

Payments Uncertain as Insurers' Agreements Expire

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LAS VEGAS — As more of the agreements signed by several large insurers to settle a class action suit alleging inappropriate billing practices expire, the possibility is increasing that the companies will return to the same behavior, especially given that many are being accused of violating the terms already, reported a compliance expert at a physicians' meeting.

Several of the health plans have said they will continue to comply with the terms of their settlements once they expire, but "not all have said that," said Edward R. Gaines III, vice president and chief compliance officer for Healthcare Business Resources in Durham, N.C., who spoke at a meeting on reimbursement sponsored by the American College of Emergency Physicians (ACEP).

Mr. Gaines said that noncompliance among all the plans that have settled has

continued to be an issue, which is being dealt with in the courts and administratively. But, "the problem is, once the settlement agreement expires, I can't go back into federal court through an easy process to make my complaint heard," he said.

The settlements were struck in response to Multidistrict Litigation 1334, which was certified as a class action in U.S. District Court for the Southern District of Florida in 2002 and named Aetna Inc., Anthem Insurance Cos. Inc., Cigna, Coventry

Health Care Inc., Health Net Inc., Humana Inc., PacifiCare Health Systems Inc., Prudential Insurance Co. of America, United Healthcare, and WellPoint Health Networks Inc. as defendants.

The suits alleged that the insurers violated the federal Racketeer Influenced and Corrupt Organizations Act by engaging in fraud and extortion in a common scheme to wrongfully deny payment to physicians.

Several state and county medical societies filed the suits on behalf of virtually every physician in the nation—about 900,000 doctors.

United Healthcare and Coventry both were summarily released from the litigation. Their release has been upheld on appeal.

Aetna and Cigna struck agreements that entailed an immediate payout in response to claims filed by physicians, some changes in billing behavior, and an agreement to provide prospective relief—\$300 million from Aetna and \$400 million from Cigna.

Cigna's 4-year agreement has now expired, and Aetna's 4-year agreement expired in June 2007; but Aetna's agreement was extended through this month because of compliance disputes. After an investigation, the New Jersey insurance department fined Aetna \$9.5 million in June 2007 for failing to properly pay for out-of-network providers. The insurer is paying nonparticipating physicians only 125% of Medicare rates and informing patients that they are not responsible for the difference.

The national-level ACEP, the North Carolina chapter of ACEP, Wake Emergency Physicians, and the North Carolina Medical Society all subsequently followed up with a complaint to the North Carolina insurance department in November, said Mr. Gaines. The North Carolina group is challenging bundling of 12-lead ECGs into evaluation and management codes, and bundling of other procedures that use the CPT-25 modifier codes.

"If we don't get prompt action from Aetna, we're going back to court [to] ask for an extension of the settlement agreement term," he said.

The American Medical Association and Aetna recently announced that they are working together to resolve outstanding complaints.

Prudential's agreement expires in 2009, and agreements with three other insurers expire in 2010: HealthNet, Anthem/WellPoint, and Humana.

Agreements were reached with 90% of the nation's Blue Cross and Blue Shield plans. The Blues plans agreed to similar terms as did the other payers, with one exception: Anthem/WellPoint and the Blues plans refused to accept assignment of benefits. In fact, the Blues plans were willing to walk away from the settlement if they did not win that concession, said Mr. Gaines.

Mr. Gaines urged physicians to hold the health plans that settled accountable to their agreements.

Information on settlement terms and how to dispute claims can be found at www.hmosettlements.com. ■

HUMALOG® Mix75/25™ 75% INSULIN LISPRO PROTAMINE SUSPENSION AND 25% INSULIN LISPRO INJECTION (rDNA ORIGIN) BRIEF SUMMARY: Consult package insert for complete prescribing information.

INDICATIONS AND USAGE: Humalog Mix75/25, a mixture of 75% insulin lispro protamine suspension and 25% insulin lispro injection (rDNA origin), is indicated in the treatment of patients with diabetes mellitus for the control of hyperglycemia. Humalog Mix75/25 has a more rapid onset of glucose-lowering activity compared with Humulin 70/30 while having a similar duration of action. This profile is achieved by combining the rapid onset of Humalog with the intermediate action of insulin lispro protamine suspension.

CONTRAINDICATIONS: Humalog Mix75/25 is contraindicated during episodes of hypoglycemia and in patients sensitive to insulin lispro or any of the excipients contained in the formulation.

WARNINGS: Humalog differs from regular human insulin by its rapid onset of action as well as a shorter duration of activity. Therefore, the dose of Humalog Mix75/25 should be given within 15 minutes before a meal.

Hypoglycemia is the most common adverse effect associated with the use of insulins, including Humalog Mix75/25. As with all insulins, the timing of hypoglycemia may differ among various insulin formulations. Glucose monitoring is recommended for all patients with diabetes. Any change of insulin should be made cautiously and only under medical supervision.

Changes in insulin strength, manufacturer, type (eg, regular, NPH, analog), species, or method of manufacture may result in the need for a change in dosage.

