

# Wyoming Drug Utilization Review

## Insulin Types and Dosage Forms Summary

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In the market today patients, physicians, and pharmacists are all faced with many options for types of insulin. In addition, there are also various dosage forms for insulin including injectable pens and aerosols. It is important to have an understanding of these products to individualize therapy to each patient, given what the patients medicinal and lifestyle needs and wants are.

### Overview of insulin products

#### Mechanism of Action of Insulin:

Insulin is released through  $\beta$ -cells in the islet of the Langerhans in the pancreas. In healthy humans insulin release is triggered in response to hyperglycemia. Insulin regulates metabolism of protein, carbohydrates, and fats in certain tissues in the body through specific membrane bound receptors. Insulin causes an uptake of glucose into muscle, adipose, and other tissues throughout the body. Some additional effects of insulin include increased glycogen synthesis in the liver and skeletal muscle, promotion of hepatic synthesis of fatty acids, and stimulation of circulation of lipoproteins within adipose tissue.<sup>1</sup> Table 1 on page 2 provides a summary of available insulin products.

#### Adverse Effects:

Hypoglycemia is the most common adverse effect of insulin therapy. Hypoglycemic symptoms include hunger, pallor, nausea/vomiting, fatigue, diaphoresis, headache, palpitations, numbness of the mouth, tingling in the fingers, tremor, muscle weakness, blurred vision, hypothermia, uncontrolled yawning, irritability, mental confusion, sinus tachycardia, shallow breathing, and coma. Prolonged hypoglycemia can result in permanent brain damage and death. Patients who experience these symptoms should quickly ingest twenty grams of glucose and a full snack or meal shortly

thereafter. In severe hypoglycemia, intravenous dextrose is the treatment of choice.<sup>2</sup>

Other effects include a “dawn phenomenon,” a result of fasting hyperglycemia as the result of inadequate insulin available to compensate for the body’s natural nocturnal increase in counterregulatory hormones, or the Somogyi effect. The Somogyi effect is a rebound reaction to nocturnal hypoglycemia after insulin peaks during sleep. Substituting long-acting insulin or using NPH closer to bedtime may help alleviate symptoms of this effect.<sup>2</sup>

Weight gain can also be an issue, especially in type 2 diabetics where weight is often already a problem. Other issues associated with insulin include lipohypertrophy and lipoatrophy, especially around the subcutaneous injection site, hypokalemia and hypertension.<sup>2</sup>

Finally, all insulin may cause insulin resistance. In type II diabetes, weight loss can often alleviate this effect. In type 1 diabetes this is usually caused by anti-insulin antibodies. Switching types of insulin and corticosteroids have been used to alleviate resistance in Type I diabetes.<sup>2</sup>

#### Storage:

Store all insulin away from light and heat. Typically you can store vials of insulin either in the refrigerator or at room temperature once they are opened. Storing opened vials at room temperature may alleviate some of the pain during injection. Once a vial is opened it can only be used for 28 days and then should be discarded.<sup>2</sup> When buying multiple vials, one should store the unopened vials in the refrigerator.<sup>3</sup>

#### Mixing insulin:

When mixing insulin, the rapid or short-acting insulin should be drawn up first.<sup>4</sup> The manufacturer recommends against mixing insulin glargine and detemir with other insulin.<sup>4,5</sup>

#### Dosage Forms

##### Inhaler:

Exubera® is a dry powdered, short-acting recombinant, regular insulin which is inhaled into the lungs and deposited in the alveoli. Pfizer has announced that they will stop manufacturing Exubera due to poor sales.

