# Rapid to Intermediate Acting Insulin Prior Authorization Program Summary

## POLICY REVIEW CYCLE

**Effective Date**
04-01-2025

**Date of Origin**

## FDA LABELED INDICATIONS AND DOSAGE

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| Admelog®<br><br>(insulin lispro)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Rapid-Acting Insulins | 1 |
| Apidra®<br><br>(insulin glulisine)<br><br>Injection | To improve glycemic control in adults and pediatric patients with diabetes mellitus | Rapid-Acting Insulins | 2 |
| Fiasp®<br><br>(insulin aspart)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Rapid-Acting Insulins | 3 |
| Humalog®, Humalog Junior®, Insulin Lispro, Insulin Lispro Junior<br><br>Injection | To improve glycemic control in adults and children with diabetes mellitus | Rapid-Acting Insulins | 4 |
| Humalog® Mix 50/50<br><br>(50% insulin lispro protamine/50 % insulin lispro)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | NPH-Lispro Combinations | 14 |
| Humalog® Mix 75/25, Insulin Lispro Protamine/Ins | To improve glycemic control in adult and pediatric patients with diabetes mellitus | NPH-Lispro Combinations | 13 |



 

| Agent(s) | FDA Indication(s) | Notes | Ref# |
|---|---|---|---|
| ulin Lispro (75/25)<br><br>Injection | | | |
| Humulin® 70/30<br><br>(70% human insulin isophane/30% regular human insulin)<br><br>Injection | To improve glycemic control in adults with diabetes mellitus | NPH-Regular Combinations | 11 |
| Humulin® N<br><br>(human isophane insulin)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Intermediate-Acting Insulins | 9 |
| Humulin® R<br><br>(regular human insulin)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Short-Acting Insulins | 7 |
| Novolin® 70/ 30, Insulin aspart protamine/ins ulin aspart<br><br>Injection | To improve glycemic control in adults and pediatric patients with diabetes mellitus | NPH-Regular Combinations | 12 |
| Lyumjev®<br><br>(insulin lispro-aabc)<br><br>Injection | To improve glycemic control in adults with diabetes mellitus | Rapid-Acting Insulins | 5 |
| Novolin® N, ReliOn® N<br><br>(human isophane insulin)<br><br>Injection | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Intermediate-Acting Insulins | 10 |
| Novolin® R, ReliOn® R | To improve glycemic control in adult and pediatric patients with diabetes mellitus | Short-Acting Insulins | 8 |



 

| Agent(s) | FDA Indication(s) | Notes | Ref# |
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| (regular human insulin)<br><br>Injection | | | |
| NovoLog®, Insulin Aspart<br><br>Injection | To improve glycemic control in adults and pediatric patients with diabetes mellitus | Rapid-Acting Insulins | 6 |
| NovoLog® Mix 70/30, Insulin aspart protamine/insulin aspart<br><br>Injection | To improve glycemic control in patients with diabetes mellitus | NPH – NovoLog Combination | 15 |

*See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm*

## CLINICAL RATIONALE

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| Overview | The American Diabetes Association Standards of Medical Care in Diabetes recommend the following therapy for type 1 diabetes mellitus:(16)<br><br>• Most individuals with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or subcutaneous insulin infusion.<br>• Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk.<br>• Individuals with type 1 diabetes should receive education on how to match mealtime insulin doses to carbohydrate intake, fat and protein content, and anticipated physical activity.<br><br>For type 2 diabetes mellitus, the American Diabetes Association recommends the following:(16)<br><br>• Healthy lifestyle behaviors, diabetes self-management education and support, avoidance of clinical inertia, and social determinants of health should be considered in the glucose-lowering management of type 2 diabetes. Pharmacologic therapy should be guided by person-centered treatment factors, including comorbidities and treatment goals.<br>• In adults with type 2 diabetes and established/high risk of atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease, the treatment regimen should include agents that reduce cardiorenal risk.<br>• Pharmacologic approaches that provide adequate efficacy to achieve and maintain treatment goals should be considered, such as metformin or other agents, including combination therapy.<br>• Weight management is an impactful component of glucose-lowering management in type 2 diabetes. The glucose-lowering treatment regimen should consider approaches that support weight management goals.<br>• Metformin should be continued upon initiation of insulin therapy (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits.<br>• Early combination therapy can be considered in some individuals at treatment initiation to extend the time to treatment failure.<br>• The early introduction of insulin should be considered if there is evidence of ongoing catabolism (weight loss), if symptoms of hyperglycemia are present, or when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (≥300 mg/dL [16.7 mmol/L]) are very high. |



