The Pharmacist Activist

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Editorial

Pfizer Should Pay Pharmacists to Counsel Patients about Exubera

Exubera (insulin human [rDNA origin] inhalation powder) is a novel formulation that permits the administration of regular insulin by oral inhalation rather than by injection. It has a rapid onset of action and is administered immediately before meals as an alternative to injections of regular insulin or another rapid-acting insulin analogue (insulin aspart [NovoLog], insulin glulisine [Apidra], insulin lispro [Humalog]). In patients with type 1 diabetes, it should be used in a regimen that also includes a longer-acting insulin and, in patients with type 2 diabetes, it may be used as monotherapy or in a regimen with a longer-acting insulin or oral antidiabetic agent.

Although millions of patients self-administer injections of insulin or other medications, many others are "needle-phobic" and a need to administer a medication by injection is a traumatic experience. It is these patients for whom the availability of Exubera offers the greatest benefit. For some patients with type 2 diabetes the use of Exubera may avoid the use of any injections of insulin. However, for patients with type 1 diabetes and some with type 2 diabetes, there will still be a need to administer a longer-acting insulin by injection.

I recently attended an educational program about Exubera that was sponsored by Pfizer, the company that markets the new product. Although the information was comprehensive and clearly presented, it was quickly apparent that a formidable challenge exists in achieving patient understanding of the procedures/techniques that are necessary for optimal use of the medication and delivery device. Even the speaker who had

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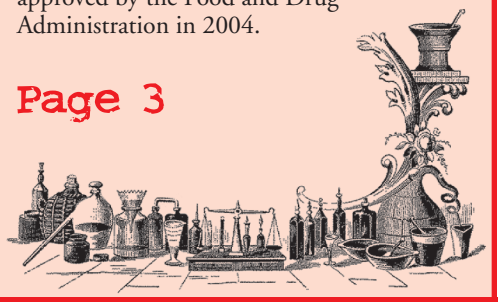

(Exubera cont.)

extensive expertise regarding Exubera was not able to answer all the questions raised by the pharmacists, although the speaker had apparently been instructed to only address information/questions for which information was provided in the package insert. Clearly, Exubera is not a product that patients will understand how to use correctly based just on written materials, telephone communication, a video, or brief verbal instructions when it is dispensed. Personalized and detailed instruction, with an opportunity for the patient to ask questions, will be required for Exubera to be used as effectively and as safely as possible.

It is my understanding that Pfizer is providing financial support for certified diabetes educators (CDEs) to provide instructions/counseling to patients regarding Exubera. I have attempted to learn the specifics of these arrangements but have not been successful in this effort in spite of numerous calls to Pfizer. I am not aware of any program through which Pfizer will provide compensation to pharmacists for the commitment of a much larger amount of time to provide counseling on the use of Exubera than is needed for the vast majority of other medications.

Pfizer should pay pharmacists to counsel patients about Exubera. With the expectation that effective counseling regarding Exubera will require on average approximately 10-15 minutes, I recommend that Pfizer provide compensation in the amount of $30 to pharmacists (that is in addition to the dispensing fee) for each new prescription for Exubera that is dispensed and for which counseling is provided. The amount of $30 may actually be low and I would quickly agree to a higher amount. If Pfizer is providing CDEs a larger amount, the compensation for pharmacists should be increased accordingly.

It is not only in the interest of patients and pharmacists that Pfizer should provide a fee to pharmacists for Exubera counseling. It is also in the interest of Pfizer itself. Pfizer has high hopes that Exubera will be a financial blockbuster that might ultimately have sales of about $2 billion a year. However, even before the product reached the market, the financial community was increasingly skeptical about these projections (*Business Week*, July 17, 2006, page 32) because of the limited dosage flexibility with the product, the potential for pulmonary adverse events, the large size of the inhaler, and health insurers possibly not placing the product on its formularies or requiring higher co-pays because it is more expensive than the insulins administered by injection.

One financial analyst has estimated that Pfizer will spend more than $50 million a year to promote Exubera directly to consumers. However, the major determinant as to whether Exubera will be clinically successful and, therefore, financially successful will be the extent to which patients use the product in the optimal manner and feel they are deriving benefit from it. Even though the product is a unique formulation, the development of which I commend, there are other alternatives and patients don't have to use Exubera. If patients feel that the use of the product is too complex, cumbersome, or frustrating, or if they conclude they are not experiencing the anticipated benefit, they won't continue to use it.