PRECAUTIONS: *General*—Hypoglycemia and hypokalemia are among the potential clinical adverse effects associated with the use of all insulins. Because of differences in the action of Humalog Mix75/25 and other insulins, care should be taken in patients in whom such potential side effects might be clinically relevant (eg, patients who are fasting, have autonomic neuropathy, or are using potassium lowering drugs or patients taking drugs sensitive to serum potassium level). Lipodystrophy and hypersensitivity are among other potential clinical adverse effects associated with the use of all insulins.

As with all insulin preparations, the time course of Humalog Mix75/25 action may vary in different individuals or at different times in the same individual and is dependent on site of injection, blood supply, temperature, and physical activity.

Adjustment of dosage of any insulin may be necessary if patients change their physical activity or their usual meal plan. Insulin requirements may be altered during illness, emotional disturbances, or other stress.

Hypoglycemia—As with all insulin preparations, hypoglycemic reactions may be associated with the administration of Humalog Mix75/25. Rapid changes in serum glucose concentrations may induce symptoms of hypoglycemia in persons with diabetes, regardless of the glucose value. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as long duration of diabetes, diabetic nerve disease, use of medications such as beta blockers, or intensified diabetes control.

Renal Impairment—As with other insulins, the requirements for Humalog Mix75/25 may be reduced in patients with renal impairment.

Hepatic Impairment—Although impaired hepatic function does not affect the absorption or disposition of Humalog, careful glucose monitoring and dose adjustments of insulin, including Humalog Mix75/25, may be necessary.

Allergy—Local Allergy—As with any insulin therapy, patients may experience redness, swelling, or itching at the site of injection. These minor reactions usually resolve in a few days to a few weeks. In some instances, these reactions may be related to factors other than insulin, such as irritants in a skin cleansing agent or poor injection technique.

Systemic Allergy—Less common, but potentially more serious, is generalized allergy to insulin, which may cause rash (including pruritus) over the whole body, shortness of breath, wheezing, reduction in blood pressure, rapid pulse, or sweating. Severe cases of generalized allergy, including anaphylactic reaction, may be life-threatening. Localized reactions and generalized myalgias have been reported with the use of cresol as an injectable excipient.

Antibody Production—In clinical trials, antibodies that cross-react with human insulin and insulin lispro were observed in both human insulin mixtures and insulin lispro mixtures treatment groups.

Information for Patients—Patients should be informed of the potential risks and advantages of Humalog Mix75/25 and alternative therapies. Patients should not mix Humalog Mix75/25 with any other insulin. They should also be informed about the importance of proper insulin storage, injection technique, timing of dosage, adherence to meal planning, regular physical activity, regular blood glucose monitoring, periodic hemoglobin A1C testing, recognition and management of hypoglycemia and hyperglycemia, and periodic assessment for diabetes complications.

Patients should be advised to inform their physician if they are pregnant or intend to become pregnant.

Refer patients to the "PATIENT INFORMATION" leaflet for information on normal appearance, timing of dosing (within 15 minutes before a meal), storing insulin, and common adverse effects.

For Patients Using Insulin Pen Delivery Devices: Before starting therapy, patients should read the "PATIENT INFORMATION" leaflet that accompanies the drug product and the User Manual that accompanies the delivery device. They should also re-read these materials each time the prescription is renewed. Patients should be instructed on how to properly use the delivery device, prime the Pen, and properly dispose of needles. Patients should be advised not to share their Pens with others.

Laboratory Tests—As with all insulins, the therapeutic response to Humalog Mix75/25 should be monitored by periodic blood glucose tests. Periodic measurement of hemoglobin A1C is recommended for the monitoring of long-term glycemic control.

Drug Interactions—Insulin requirements may be increased by medications with hyperglycemic activity, such as corticosteroids, isoniazid, certain lipid-lowering drugs (eg, niacin), estrogens, oral contraceptives, phenothiazines, and thyroid replacement therapy.

Insulin requirements may be decreased in the presence of drugs that increase insulin sensitivity or have hypoglycemic activity, such as oral antidiabetic agents, salicylates, sulfa antibiotics, certain antidepressants (monoamine oxidase inhibitors), angiotensin-converting-enzyme inhibitors, angiotensin II receptor blocking agents, beta-adrenergic blockers, inhibitors of pancreatic function (eg, octreotide), and alcohol. Beta-adrenergic blockers may mask the symptoms of hypoglycemia in some patients.

Pregnancy—Teratogenic Effects—Pregnancy Category B—Reproduction studies with insulin lispro have been performed in pregnant rats and rabbits at parenteral doses up to 4 and 0.3 times, respectively, the average human dose (40 units/day) based on body surface area. The results have revealed no evidence of impaired fertility or harm to the fetus due to insulin lispro. There are, however, no adequate and well-controlled studies with Humalog, Humalog Mix75/25, or Humalog Mix50/50 in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Although there are limited clinical studies of the use of Humalog in pregnancy, published studies with human insulins suggest that optimizing overall glycemic control, including postprandial control, before conception and during pregnancy improves fetal outcome. Although the fetal complications of maternal hyperglycemia have been well documented, fetal toxicity also has been reported with maternal hypoglycemia. Insulin requirements usually fall during the first trimester and increase during

the second and third trimesters. Careful monitoring of the patient is required throughout pregnancy. During the perinatal period, careful monitoring of infants born to mothers with diabetes is warranted.