 

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| | • A person-centered approach should guide the choice of pharmacologic agents. Consider the effects on cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost and access, risk for side effects, and individual preferences.<br>• Among individuals with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high cardiovascular risk, established kidney disease, or heart failure, a sodium–glucose cotransporter 2 inhibitor and/or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit is recommended as part of the glucose-lowering regimen and comprehensive cardiovascular risk reduction, independent of A1C and in consideration of person-specific factors.<br>• In adults with type 2 diabetes, a glucagon-like peptide 1 receptor agonist is preferred to insulin when possible.<br>• If insulin is used, combination therapy with a glucagon-like peptide 1 receptor agonist is recommended for greater efficacy, durability of treatment effect, and weight and hypoglycemia benefit. Recommendation for treatment intensification for individuals not meeting treatment goals should not be delayed.<br>• Medication regimen and medication-taking behavior should be reevaluated at regular intervals (every 3–6 months) and adjusted as needed to incorporate specific factors that impact choice of treatment.<br>• Clinicians should be aware of the potential for overbasalization with insulin therapy. Clinical signals that may prompt evaluation of overbasalization include basal dose more than approximately typ0.5 units/kg/day, high bedtime–morning or postpreprandial glucose differential, hypoglycemia (aware or unaware), and high glycemic variability. Indication of overbasalization should prompt reevaluation to further individualize therapy.<br><br>The American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) 2023 algorithm for type 2 diabetes recommends the overall goal of insulin therapy is to achieve glycemic control after failure of noninsulin antihyperglycemic agents. Glycemic targets should be individualized, although an A1C of 6.5% to 7% for persons on insulin is recommended for most patients. Although A1C is a key measure, insulin titration requires use of multiple glycemic parameters including fasting blood glucose (FBG), premeal or 2-hour postprandial blood glucose, and data from continuous glucose monitoring (CGM), when available. In general, targets for fasting and premeal glucose are <110 mg/dL without hypoglycemia and can be individualized based on a person's comorbidities and clinical status. The use of CGM is recommended for persons treated with insulin to optimize glycemic control while minimizing hypoglycemia.(17)<br><br>Given that type 2 diabetes is a progressive disease, many individuals will require >1 antihyperglycemic medication to achieve their individualized A1C target over the course of the disease. Clinicians should consider multiple factors when selecting the second agent, including presence of overweight or obesity, hypoglycemia risk, access/cost, and presence of severe hyperglycemia. Patients often present with >1 of these factors, so using a patient-centered, shared decision-making approach is important. The order that medications are listed in the algorithm denotes the suggested preference hierarchy for selection. In those patients with overweight or obesity and the additional goal of weight loss, dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist (GIP/GLP-1 RA), GLP-1 RA, or sodium glucose cotransporter 2 inhibitor (SGLT2i) class are preferred options. Persons with a history of hypoglycemia, at high risk of hypoglycemia, and/or at risk for severe complications from hypoglycemia should preferentially be initiated with an agent associated with low risk for hypoglycemia, including GLP-1 RA, SGLT2i, dual GIP/GLP-1 RA, thiazolidinedione (TZD), or dipeptidyl peptidase-4 inhibitor (DPP-4i).(17)<br><br>Patients with symptomatic hyperglycemia and/or an A1C >10% suggestive of marked insulin deficiency should start basal insulin to improve glycemia as quickly as possible. Basal insulin can be initiated with or without initiation and titration of a GLP-1 RA if the |



 