By compensating pharmacists to provide counseling, Pfizer has an opportunity to increase patient understanding to a level that should result in the effective and safe use of Exubera, recognize and support the role of pharmacists in providing effective counseling, and increase the clinical success, as well as the financial success, of its product.

Daniel A. Hussar

Sesquicentennial

The title is used infrequently enough that many of us may check our dictionary to confirm that we know how many years are represented. 150! How many organizations, businesses, publications, or anything else can we quickly identify as having been established 150 years ago or more? Not many.

Drug Topics is celebrating its 150th anniversary this year. Its longevity is a tribute to the high quality and broad scope that characterize its coverage of so many issues that are of importance to our profession. I personally find it to be of sufficient interest and value that I go through each issue page by page, and remove and retain many pages with stories about the topics in which I have the strongest interest.

Congratulations to Judy Chi, Editor-in-Chief, and her colleagues on their excellent work and dedicated service to the profession of pharmacy. They have recognized the value of the legacy that has been entrusted to them and are committed to not only maintain, but to enhance even further the value of *Drug Topics* to pharmacists. Their leadership positions *Drug Topics* to serve pharmacy for many years to come.

This is the seventh issue in the first year of publication of *The Pharmacist Activist*. Only 149 and a half years to go until its sesquicentennial.

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New Drug Review

Insulin glulisine (Apidra)

New Drug Comparison Rating (NDCR) = 2
(significant disadvantage[s])
in a scale of 1 to 5, with 5 being the highest rating

Indications:

For subcutaneous administration for the treatment of adult patients with diabetes mellitus for the control of hyperglycemia.

Comparative drugs:

Insulin aspart (NovoLog), insulin lispro (Humalog)

Advantages:

- None

Disadvantages:

- Indication is only for adult patients (indication for insulin lispro is not limited to adults);
- Indication does not include concurrent use with a sulfonylurea (indication for insulin lispro includes use in combination with a sulfonylurea antidiabetic agent instead of a longer-acting insulin in patients with type 2 diabetes);
- Not available in a combination formulation with a longer-acting insulin (insulin aspart and insulin lispro are available in combination formulations that also include insulin aspart protamine and insulin lispro protamine, respectively);
- Is in Pregnancy Category C (insulin lispro is in Category B).

Conclusions:

Insulin glulisine has a rapid onset of action and short duration of action. Its properties and use are most similar to those of insulin aspart and insulin lispro, and each of the three agents is administered at mealtimes. Although regular insulin is also generally considered to be a rapid-acting insulin, it should be administered at least 30 minutes before meals to achieve optimum postprandial glucose control. The administration of insulin glulisine, insulin aspart, and insulin lispro is more convenient because they may be administered closer to mealtimes or in conjunction with meals.

Insulin glulisine was compared with insulin lispro and with regular insulin in the clinical studies. Glycemic control and the rates of hypoglycemia were similar in the patients receiving insulin glulisine and those receiving insulin lispro or regular insulin. There is no evidence that the new agent is either more effective or safer than the other insulins with similar properties.

Insulin glulisine has no documented advantages when compared with insulin aspart and insulin lispro, but it does have disadvantages (identified above), particularly when compared with insulin lispro. Insulin lispro should be the first choice from among the three agents. The more extensive studies and experience with its use have resulted in evidence for its effective use in a broader range of situations than have been evaluated for either insulin glulisine or insulin aspart.

Discussion

Insulin glulisine (Apidra-Sanofi Aventis) is a human insulin analogue with a rapid onset of action and short duration of action following subcutaneous administration. It was approved by the Food and Drug Administration in 2004, but its marketing was delayed until its use in the OptiClik pen delivery device was also approved. The new agent is produced by recombinant DNA technology and differs from human insulin in that the amino acid asparagine at position B3 is replaced by lysine and the lysine in position B29 is replaced by glutamic acid. The properties of insulin glulisine are most similar to those of insulin aspart (NovoLog) and insulin lispro (Humalog).

