

Steroid-Induced Osteoporosis Is a Top Challenge

BY BRUCE JANCIN

ESTES PARK, COLO. — Poor adherence accounts for more than 90% of all cases of failure to respond to osteoporosis therapy as evidenced by declining bone density or a fracture.

Lack of medication efficacy, on the other hand, is the least likely of the common causes for failure to respond. It ranks behind calcium/vitamin D deficiency, hyperthyroidism and other comorbid conditions, and the use of corticosteroids or other osteoporosis-inducing medications to treat comorbid conditions, Dr. Michael T. McDermott said at a conference on internal medicine sponsored by the University of Colorado.

He singled out failure to respond to treatment as one of the five top challenges in osteoporosis management today. Here are the other challenges highlighted by Dr. McDermott, professor of medicine and director of endocrinology and diabetes practice at University of Colorado Hospital, Denver:

► **Osteoporosis-inducing medications.** Glucocorticoids top the list. They simultaneously reduce bone formation and increase bone resorption, resulting in quick bone loss in patients taking

invasive dental procedure such as tooth extraction. Dr. McDermott said that he doesn't see it often, but he fields many phone calls about it. The great majority of cases have occurred in patients on high-dose intravenous bisphosphonate therapy for underlying bone cancer; oral bisphosphonates have not been shown to cause the disorder. Nevertheless, when Dr. McDermott is ready to start a patient on a bisphosphonate, he asks if a tooth

extraction or dental implant is planned; if so, he'll wait to start the drug until after the procedure.

► **Osteoporosis medications and renal disease.** Citing a lack of safety data, the Food and Drug Administration recommends against using bisphosphonates in patients with an estimated glomerular filtration rate (eGFR) below 30 mL/min per 1.73 m². However, limited experience indicates that treatment is reassuringly

safe and effective in patients with an eGFR of 15-30 mL/min per 1.73 m², according to Dr. McDermott.

"I do caution against antiresorptive therapy in patients with an eGFR below 15 mL/min—stage 5 chronic kidney disease—because it may predispose to adynamic bone disease," he added.

Dr. McDermott disclosed serving on the speakers bureaus of several pharmaceutical companies. ■



Anticonvulsants are the second most common cause of medication-induced osteoporosis.

DR. McDERMOTT

steroids. Serious consideration should be given to prescribing osteoporosis therapy in any patient who has ever been on 5 mg/day or more of prednisone for at least 3 months, he said.

Compelling 18-month data from a randomized trial of teriparatide (Forteo) versus alendronate (Fosamax) for the treatment of glucocorticoid-induced osteoporosis showed teriparatide to be the clear winner, both in terms of increased bone density and fewer vertebral fractures (N. Engl. J. Med. 2007;357:2028-39). The soon-to-be-published 3-year follow-up data confirm this. Both drugs have FDA approval for this indication.

Anticonvulsants are the No. 2 class of medications causing osteoporosis. "Anti-convulsant-induced osteoporosis hasn't been recognized as much, but it's emerging as quite important. It's a much bigger problem with phenobarbital, Dilantin, and Tegretol than with the newer anticonvulsants," he said.

► **Atypical fractures of the femoral diaphysis.** These fractures are the most recent and worrisome development in the osteoporosis field. Many experts now informally advocate a bisphosphonate therapy holiday after 5 years of use in an effort to avoid these fractures.

► **Osteonecrosis of the jaw.** This condition is marked by nonhealing exposed bone for at least 8 weeks following an in-



To access Complimentary E-Learning Programs, visit novomedlink.com/Levemir

*Model is for illustrative purposes only.

Indications and usage

Levemir® is indicated for once- or twice-daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

Important safety information

Levemir® is contraindicated in patients hypersensitive to insulin detemir or one of its excipients.

Hypoglycemia is the most common adverse effect of all insulin therapies, including Levemir®. As with other insulins, the timing of hypoglycemic events may differ among various insulin preparations. Glucose monitoring is recommended for all patients with diabetes. Levemir® is not to be used in insulin infusion pumps. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetes treatment may require adjustment.

Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic

ketoacidosis. Levemir® should not be diluted or mixed with any other insulin preparations. Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. Dose and timing of administration may need to be adjusted to reduce the risk of hypoglycemia in patients being switched to Levemir® from other intermediate or long-acting insulin preparations. The dose of Levemir® may need to be adjusted in patients with renal or hepatic impairment. Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

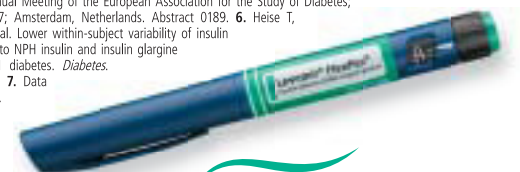
Whether these observed differences represent true differences in the effects of Levemir®, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

For your patients with type 2 diabetes, start once-daily Levemir®

Levemir® helps patients with diabetes achieve their A1C goal.^{1,2}

- 24-hour action at a once-daily dose^{3,4}
- Provides consistent insulin absorption and action, day after day^{3,5,6}
- Less weight gain^{7†}

References: 1. Meneghini LF, Rosenberg KH, Koenen C, Meriläinen MJ, Lüddeke H-J. Insulin detemir improves glycaemic control with less hypoglycaemia and no weight gain in patients with type 2 diabetes who were insulin naive or treated with NPH or insulin glargine: clinical practice experience from a German subgroup of the PREDICTIVE study. *Diabetes Obes Metab.* 2007;9(3):418-427. 2. Hermansen K, Davies M, Derezinski T, Ravn GM, Clauson P, Home P, for the Levemir Treat-to-Target Study Group. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetes Care.* 2006;29(6):1269-1274. 3. Klein O, Lyngé J, Endahl L, Damholt B, Nosek L, Heise T. Albumin-bound basal insulin analogues (insulin detemir and NN344): comparable time-action profiles but less variability than insulin glargine in type 2 diabetes. *Diabetes Obes Metab.* 2007;9(3):290-299. 4. Philis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther.* 2006;28(10):1569-1581. 5. Danne T, Endahl L, Haahr H, et al. Lower within-subject variability in pharmacokinetic profiles of insulin detemir in comparison to insulin glargine in children and adolescents with type 1 diabetes. Presented at: 43rd Annual Meeting of the European Association for the Study of Diabetes; September 17-21, 2007; Amsterdam, Netherlands. Abstract 0189. 6. Heise T, Nosek L, Renn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes.* 2004;53(6):1614-1620. 7. Data on file. NDA21-536. Novo Nordisk Inc, Princeton, NJ.



Levemir®
insulin detemir (rDNA origin) injection



Please see brief summary of Prescribing Information on adjacent page.

FlexPen® and Levemir® are registered trademarks of Novo Nordisk A/S. © 2008 Novo Nordisk Inc. 133236R1

May 2008