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| | patient is not already on this class of agents. Some patients with severe hyperglycemia may need simultaneous initiation of bolus insulin. Clinicians should be cognizant that combination of incretin-based therapies is not recommended (ie, DPP-4i with GLP-1 RA or dual GIP/GLP-1 RA). Antihyperglycemic medications should be titrated to the maximally tolerated dose to achieve the individualized A1C goal, and additional antihyperglycemic agents should be considered in a timely fashion to avoid therapeutic inertia. If the A1C is >9% or >1.5% above goal, greater than 2 antihyperglycemic agents may need to be initiated at once.(17)<br><br>Basal with or without prandial insulin treatment may be needed as initial therapy if the A1C is >10% and/or glucose values are >300 mg/dL, combined with catabolic symptoms, such as weight loss. If symptomatic hyperglycemia is present, a GLP-1 RA alone is not recommended as it requires titration and may delay glucose control. The goal of initial intensive insulin therapy for symptomatic hyperglycemia is to reduce glucose levels safely and promptly. After improved glycemic control is achieved with short-term insulin therapy, especially with a new diagnosis of DM, a role for noninsulin antihyperglycemic agents could be considered. For most persons who need intensification of glycemic control and who are already undergoing 3 to 4 oral therapies, a GLP-1 RA or GIP/GLP-1 RA should be the initial choice, if not already in use. If glycemic targets are not achieved with these therapies, basal insulin should be added alone or as a basal insulin/GLP-1 RA combination injection. Stepwise addition of prandial insulin at 1 to 3 meals is recommended if additional glycemic control is required. The dose of basal insulin can be based on A1C levels at the time of initiation. For an A1C <8%, basal insulin can be started at 0.1 to 0.2 U/kg/day and for an A1C >8%, 0.2 to 0.3 U/kg/day can be considered. Analog insulins, including detemir, glargine, or degludec are preferred over human insulins such as neutral protamine Hagedorn (NPH) to reduce hypoglycemia.(17) |
| Safety | All rapid to intermediate-acting insulin agents have the following contraindications:(1-15)<br><br>• Do not use during episodes of hypoglycemia.<br>• Do not use in patients with hypersensitivity to the insulin agent or any of the excipients. |

## REFERENCES


| Number | Reference |
|---|---|
| 1 | Admelog prescribing information. Sanofi-Aventis US, LLC. August 2023. |
| 2 | Apidra (insulin glulisine [rDNA origin] injection) prescribing information. Sanofi-Aventis. November 2022. |
| 3 | Fiasp prescribing information. Novo Nordisk Inc. June 2023. |
| 4 | Humalog, Humalog Kwikpen, Humalog Junior Kwikpen, Humalog Tempo Pen (insulin lispro injection [rDNA origin] solution for subcutaneous injection) prescribing information. Eli Lilly and Company. August 2023. |
| 5 | Lyumjev, Lyumjev Kwikpen, Lyumjev Junior Kwikpen, Lyumjev Kwikpen prescribing information. Eli Lilly and Company. October 2022. |
| 6 | NovoLog (insulin aspart [rDNA origin] injection) prescribing information. Novo Nordisk, Inc. December 2023. |
| 7 | Humulin R (insulin human injection [rDNA origin]) prescribing information. Eli Lilly and Company. June 2022. |
| 8 | Novolin R (human insulin injection [rDNA origin]) prescribing information. Novo Nordisk, Inc. November 2022. |
| 9 | Humulin N (insulin [rDNA origin] isophane suspension) prescribing information. Eli Lilly and Company. March 2023. |




 

| Number | Reference |
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| 10 | Novolin N (human insulin isophane suspension injection) prescribing information. Novo Nordisk. November 2022. |
| 11 | Humulin 70/30 (70% human insulin isophane suspension and 30% human insulin injection (rDNA origin) prescribing information. Eli Lilly and Company. January 2024. |
| 12 | Novolin 70/30 (70% NPH, Human Insulin Isophane Suspension and 30% Regular, Human Insulin Injection, [rDNA]) prescribing information. Novo Nordisk. November 2022. |
| 13 | Humalog Mix 75/25 (75% insulin lispro protamine suspension and 25% insulin lispro injection (rDNA origin) prescribing information. Eli Lilly and Company. July 2023. |
| 14 | Humalog Mix 50/50 (50% insulin lispro protamine suspension and 50% insulin lispro injection [rDNA origin]) prescribing information. Eli Lilly and Company. July 2023. |
| 15 | NovoLog 70/30 (70% insulin aspart protamine suspension and 30% insulin aspart injection prescribing information. Novo Nordisk Inc. February 2023. |
| 16 | ElSayed NA, Aleppo G, Bannuru RR, et al. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. Diabetes Care. 2023;47(Supplement_1):S158-S178. doi:10.2337/dc24-s009 |
| 17 | Samson, S. L., Vellanki, P., Blonde, L., et. al. (2023). American association of clinical endocrinology consensus statement: Comprehensive type 2 diabetes management algorithm – 2023 update. Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists, 29(5), 305–340. https://doi.org/10.1016/j.eprac.2023.02.001 |