##### Insulin Injection Pen Device (IIPD):

IIPDs are a dosage form for insulin delivery that is not widely used in America. One major advantage of using a pen is that it has been found to be more accurate for children in doses that are less than five units of insulin.<sup>6</sup> Furthermore, a mail survey, conducted in both insulin users and non-users, revealed statistically significant preference in ease of use, activity interfer-

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# WY-DUR Board Meeting Update

The DUR Board met for its bimonthly business meeting on November 29, 2007. Highlights of this meeting include:

- The Department of Health announced that the Governor's budget would be released on November 30, 2007.
- Epocrates is now available for the Blackberry handheld. The Wyoming Medicaid Preferred Drug List is available free of charge through Epocrates.
- The Board approved the final criteria for antidepressants and Invega. The criteria can be viewed at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR).

- Draft prior authorization criteria for newer insomnia medications were released for public comment by the Board and can be viewed at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR). Public comment can be emailed to [alewis13@uwyo.edu](mailto:alewis13@uwyo.edu) or [lgm@uwyo.edu](mailto:lgm@uwyo.edu) or can be mailed to:

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The next DUR Board meeting will be held January 31, 2008 in Cheyenne. Topics for discussion will include the insomnia criteria, combination drugs and newly approved medications. An agenda will be posted approximately two weeks prior to the meeting.

## Insulin Types and Dosage Forms Summary

ence, and social acceptability of the insulin pen over a vial. The data was stronger for the non-user group than the users of insulin, suggesting that a pen may be a preferred alternative for patients new to insulin therapy.<sup>7</sup>

### Continuous Subcutaneous Insulin Infusion (CSII):

CSII is a method of delivery that utilizes a pump to deliver insulin to the patient at all times of the day. CSII can help improve lifestyle flexibility, though this method should be used by patients who are willing to assume substantial responsibility for their care.<sup>8</sup> Other uses could include patients with unpredictable hypoglycemia and patients suffering from the "dawn phenomenon."<sup>9</sup> Other practitioners argue that CSII is preferable to multiple insulin injections for metabolic control of pregnant patients, however a meta-analysis of several studies showed no significant difference between these two regimens in either hypoglycemia rates or glycemic control (HbA<sub>1c</sub>).<sup>10</sup> One large disadvantage of CSII is that the equipment is expensive, which may be an issue for some patients.

Overall, CSII has shown statistically significant improvement of mean blood glucose concentrations as compared to multiple insulin injections. In addition, the number of hypoglycemic comas and mild to moderate hypoglycemic episodes were all reduced by CSII versus normal insulin injection. Diabetic ketoacidosis is more common with CSII when used by inexperienced patients and practitioners as compared with insulin injection therapy, though other studies suggest that with proper education and pump practice, the frequency of ketoacidosis is the same.<sup>8</sup>

