

Compliance and ethics program (§483.85). Facilities will be required to have a compliance and ethics program with written standards, and policies and procedures that can reduce the prospect of criminal, civil and administrative violations.

Training requirements (§483.95). A section on training will require facilities to develop, implement, and maintain an effective training program for new and existing staff, contracted individuals, and volunteers.

CMS estimated that the projected estimated cost of the final rule will be \$831 million in the first year, and \$736 million annually thereafter. The average facility costs are estimated to be \$62,900 the first year, and \$55,000 per year for subsequent years.

The Society and many other stakeholders submitted comments to the proposed rule last summer, and CMS clearly responded to these by removing some of the original regulations, including a requirement that every resident be

evaluated by a physician or non-physician practitioner before any transfer to the emergency department.

Caring will provide more information on the final rule in future issues. The Society also will post a webinar on this topic sometime in November. For more information, go to <https://federalregister.gov/d/2016-23503>.

Carey Cowles is the managing editor of *Caring for the Ages*.

FDA: New Boxed Warning on Combining Opioids, Benzodiazepines

Sharon Worcester

Labeling for prescription opioid pain or cough medicines and benzodiazepines will now carry the strongest available warning regarding serious side effects and death associated with their combined use, according to the Food and Drug Administration.

The new boxed warnings urge health care professionals to limit prescribing opioid pain medicines with benzodiazepines or other central nervous system depressants only to patients for whom alternative treatment options are inadequate, and to limit dosages and treatment duration to the minimum possible while achieving the desired clinical effect.

Opioids will include a warning regarding prescribing with benzodiazepines and other central nervous system depressants, including alcohol. Benzodiazepines will include a warning regarding prescribing with opioids.

The action comes amid ongoing efforts to address an epidemic of opioid addiction across the United States, and in response to a first-of-its-kind “citizen petition” calling for the boxed warnings.

Sharon Worcester is with the Southeast bureau of Frontline Medical News.

EDITOR'S NOTE

Most of us should know the potentiation of respiratory depression with concomitant administration of benzodiazepines and opioids. Although the risk of clinically significant respiratory depression with pure opioids (e.g., morphine) has been overblown and is rare in clinical practice, mixing opioids with benzos is known to increase the risk of serious respiratory compromise. The new boxed warning won't mean we can't use them together, but we can expect to get the usual communications from our consultant pharmacists when we do. Benzodiazepines — although most of us still prescribe them at times — are pretty risky and not that effective for many conditions they're commonly used for, most notably dementia-related agitation. They disinhibit behavior and increase the risk of falls, among other adverse effects. The FDA is taking an appropriate step to remind us not to combine opioids and benzos indiscriminately. As always, let's keep our individual patients' situations always at the forefront of decision making.

—Karl Steinberg, MD, CMD, HMDC
Editor in Chief

Adverse reactions occurring in ≥5% of adult patients with type 1 diabetes treated with BASAGLAR (combined with insulin lispro) in a 52-week trial were infection (24%), nasopharyngitis (16%), and upper respiratory tract infection (8%). Adverse reactions occurring in ≥5% of adult patients with type 2 diabetes treated with BASAGLAR in a 24-week trial were infection (17%), nasopharyngitis (6%), and upper respiratory tract infection (5%).

Allergic Reactions

Some patients taking insulin therapy, including BASAGLAR have experienced erythema, local edema, and pruritus at the site of injection. These conditions were usually self-limiting. Severe cases of generalized allergy (anaphylaxis) have been reported [see Warnings and Precautions (5.5)].

Weight Gain

Weight gain can occur with insulin therapy, including BASAGLAR, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

Peripheral Edema

Some patients taking BASAGLAR have experienced sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy.

Lipodystrophy

Administration of insulin subcutaneously, including BASAGLAR, has resulted in lipoatrophy (depression in the skin) or lipohypertrophy (enlargement or thickening of tissue) in some patients [see Dosage and Administration (2.1)].

Weight Gain

Weight gain has occurred with some insulin therapies including BASAGLAR and has been attributed to the anabolic effects of insulin and the decrease in glucosuria.

Severe Hypoglycemia

Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including BASAGLAR [see Warnings and Precautions]. The rates of reported hypoglycemia depend on the definition of hypoglycemia used, diabetes type, insulin dose, intensity of glucose control, background therapies, and other intrinsic and extrinsic patient factors. For these reasons, comparing rates of hypoglycemia in clinical trials for BASAGLAR with the incidence of hypoglycemia for other products may be misleading and also, may not be representative of hypoglycemia rates that will occur in clinical practice. Severe symptomatic hypoglycemia was defined as an event with symptoms consistent with hypoglycemia requiring the assistance of another person and associated with either a blood glucose below 50 mg/dL or prompt recovery after oral carbohydrate, intravenous glucose or glucagon administration. The incidence of severe symptomatic hypoglycemia in patients receiving BASAGLAR with type 1 diabetes mellitus and type 2 diabetes mellitus [see Clinical Studies] was 4% at 52 weeks and 1% at 24 weeks, respectively.

USE IN SPECIFIC POPULATIONS

Pregnancy—Pregnancy Category C. Female patients should be advised to tell their physicians if they intend to become, or if they become pregnant while taking BASAGLAR.

There are no well-controlled clinical studies of the use of insulin glargine in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—It is unknown whether insulin glargine is excreted in human milk. Use of insulin glargine is compatible with breastfeeding, but women with diabetes who are lactating may require adjustments of their insulin doses.

Pediatric Use—The safety and effectiveness of BASAGLAR have been established in pediatric patients (age 6 to 15 years) with type 1 diabetes based on an adequate and well-controlled trial of another insulin glargine product, 100 units/mL, in pediatric patients (age 6 to 15 years) with type 1 diabetes and additional data in adults with type 1 diabetes [see Clinical Studies (14.2)]. The safety and effectiveness of BASAGLAR in pediatric patients younger than 6 years of age with type 1 diabetes and pediatric patients with type 2 diabetes has not been established.

In the pediatric clinical trial of another insulin glargine, pediatric patients (age 6 to 15 years) with type 1 diabetes had a higher incidence of severe symptomatic hypoglycemia compared to the adults in trials with type 1 diabetes [see Adverse Reactions].

Geriatric Use—Of the total number of subjects in clinical studies of patients with type 2 diabetes who were treated with BASAGLAR or another insulin glargine product, 100 units/mL, each in combination with oral agents in a controlled clinical trial environment, 28.3% were 65 and over, while 4.5% were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Nevertheless, caution should be exercised when BASAGLAR is administered to geriatric patients. In elderly patients with diabetes, the initial dosing, dose increments, and maintenance dosage should be conservative to avoid hypoglycemic reactions. Hypoglycemia may be difficult to recognize in the elderly.

Renal Impairment—The effect of renal impairment on the pharmacokinetics of BASAGLAR has not been studied.

Hepatic Impairment—The effect of hepatic impairment on the pharmacokinetics of BASAGLAR has not been studied.

Obesity—In controlled clinical trials, subgroup analyses based on BMI did not show differences in safety and efficacy between BASAGLAR and another insulin glargine product, 100 units/mL.

OVERDOSAGE

Excess insulin administration relative to food intake, energy expenditure, or both may lead to severe and sometimes prolonged and life-threatening hypoglycemia and hypokalemia [see Warnings and Precautions (5.3, 5.6)]. Mild episodes of hypoglycemia can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or physical activity level may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

PATIENT COUNSELING INFORMATION: See FDA-approved patient labeling and Patient Counseling Information section of the Full Prescribing Information.

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Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA and Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT 06877, USA

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Additional information can be found at www.BASAGLAR.com.

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