## POLICY AGENT SUMMARY PRIOR AUTHORIZATION

| Target Brand Agent(s) | Target Generic Agent(s) | Strength | Targeted MSC | Available MSC | Final Age Limit | Preferred Status |
|---|---|---|---|---|---|---|
| | | | | | | |
| Apidra ; Apidra solostar | insulin glulisine inj ; insulin glulisine soln pen-injector inj | 100 UNIT/ML | M ; N ; O ; Y | N | | |
| Admelog ; Admelog solostar ; Insulin lispro ; Insulin lispro junior kwi ; Insulin lispro kwikpen ; Lyumjev | insulin lispro inj ; insulin lispro inj soln ; insulin lispro soln pen-injector ; insulin lispro subcutaneous soln ; insulin lispro-aabc inj | 100 UNIT/ML ; 200 UNIT/ML | M ; N ; O ; Y | N | | |
| Insulin aspart ; Insulin aspart flexpen ; Insulin aspart penfill | insulin aspart inj soln ; insulin aspart soln cartridge ; insulin aspart soln pen-injector | 100 UNIT/ML | M ; N ; O ; Y | N | | |
| Insulin aspart protamine/ | insulin aspart prot & aspart (human) inj ; insulin aspart prot & aspart sus pen-inj | (70-30) 100 UNIT/ML | M ; N ; O ; Y | N | | |
| Insulin lispro protamine/ | insulin lispro prot & lispro inj ; insulin lispro prot & lispro sus pen-inj | (50-50) 100 UNIT/ML ; (75-25) 100 UNIT/ML | M ; N ; O ; Y | N | | |

## CLIENT SUMMARY – PRIOR AUTHORIZATION

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| | | 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| | insulin nph isophane & regular human inj | (70-30) 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Admelog ; Admelog solostar ; Humalog ; Humalog junior kwikpen ; Humalog kwikpen ; Humalog tempo pen ; Insulin | insulin lispro inj soln ; insulin lispro soln cartridge ; insulin lispro soln pen-inj w/transmitter port ; insulin lispro soln | 100 UNIT/ML ; 200 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |



 

| Target Brand Agent Name(s) | Target Generic Agent Name(s) | Strength | Client Formulary |
|---|---|---|---|
| lispro ; Insulin lispro junior kwi ; Insulin lispro kwikpen ; Lyumjev ; Lyumjev kwikpen ; Lyumjev tempo pen | pen-injector ; insulin lispro-aabc inj ; insulin lispro-aabc soln pen-inj ; insulin lispro-aabc soln pen-inj w/transmit port ; insulin lispro-aabc soln pen-injector | | |
| Admelog ; Admelog solostar ; Insulin lispro ; Insulin lispro junior kwi ; Insulin lispro kwikpen ; Lyumjev | insulin lispro inj ; insulin lispro inj soln ; insulin lispro soln pen-injector ; insulin lispro subcutaneous soln ; insulin lispro-aabc inj | 100 UNIT/ML ; 200 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Apidra ; Apidra solostar | insulin glulisine inj ; insulin glulisine soln pen-injector inj | 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Humalog mix 50/50 ; Humalog mix 50/50 kwikpen ; Humalog mix 75/25 ; Humalog mix 75/25 kwikpen ; Insulin lispro protamine/ | insulin lispro prot & lispro inj ; insulin lispro prot & lispro sus pen-inj ; insulin lispro protamine & lispro inj | (50-50) 100 UNIT/ML ; (75-25) 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Insulin aspart ; Insulin aspart flexpen ; Insulin aspart penfill | insulin aspart inj soln ; insulin aspart soln cartridge ; insulin aspart soln pen-injector | 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Insulin aspart protamine/ | insulin aspart prot & aspart (human) inj ; insulin aspart prot & aspart sus pen-inj | (70-30) 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |
| Insulin lispro protamine/ | insulin lispro prot & lispro inj ; insulin lispro prot & lispro sus pen-inj | (50-50) 100 UNIT/ML ; (75-25) 100 UNIT/ML | Commercial ; HIM 5 and 6 Tiers ; HIM 7 Tiers |

## PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

| Module | Clinical Criteria for Approval |
|---|---|
| PA | |

| Formulation | Preferred Target Agent(s) | Non-Preferred Target Agent(s) | Stand-Alone Agent(s) |
|---|---|---|---|
| **Rapid Insulin** | **Fiasp** (insulin aspart)<br>**Humalog** (insulin lispro)<br>**Humalog U200** (insulin lispro)<br>**Lyumjev** (insulin lispro-aabc)<br>**NovoLog** (insulin aspart) | **Admelog** (insulin lispro)<br>**Apidra** (insulin glulisine)<br>**Insulin aspart**<br>**Insulin lispro** | **None** |
| **Regular Insulin** | **Humulin R U-100** (regular human insulin)<br>**Novolin R** (regular human insulin) | **None** | **Humulin R U-500**(regular human insulin concentrated)<br>**ReliOn R** (regular human insulin) |
| **NPH Insulin** | **Humulin N** (human insulin isophane suspension)<br>**Novolin N** (human insulin NPH) | **None** | **None** |
| **Mix Insulin** | **Humalog 75/25** (75% insulin lispro protamine suspension/25% insulin lispro)<br>**Humalog 50/50** (50% | **Insulin aspart protamine/insulin aspart Mix 70/30**<br><br>**Insulin lispro protamine/ insulin lispro 75/25** | **None** |



 

| Module | Clinical Criteria for Approval |
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|---|---|---|---|
| | insulin lispro protamine suspension/50% insulin lispro) **Humulin 70/30** (70% human insulin isophane suspension/30% human insulin) **Novolin 70/30** (70% human insulin isophane suspension/30% human insulin) **NovoLog 70/30** (70% insulin aspart protamine/30% insulin aspart) | | |

**Non-Preferred Insulin Target Agent(s)** will be approved when ONE of the following is met:

1. BOTH of the following:
   A. The requested agent is a rapid insulin **AND**
   B. ONE of the following:
      1. The patient is currently using an insulin pump that has an incompatibility with ALL preferred rapid insulin agents that is not expected to occur with the requested agent **OR**
      2. The patient has tried and had an inadequate response to ALL preferred rapid acting insulin agents that is not expected to occur with the requested agent* **OR**
      3. The patient has an intolerance or hypersensitivity to ALL preferred rapid acting insulin agents that is not expected to occur with the requested agent **OR**
      4. The patient has an FDA labeled contraindication to ALL preferred rapid acting insulin agents that is not expected to occur with the requested agent **OR**
2. BOTH of the following:
   A. The requested agent is a regular insulin **AND**
   B. ONE of the following:
      1. The patient has tried and had an inadequate response to ALL preferred regular insulin agents that is not expected to occur with the requested agent* **OR**
      2. The patient has an intolerance or hypersensitivity to ALL preferred regular insulin agents that is not expected to occur with the requested agent **OR**
      3. The patient has an FDA labeled contraindication to ALL preferred regular insulin agents that is not expected to occur with the requested agent **OR**
3. BOTH of the following:
   A. The requested agent is a mixed insulin **AND**
   B. ONE of the following:
      1. The patient has tried and had an inadequate response to ALL preferred mixed insulin agents that is not expected to occur with the requested agent* **OR**
      2. The patient has an intolerance or hypersensitivity to ALL preferred mixed insulin agents that is not expected to occur with the requested agent **OR**



 

| Module | Clinical Criteria for Approval |
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| | 3. The patient has an FDA labeled contraindication to ALL preferred mixed insulin agents that is not expected to occur with the requested agent **OR**<br>4. The patient has a physical or a mental disability that would prevent them from using ALL preferred insulin agents **OR**<br>5. The patient is pregnant<br><br>**Length of Approval:** 12 months<br><br>* Step therapy requirement may not apply if a prior health plan paid for the medication - documentation of a paid claim may be required<br><br>NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. |



 