining of 3 instances of low blood sugar over the last week. These hypoglycemic episodes are confirmed by her daily blood glucose log. She is being treated with metformin 1000 mg twice daily and insulin glargine 20 units each morning. After completing the enduring educational program, which of the following potential changes to her treatment regimen are you NOW most likely to recommend?

   a) Discontinue metformin
   b) Discontinue insulin
   c) **Reduce her daily insulin glargine dose by 4 units**
   d) Reduce her daily insulin glargine dose by 10 units
   e) Add a sulfonylurea to her treatment regimen

**Rationale:** The latest guidelines from the American Diabetes Association recommend that clinicians respond to hypoglycemic episodes in patients with T2DM who are on insulin therapy by determining cause, and reducing the daily insulin by the greater of 4 units or 10% to 20% (ADA, *Diabetes Care*. 2016;39(suppl 1):S1-S112). Moreover, providers should consider stopping or reducing the doses of other noninsulin medications that may be significantly contributing to episodes of low blood sugar (eg, sulfonylureas).