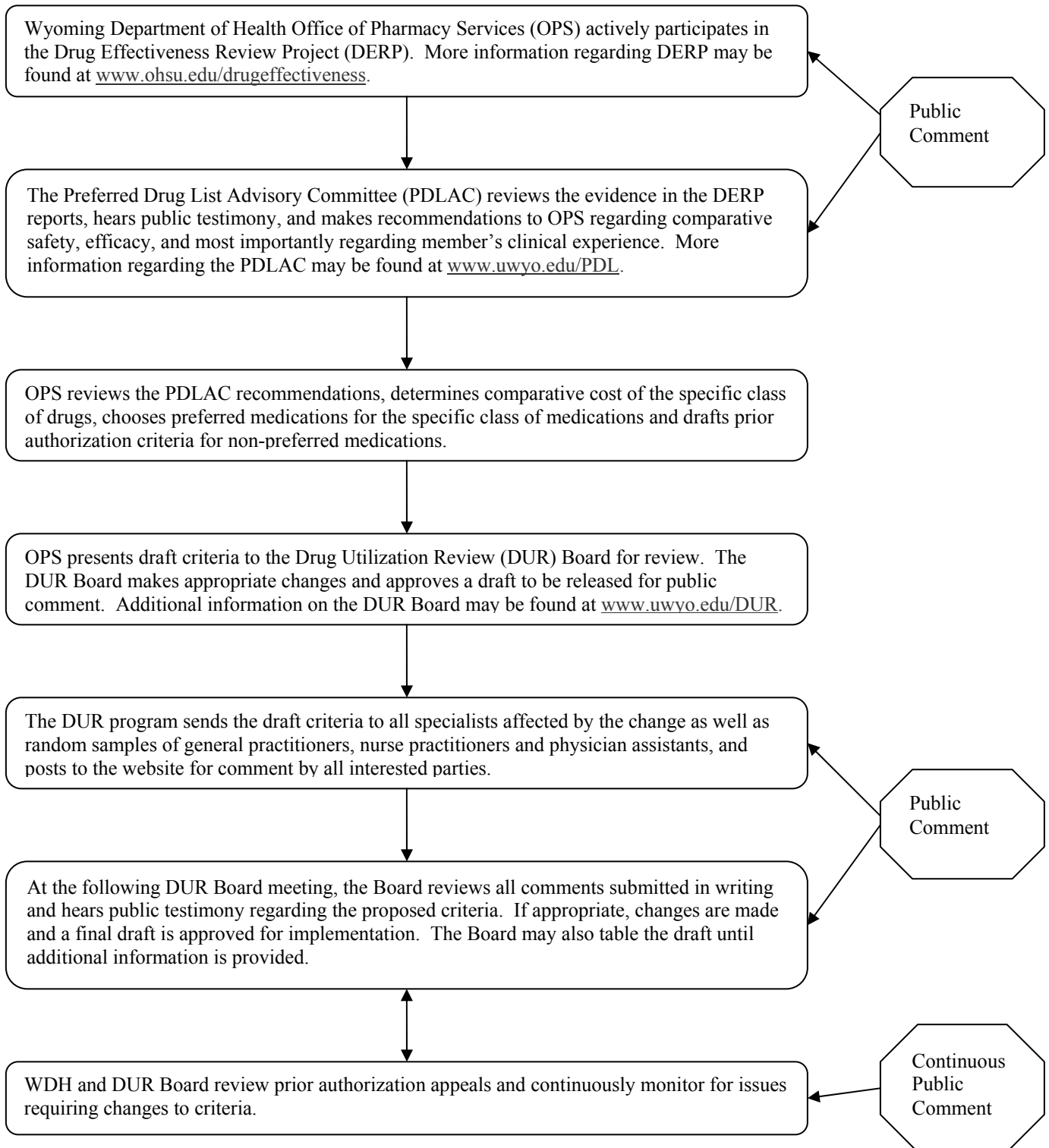
Table 1: Summary of Insulin Products<sup>3,4</sup>

	Insulin type/name	Brand name	Manufacturer	Onset of action (minutes)	Peak (hours)	Duration of action (hours)	Cost (10 mL vial)
Rapid Acting	Insulin glulisine	Apidra®	Sanofi-Aventis	20	0.5 - 1.5	4.5	\$79.99
	Insulin lispro	Humalog®	Eli Lilly and Company	15 - 30	0.5 - 1.5	3 - 5	\$78.47
	Insulin aspart	Novolog®	Novo Nordisk, Inc	15	1 - 3	3 - 5	\$88.52
Regular Insulin	Regular	Humulin R®	Eli Lilly and Company	30	2 - 4	8 - 12	\$36.89
	Regular	Novolin R®	Novo Nordisk, Inc	30	2 - 4	8 - 12	\$38.44
Intermediate Acting	NPH	Humulin N®	Eli Lilly and Company	60 - 120	6 - 12	18 - 24	\$36.89
	NPH	Novolin N®	Novo Nordisk, Inc	60 - 120	6 - 12	18 - 24	\$38.44
Long Acting	Insulin glargine	Lantus®	Sanofi-Aventis	180 - 240	peakless	24	\$83.54
	Insulin detemir	Levemir®	Novo Nordisk, Inc	180 - 240	6 - 8	6 - 23	\$84.15

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# Evidence-Based Decision Process



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