Nursing Mothers—It is unknown whether insulin lispro is excreted in significant amounts in human milk. Many drugs, including human insulin, are excreted in human milk. For this reason, caution should be exercised when Humalog Mix75/25 is administered to a nursing woman. Patients with diabetes who are lactating may require adjustments in Humalog Mix75/25 dose, meal plan, or both.

Pediatric Use—Safety and effectiveness of Humalog Mix75/25 in patients less than 18 years of age have not been established.

Geriatric Use—Clinical studies of Humalog Mix75/25 did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients. In general, dose selection for an elderly patient should take into consideration the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy in this population.

ADVERSE REACTIONS: Clinical studies comparing Humalog Mix75/25 with human insulin mixtures did not demonstrate a difference in frequency of adverse events between the 2 treatments.

Adverse events commonly associated with human insulin therapy include the following:

Body as a Whole—allergic reactions (see PRECAUTIONS).

Skin and Appendages—injection site reaction, lipodystrophy, pruritus, rash.

Other—hypoglycemia (see WARNINGS and PRECAUTIONS).

OVERDOSAGE: Hypoglycemia may occur as a result of an excess of insulin relative to food intake, energy expenditure, or both. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise 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.

DOSAGE AND ADMINISTRATION: Humalog Mix75/25 is intended for subcutaneous administration. Humalog Mix75/25 should not be administered intravenously. Dosage regimens of Humalog Mix75/25 will vary among patients and should be determined by the healthcare provider familiar with the patient's metabolic needs, eating habits, and other lifestyle variables. Humalog has been shown to be equipotent to regular human insulin on a molar basis. One unit of Humalog has the same glucose-lowering effect as one unit of regular human insulin, but its effect is more rapid and of shorter duration. Humalog Mix75/25 has a similar glucose-lowering effect as compared with Humulin 70/30 on a unit-for-unit basis. The quicker glucose-lowering effect of Humalog is related to the more rapid absorption rate of insulin lispro from subcutaneous tissue.

Humalog Mix75/25 starts lowering blood glucose more quickly than regular human insulin, allowing for convenient dosing immediately before a meal (within 15 minutes). In contrast, mixtures containing regular human insulin should be given 30 to 60 minutes before a meal.

The rate of insulin absorption and consequently the onset of activity are known to be affected by the site of injection, exercise, and other variables. As with all insulin preparations, the time course of action of Humalog Mix75/25 may vary considerably in different individuals or within the same individual. Patients must be educated to use proper injection techniques.

Humalog Mix75/25 should be inspected visually before use. Humalog Mix75/25 should be used only if it appears uniformly cloudy after mixing. Humalog Mix75/25 should not be used after its expiration date.

HOW SUPPLIED:

Humalog Mix75/25 (75% insulin lispro protamine suspension and 25% insulin lispro injection [rDNA origin]) is available in the following package sizes (with each presentation containing 100 units insulin lispro per mL [U-100]):

10 mL vials	NDC 0002-7511-01	(VL-7511)
5 x 3 mL cartridges ¹	NDC 0002-7516-59	(VL-7516)
5 x 3 mL disposable insulin delivery devices (Pen)	NDC 0002-8794-59	(HP-8794)
5 x 3 mL disposable insulin delivery devices (KwikPen [®])	NDC 0002-8797-59	(HP-8797)

¹ 3 mL cartridge is for use in Eli Lilly and Company's HumaPen[®] MEMOIR[™] and HumaPen[®] LUXURA[™] HD insulin delivery devices, Owen Mumford, Ltd.'s Autopen[®] 3 mL insulin delivery device, and Disetronic D-TRON[®] and D-TRONplus[®] pumps. Autopen[®] is a registered trademark of Owen Mumford, Ltd. HumaPen[®], HumaPen[®] MEMOIR[™], and HumaPen[®] LUXURA[™] HD are trademarks of Eli Lilly and Company.

Other product and company names may be the trademarks of their respective owners.

Storage—Humalog Mix75/25 should be stored in a refrigerator (2° to 8°C [36° to 46°F]), but not in the freezer. Do not use Humalog Mix75/25 if it has been frozen. Unrefrigerated (below 30°C [86°F]) vials must be used within 28 days or be discarded, even if they still contain Humalog Mix75/25. Unrefrigerated (below 30°C [86°F]) Pens and KwikPens must be used within 10 days or be discarded, even if they still contain Humalog Mix75/25. Protect from direct heat and light.

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KwikPens manufactured by Eli Lilly and Company, Indianapolis, IN 46285, USA.
Pens manufactured by Eli Lilly and Company, Indianapolis, IN 46285, USA or Lilly France, F-67640 Fegersheim, France.
Vials manufactured by Eli Lilly and Company, Indianapolis, IN 46285, USA or Hospira, Inc., Lake Forest, IL 60045, USA or Lilly France, F-67640 Fegersheim, France.
Cartridges manufactured by Lilly France, F-67640 Fegersheim, France for Eli Lilly and Company, Indianapolis, IN 46285, USA.
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