PREFERRED STEP THERAPY POLICY

POLICY: Diabetes – Insulin (Other) Preferred Step Therapy

TAC REVIEW DATE: 11/08/2017

DRUGS AFFECTED:

- Humulin® R (Regular insulin human injection, USP [rDNA origin] U-100 only [vials] - Lilly)
- Humulin® 70/30 (70% NPH, human insulin isophane suspension and 30% regular, human insulin injection [recombinant DNA origin] [vials, and KwikPen] – Lilly)
- Novolin® N (NPH, human insulin isophane suspension [recombinant DNA origin] injection [vials] - NovoNordisk)
- Novolin® R (Regular, human insulin injection [recombinant DNA origin] solution for subcutaneous or intravenous use [vials] – NovoNordisk)
- Novolin® 70/30 (70% NPH, human insulin isophane suspension and 30% regular, human insulin [recombinant DNA origin] injection [vials] – NovoNordisk)

OVERVIEW

Insulin is an anabolic and anticatabolic hormone and plays a major role in protein, carbohydrate, and fat metabolism. Humulin and Novolin are lines of human insulin indicated for to improve glycemic control in adults and children with diabetes mellitus. These products substitute for inadequate endogenous insulin secretion and partially correct the disordered metabolism and inappropriate hyperglycemia of diabetes mellitus, which are caused by either a deficiency or reduction in the biologic effectiveness of insulin. As with all insulin preparations, the duration of action is dependent on the dose, site of injection, blood supply, temperature, and physical activity. All patients with type 1 diabetes require insulin therapy. There have been numerous randomized-controlled studies comparing basal insulin analogues with NPH insulin in addition to rapid-acting analogues with regular human insulin. With the insulin analogues no additional improvements of mean glucose as measured by glycosylated hemoglobin (HbA1C) have been shown, but there is a consistent reduction of hypoglycemia.

Humulin R and Novolin R have short durations of action. With subcutaneous (SC) use, the pharmacologic effect begins approximately 30 minutes (range 10 to 75 minutes). The effect is maximal at approximately 3 hours (range 20 minutes to 7 hours) and terminates after approximately 8 hours (range 3 to 14 hours). Humulin R and Novolin R can also be administered intravenously (IV), with a faster onset and termination.

Humulin N and Novolin N are Neutral Protamine Hagedorn (NPH) or isophane insulins. These intermediate-acting insulins are produced by adding zinc and protamine to regular insulin which causes a
delay in absorption and prolongs the duration of action after SC administration. NPH insulin is commonly administered twice daily (BID) in combination with a quick-acting insulin (either a short-acting insulin or a rapid-acting analogue) to patients with type 2 diabetes and during the honeymoon phase of type 1 diabetes mellitus. The duration of action of NPH insulin is variable; some patients may require only one injection while others require three or more injections daily. NPH insulin is not the ideal basal insulin as it has variable absorption, unwanted peaks leading to hypoglycemia including nocturnal hypoglycemia, and often an inadequate duration of action (even when administered twice daily) causing fasting hyperglycemia.

Humulin 70/30 and Novolin 70/30 contain a combination of regular insulin and NPH insulin.¹ Humulin 70/30 and Novolin 70/30 are equipotent to other insulin mixtures including insulin and Humalog Mix 75/25 (insulin lispro; insulin lispro protamine suspension for injection) NovoLog Mix 70/30 (insulin aspart [recombinant]; insulin aspart protamine [recombinant] suspension for injection). Insulin mixtures provide convenience to patients as they have the onset of action of the quick-acting insulin component with a duration of activity of the intermediate component allowing for BID injections in many patients.

**Guidelines/Consensus Statements**

There are several position statements and guidelines that address the treatment of patients with diabetes from the ADA/EASD and AACE/American College of Endocrinology (ACE).⁵,⁶,⁸,¹⁰ In general for patients with type 2 diabetes metformin remains the first-line therapy unless contraindicated due to proven safety, weight neutrality, and possible benefits on CV outcomes.⁵ Basal insulins may be added to gain additional glycemic control in patients that are not attaining the desired HbA₁C with oral therapy or added for patients with very high baseline HbA₁C values. In patients with Type 1 diabetes, insulin to mimic physiological patterns is required (bolus insulin plus basal insulin).¹⁰ The ADA continues to recommend a goal HbA₁C of 7.0%, with individualized goals based on age and co-morbid conditions to balance the risk of hyperglycemia and hypoglycemia⁵,⁶,⁸,¹⁰ while the AACE continue to recommend a goal HbA₁C of 6.5%.⁶ None of the position statements or guidelines recommend a specific regular insulin product; rapid-acting insulin analogs are preferred.

This step therapy program encourages the use of Humulin products prior to the use of Novolin products. If the step therapy rule is not met, coverage will be determined by prior authorization criteria.

**Automation:** Patients 18 years of age and older will be targeted in this preferred step therapy program. Patients with a history of one Step 1 drug within the 130-day look-back period are excluded from step therapy.
**Regular Insulins**

**Step 1 Regular:** Humulin R vials

**Step 2 Regular:** Novolin R vials

**NPH Insulins**

**Step 1 NPH:** Humulin N vials, Humulin KwikPens.

**Step 2 NPH:** Novolin N vials

**70/30 Mix Insulins**

**Step 1 Mix:** Humulin 70/30 vials, Humulin 70/30 KwikPens.

**Step 2 Mix:** Novolin 70/30 vials.

**CRITERIA.**

1. If a patient has tried Humulin R, approve Novolin R.

2. If a patient has tried Humulin N (vials KwikPens), approve Novolin N.

3. If a patient has tried Humulin 70/30 (vialsKwikPens), approve Novolin 70/30.

4. No other exceptions are recommended.

**REFERENCES**


2. Humulin® R injection [prescribing information]. Indianapolis, IN: Eli Lilly; March 2015.


### HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes*</th>
<th>TAC Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integrated policy</td>
<td>New policy</td>
<td>10/09/2013</td>
</tr>
<tr>
<td>DEU revision</td>
<td>Add Humulin KwikPens to Step 2 (already rolled in)</td>
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<tr>
<td>Annual revision</td>
<td>Automation updated to reflect how the rule operates.</td>
<td>11/05/2014</td>
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<tr>
<td>Annual revision</td>
<td>No Changes to criteria</td>
<td>11/11/2015</td>
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<tr>
<td>Annual revision</td>
<td>No Changes to criteria</td>
<td>11/06/2016</td>
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<tr>
<td>Annual revision</td>
<td>Removed Humulin Pens from policy, no longer manufactured</td>
<td>11/08/2017</td>
</tr>
</tbody>
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TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: [http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx](http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx).