PREMERA HMO

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PHARMACY / MEDICAL POLICY – 5.01.648

Insulin Therapy

Effective Date:	Jan. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	Dec. 10, 2024	5.01.569 Pharmacotherapy of Type I and Type II Diabetes Mellitus
Replaces:	N/A	

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Metabolism refers to how the body converts the energy supplied by food into energy the body can use. Diabetes is a disease of the metabolic system. Diabetes involves production of and response to insulin. Insulin is a hormone produced by certain cells in the pancreas called beta cells. These cells regulate the amount of glucose (sugar) in the blood. There are two types of diabetes: type 1 and type 2. In type 1 diabetes, the pancreas no longer makes insulin. The beta cells of the pancreas have been destroyed. The body needs an external supply of insulin to use glucose. Type 1 diabetes is usually diagnosed in children and young adults. In type 2 diabetes, people can still make insulin, but their bodies don't respond well to it. This is known as insulin resistance. Type 2 diabetes can be diagnosed at any age and can be affected and modified by a number of factors, such diet and exercise and other health conditions. This policy discusses when each type of insulin therapy may be considered medically necessary for the treatment of diabetes.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

This policy contains separate criteria to be used based on the member's formulary. Please check the member Plan booklet or member ID card for coverage and click the links below to navigate to the appropriate section:

Section 1: Non-Metallic Formulary Plans (Rx Plan A1, A2, B3, B4, C4, E1, E3, E4, F1, and G3) and Plans with No Pharmacy Benefit Coverage

Section 2: Individual/Small Group/Student ISHIP Metallic Formulary Plans (Rx Plan M1, M2, and M4)

Insulin Products (Vials and Prefilled Pens)

The following section applies to non-Metallic formulary plans (Rx Plan A1, A2, B3, B4, C4, E1, E3, E4, F1, and G3) and plans with no pharmacy benefit coverage only. Please refer to the member plan booklet or member ID card.

Section 1: Non-Metallic Formulary Plans (Rx Plan A1, A2, B3, B4, C4, E1, E3, E4, F1, and G3) and Plans with No Pharmacy Benefit Coverage ONLY

Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
Rapid–Acting Insulin	
• Fiasp (aspart) • Insulin aspart • Novolog (aspart) **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Admelog (lispro) • Admelog Solostar (lispro) • Apidra (glulisine) • Humalog (lispro)

Section 1: Non-Metallic Formulary Plans (Rx Plan A1, A2, B3, B4, C4, E1, E3, E4, F1, and G3) and Plans with No Pharmacy Benefit Coverage ONLY

Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
	• Insulin lispro • Lyumjev (lispro)
Regular–Acting/Short-Acting Insulin	
• Novolin R **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humulin R
Intermediate–Acting NPH Insulin	
• Novolin N **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humulin N
Mix of Intermediate-Acting NPH and Regular (Short-Acting) Insulin	
• Novolin Mix 70/30 **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humulin Mix 70/30
Mix of Intermediate Insulin Lispro Protamine + Rapid-Acting Insulin Lispro and Mix of Intermediate-Acting Insulin Aspart Protamine + Rapid-Acting Insulin Aspart	

Section 1: Non-Metallic Formulary Plans (Rx Plan A1, A2, B3, B4, C4, E1, E3, E4, F1, and G3) and Plans with No Pharmacy Benefit Coverage ONLY

Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
• Novolog Mix 70/30 • Insulin aspart protamine + insulin aspart mix 70/30 **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humalog Mix 75/25 • Humalog Mix 50/50
Long–Acting Insulin	
• Lantus (glargine) • Levemir (detemir) • Toujeo (glargine) • Tresiba (degludec) **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to TWO preferred insulins OR these insulin products were ineffective in reducing A1C to goal after three months of therapy:** • Basaglar (glargine) • Insulin Degludec (degludec) • Insulin Glargine (glargine) • Insulin Glargine (glargine-yfgn) • Rezvoglar (glargine-aglr) • Semglee (glargine-yfgn)

The following section applies to Individual and Small Group Metallic Formulary Plans (Rx Plan M1, M2, and M4) only. Please refer to the member's Plan.

Section 2: Individual/Small Group/Student ISHIP METALLIC Formulary Plans (Rx Plan M1, M2, and M4) ONLY

Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
Rapid–Acting Insulin	
• Novolog (aspart) pen • Fiasp (aspart) pen and vial • Insulin aspart pen • Insulin lispro vial **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Apidra (glulisine) pen and vial • Admelog (lispro) vial • Admelog Solostar (lispro) pen • Humalog (lispro) pen and vial • Insulin aspart vial • Insulin lispro pen • Lyumjev (lispro) pen and vial • Novolog (aspart) vial
Regular-Acting/Short-Acting Insulin	
• Novolin R **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humulin R
Intermediate-Acting NPH Insulin	
• Novolin N **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was**

Section 2: Individual/Small Group/Student ISHIP METALLIC Formulary Plans (Rx Plan M1, M2, and M4) ONLY	
Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
	ineffective in reducing A1C to goal after three months of therapy: • Humulin N
Mix of Intermediate-Acting NPH and Regular (Short-Acting) Insulin	
• Novolin Mix 70/30 **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humulin Mix 70/30
Mix of Intermediate Insulin Lispro Protamine + Rapid-Acting Insulin Lispro and Mix of Intermediate-Acting Insulin Aspart Protamine + Rapid-Acting Insulin Aspart	
• Novolog Mix 70/30 • Insulin aspart protamine + insulin aspart mix 70/30 **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to the preferred insulin OR this insulin product was ineffective in reducing A1C to goal after three months of therapy:** • Humalog Mix 75/25 • Humalog Mix 50/50
Long–Acting Insulin	
• Lantus (glargine) • Levemir (detemir) • Toujeo (glargine) • Tresiba (degludec) **Note:** The medications listed above do not require pre-approval for coverage.	**Considered medically necessary when the individual has a diagnosis of type I or type II diabetes (Related Information), and has a contraindication or intolerance to TWO preferred insulins OR these insulin products were ineffective in reducing A1C to goal after three months of therapy:** • Basaglar (glargine)

Section 2: Individual/Small Group/Student ISHIP METALLIC Formulary Plans (Rx Plan M1, M2, and M4) ONLY	
Medical Necessity	
Preferred Insulin	**Non-preferred Insulin**
	• Insulin Degludec (degludec) • Insulin Glargine (glargine) • Insulin Glargine (glargine-yfgn) • Rezvoglar (glargine-aglr) • Semglee (glargine-yfgn)

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of the drugs for conditions not listed in this policy are considered investigational.**

Drug	Not Medically Necessary
As listed	**All other uses of the drugs for approved conditions listed in this policy are considered not medically necessary.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in this policy may be approved for up to 3 years.**
Re-authorization criteria	**Future re-authorization of all drugs listed in the policy may be approved for up to 3 years as long as the medical necessity criteria are met, and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation, and medication history

Coding

Code	Description
HCPCS	
J1813	Insulin (Lyumjev) for administration through DME (i.e., insulin pump) per 50 units
J1814	Insulin (Lyumjev), per 5 units

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Benefit Application

Lyumjev (insulin lispro-aabc) is managed through the pharmacy and medical benefit. All other drugs addressed in this policy are managed through the pharmacy benefit.

Criteria for Diagnosis of Diabetes in Nonpregnant Individuals[1]

Criteria for Diagnosis of Diabetes in Nonpregnant Individuals
A1C ≥6.5% (≥48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
FPG ≥126 mg/dL (≥7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

Criteria for Diagnosis of Diabetes in Nonpregnant Individuals
OR
2-h PG ≥200 mg/dL (≥11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (≥11.1 mmol/L). Random is any time of the day without regard to time since previous meal.

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization; 2-h PG, 2-h plasma glucose. *In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results obtained at the same time (e.g., A1C and FPG) or at two different time points.

Staging of Type 1 Diabetes[1]

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• Autoimmunity • Overt hyperglycemia • Symptomatic
Diagnostic Criteria	• Multiple islet autoantibodies • No IGT or IFG	• Islet autoantibodies (usually multiple) • Dysglycemia: IFG and/or IGT • FPG 100-125 mg/dL (5.6-6.9 mmol/L) • 2-h PG 140-199 mg/dL (7.8-11.0 mmol/L) • A1C 5.7-6.4% (39-47 mmol/mol) or ≥10% increase in A1C	• Autoantibodies may become absent • Diabetes by **standard criteria**

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose. Alternative additional stage 2 diagnostic criteria of 30-, 60-, or 90-min plasma glucose on oral glucose tolerance test ≥200 mg/dL (≥11.1 mmol/L) and confirmatory testing in those aged ≥18 years have been used in clinical trials.

Evidence Review

Insulin Agents

Table 1. Types and Characteristics of Commonly Used Insulin Products

Insulin	Brand Name	Onset of Action	Peak Effect	Duration of Action
Rapid-acting Insulin				
Lispro	Humalog	< 15 minutes	30 to 90 minutes	3 to 5 hours
Aspart	Novolog	< 15 minutes	30 to 90 minutes	3 to 5 hours
Glulisine	Apidra	< 15 minutes	30 to 90 minutes	3 to 5 hours
Short-acting Insulin				
Regular	Humulin R	0.5 to 1 hour	2 to 4 hours	4 to 8 hours
	Novolin R	0.5 to 1 hour	2 to 4 hours	4 to 8 hours
Intermediate-acting Insulin				
NPH	Humulin N	1 to 2 hours		
	Novolin N	1 to 2 hours	4 to 10 hours	10 to 18 hours
Long-acting Insulins				
Degludec	Tresiba	0.5 to 1.5 hours	No peak	42 to 45 hours
Detemir	Levemir	1 to 2 hours	3 to 9 hours	6 to 24 hours *
Glargine	Basaglar	1 to 2 hours	No peak	20 to 24 hours
Glargine	Lantus	1 to 2 hours	No peak	20 to 24 hours
Glargine	Semglee	1 to 2 hours	No peak	20 to 24 hours
Glargine	Toujeo	6 hours	No peak	Up to 36 hours
Combination Insulins				
Mix of intermediate insulin lispro protamine and rapid-acting insulin lispro and	Humulin 70/30 and Novolin 70/30	0.5 to 1 hour	2 to 10 hours	10 to 18 hours
Mix of intermediate-acting insulin aspart protamine and rapid-acting insulin aspart	Humalog 75/25 and Novolog 70/30	<15 minutes	1 to 2 hours	10 to 19 hours

*Duration of action for detemir is dose-dependent.

Insulin Interchangeability

As shown in the table above, different brand name insulin products can have similar pharmacokinetic profiles. Currently, there is no scientific literature or evidence to suggest that one insulin brand is superior over the other. Switching between insulin brands should be done in consultation with a physician and requires medical supervision (close monitoring of blood glucose) during the initial phase.

References

1. American Diabetes Association Professional Practice Committee; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024. Diabetes Care 1 January 2024; 47 (Supplement_1): S20–S42. https://doi.org/10.2337/dc24-S002
2. U.S. Food and Drug Administration: Emergency Preparedness: Information Regarding Insulin Storage and Switching Between Products in an Emergency. [Online database): Updated September, 2017. Available at: **http://www.fda.gov/Drugs/EmergencyPreparedness/ucm085213.htm** Accessed November 28, 2024.
3. Dowlat HA, Kuklmann MK, Khatami H, Ampudia-Blasco FJ. Diabetes Obes Metab 2016 Aug; 18(8):737-46 doi: 10.1111/dom. 12676. Epub May 2016. Interchangeability among reference insulin analogues and their biosimilars: regulatory framework, study design and clinical implications. Available at: **http://www.ncbi.nlm.nih.gov/pubmed/27097592** Accessed November 28, 2024.
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5. Plank J, Wutte A, Brunner G, et al. A Direct Comparison of Insulin Aspart and Insulin Lispro in Patients with Type I Diabetes. Diabetes Care. 2002; 25:2053-2057. Available at: **http://care.diabetesjournals.org/content/25/11/2053** Accessed November 28, 2024.
6. Hedman CA, Lindstrom T, Arnqvist HJ. Direct Comparison of Insulin Lispro and Aspart Shows Small Differences in Plasma Insulin Profiles After Subcutaneous Injection in Type 1 Diabetes. Diabetes Care. 2001; 24:1120-1121. Available at: **http://care.diabetesjournals.org/content/24/6/1120** Accessed November 28, 2024.
7. Von Mach MA, et al. Differences in Pharmacokinetics and Pharmacodynamics of Insulin Lispro and Aspart in Healthy Volunteers. Exp Clin Endocrinol Diabetes. 2002; 110:416-419. Available at: **http://www.ncbi.nlm.nih.gov/pubmed/12518253** Accessed November 28, 2024.
8. Package insert for Novolog (insulin aspart). Novo Nordisk Inc, Plainsboro, NJ. Revised February 2023.
9. Package insert for Fiasp (insulin aspart). Novo Nordisk Inc, Plainsboro, NJ. Revised June 2023.
10. Package insert for Humalog (insulin lispro). Eli Lilly and Company, Indianapolis, IN. Revised August 2023.
11. Package insert for Apidra (insulin glulisine). sanofi-aventis, Bridgewater, NJ. Revised November 2022.
12. Package insert for Admelog (insulin lispro). sanofi-aventis, Bridgewater, NJ. Revised December 2020.
13. Package insert for Lyumjev (insulin lispro-aabc). Eli Lilly and Company, Indianapolis, IN. Revised October 2022.

History

Date	Comments
01/01/25	New policy, approved December 10, 2024. Moved Novolog, Fiasp, insulin aspart, Humalog, insulin lispro, Apidra, Admelog, Admelog Solostar, Lyumjev, Novolin R, Humulin R, Novolin R, Humulin N, Novolin Mix 70/30, Humulin Mix 70/30, Novolog Mix 70/30, insulin aspart protamine-insulin aspart mix 70/30, Humalog Mix 75/25, Humalog Mix 50/50, Lantus, Levemir, Toujeo, Tresiba, Basaglar, insulin degludec, insulin glargine (insulin glargine), insulin glargine (insulin glargine-yfgn), Rezvoglar, and Semglee from Policy 5.01.569 to 5.01.648 with no changes to Section 1 (non-individual formulary plans) coverage criteria. New policy section with headers added for Section 2 (individual/small group/student ISHIP Metallic formulary plans) with hyperlinks to aid navigation. Added separate coverage criteria for Metallic (individual/small group/student ISHIP plans) formulary members for the following drugs: Novolog, Fiasp, insulin aspart, Humalog, insulin lispro, Apidra, Admelog, Admelog Solostar, Lyumjev, Novolin R, Humulin R, Novolin R, Humulin N, Novolin Mix 70/30, Humulin Mix 70/30, Novolog Mix 70/30, insulin aspart protamine-insulin aspart mix 70/30, Humalog Mix 75/25, Humalog Mix 50/50, Lantus, Levemir, Toujeo, Tresiba, Basaglar, insulin degludec, insulin glargine (insulin glargine), insulin glargine (insulin glargine-yfgn), Rezvoglar, and Semglee. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added HCPCS codes J1813 and J1814 for Lyumjev.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.