Although regular insulin is generally considered to be a rapid-acting insulin, it should be administered at least 30 minutes before meals to achieve optimal postprandial glucose control. Regular insulin tends to form hexamers, and its absorption is delayed as the drug dissociates into dimers and monomers. However, insulin glulisine, insulin aspart, and insulin lispro do not tend to form hexamers and, following subcutaneous administration, these analogues have faster rates of absorption, faster onsets of action, and shorter durations of action than regular insulin. Insulins glulisine, aspart, and lispro are administered in conjunction with meals and they may be administered closer to the time of a meal than regular insulin, thereby making their use more convenient for many patients. By more closely mimicking the body's natural rapid insulin output after a meal, these agents may improve postprandial glycemic control.

Insulin glulisine is indicated for the treatment of adult patients with diabetes mellitus for the control of hyperglycemia. Insulin aspart has the same indication, whereas insulin lispro has also been studied in pediatric patients and its indication does not limit use to adult patients. The short duration of action of insulin glulisine, as well as insulin aspart and insulin lispro, usually necessitates use in a regimen that also includes a longer-acting insulin (e.g., insulin glargine [Lantus]). Although insulin lispro should be used with a longer-acting insulin in patients with type 1 diabetes, in patients with type 2 diabetes it may be used in conjunction with a sulfonylurea antidiabetic agent (e.g., glyburide) instead of a longer-acting insulin. In addition to being administered by subcutaneous injection, insulins glulisine, aspart, and lispro may also be administered subcutaneously by external infusion pumps.

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One of the clinical studies with insulin glulisine, in which it was administered within 15 minutes before a meal, compared it with insulin lispro in patients with type 1 diabetes who were also being treated with insulin glargine (Lantus) once a day. Glycemic control and the rates of hypoglycemia were similar for the two regimens. In another study, insulin glulisine was compared with regular insulin in patients with type 2 diabetes who were also treated with NPH insulin twice a day. The results were similar for the two regimens.

The primary concern with the use of any of the insulins is the potential for hypoglycemia, and glucose concentrations should be closely monitored. The risk of hypoglycemia may be increased by the concurrent use of certain other medications such as the salicylates. Caution should also be exercised in patients treated with certain beta-adrenergic blocking agents (e.g., propranolol [e.g., Inderal]) because these agents may mask the symptoms of hypoglycemia in some patients. Other adverse events associated with the use of the insulins include injection site reactions, allergic reactions, rash, pruritus and lipodystrophy.

Insulin requirements may be increased by the use of medications that may increase glucose concentrations (e.g., thiazide diuretics, corticosteroids), and the concurrent use of these agents should be closely monitored.

Insulin glulisine and insulin aspart are classified in Pregnancy Category C, whereas insulin lispro is in Category B. The effectiveness and safety of insulin glulisine and insulin aspart in pediatric patients have not been established.

Insulin glulisine should be administered within 15 minutes before a meal or within 20 minutes after starting a meal. The dosage should be individualized and appropriately balanced with the dosage of the longer-acting insulin being used concurrently, and adjusted based on blood glucose determinations. The drug is administered by subcutaneous injection in the abdominal wall, the thigh, or the deltoid, or by continuous subcutaneous infusion in the abdominal wall. Injection sites and infusion sites within an injection area should be rotated from one injection to the next.

Insulin glulisine injection is supplied in vials (10 mL) and cartridges (3 mL) containing 100 units/mL of the drug. The cartridges are for use only in the OptiClik insulin delivery device. Unopened vials and cartridges should be stored in a refrigerator, but should not be frozen. Opened vials or cartridges should be used within 28 days of opening or discarded after that time. Opened cartridges and the OptiClik devices must not be stored in a refrigerator.

If insulin glulisine is mixed with NPH insulin, the new agent should be drawn into the syringe first. The injection should be administered immediately after mixing. Data are not available with respect to mixing insulin glulisine with insulin preparations other than NPH. Insulin lispro is also available in a formulation (Humalog Mix 75/25) containing 25% insulin lispro injection, which provides a rapid onset of action, and 75% insulin lispro protamine suspension, which has an intermediate duration of action. An analogous combination (NovoLog Mix 70/30) with insulin aspart contains 30% insulin aspart injection and 70% insulin aspart protamine suspension. Insulin glulisine is not yet available in such a combination formulation.

Daniel A. Hussar