MAYO CLINIC LABORATORIES

Test Definition: INSAL

Insulin Analogs, Serum

Overview

Useful For

Detection and quantitation of native human insulin and insulin analogs in serum

Assessment of factitious hypoglycemia from misuse or surreptitious administration of insulin analogs

Monitoring treatment adherence of prescribed insulin therapy

Providing an alternative testing methodology for insulin measurements when immunoassay test results do not align with the clinical presentation and/or interference is suspected

Method Name

Liquid Chromatography Mass Spectrometry, High-Resolution Accurate Mass-Mass Spectrometry (LC-MS HRAM)

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Patient Preparation:
Fasting: 8 hours, required for human insulin reference values to apply
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red Top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 1.5 mL Serum
Collection Instructions: Within 2 hours of collection, centrifuge and aliquot serum into a plastic vial
Additional Information: Human insulin reference values are not applicable to patients who were not fasting for 8 hours or received pharmaceutical/synthetic insulin analogs.

Specimen Minimum Volume

Serum: 0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Insulin is a peptide hormone that plays a critical role in regulation of blood glucose levels; thus, prescribed insulin therapy is widely used for treatment of type 1 or type 2 diabetes mellitus. However, a large and increasing proportion of clinically used insulin preparations are no longer based on naturally occurring insulin but are instead insulin analogs created using recombinant DNA technology to modify human insulin to alter its pharmacokinetics and pharmacodynamics. This results in insulin analogs with rapid onset and offset of action, or conversely, delayed onset but a concomitant delay in the offset of insulin action. Current immunoassays for insulin have been designed to detect the native (natural) form of human insulin in serum or plasma. No currently available insulin immunoassays detect these insulin analogs with the same reliability as natural insulin, while the degree of detection cross-reactivity with insulin analogs varies between different insulin immunoassays. Thus, insulin analogs present unique challenges when assessing patients exhibiting hypo- or hyperglycemia. This novel liquid chromatography-high-resolution mass spectrometry test overcomes the limitations of currently available immunoassays by enabling simultaneous detection and quantitation of native human insulin and the insulin analogs aspart, glulisine, lispro, and glargine. These measurements are beneficial for monitoring treatment adherence of prescribed insulin therapy in patients with diabetes and unexpected hyperglycemia. This test is also useful in assessment of patients with unexplained hypoglycemia and it is uniquely suited to identify factitious hypoglycemia caused by the surreptitious use of insulin analogs or insulin.

Reference Values

Human insulin: 2.6-24.9 mcIU/mL

Reference values only apply to fasting patients not being administered pharmaceutical/synthetic insulins.

Therapeutic reference intervals for synthetic insulin analogs have not been established.

Interpretation

The human insulin reference values only apply to fasting patients not being administered pharmaceutical/synthetic insulins.

Detection of insulin analogs indicates exposure to insulin analogs, but the detection window and levels of insulin analogs after administration vary significantly based on the unique pharmacokinetics of the various insulin analogs. Intra- and inter-individual variability of insulin pharmacokinetics can also be significant.

Therapeutic reference intervals for insulin analogs have not been established.

Cautions

This test cannot currently detect or measure the long-acting insulin analogs detemir, degludec, or icodec.

This test cannot differentiate between endogenous human insulin and exogenous/synthetic forms of human insulin (Novolin R and Novolin N)

Human insulin reference values are only applicable to patients who are fasting and not being administered pharmaceutical/synthetic insulin analogs.

Hemolysis interferes with this assay, as insulin-degrading peptidases are released from erythrocytes.

Clinical Reference

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2. Cryer PE, Axelrod L, Grossman AB, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009;94(3):709-728. doi:10.1210/jc.2008-1410
3. Grunberger G, Weiner JL, Silverman R, Taylor S, Gorden P. Factitious hypoglycemia due to surreptitious administration of insulin. Diagnosis, treatment, and long-term follow-up. Ann Intern Med. 1988;108(2):252-257. doi:10.7326/0003-4819-108-2-252
4. Parfitt C, Church D, Armston A, et al. Commercial insulin immunoassays fail to detect commonly prescribed insulin analogues. Clin Biochem. 2015;48(18):1354-1357. doi:10.1016/j.clinbiochem.2015.07.017
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6. Lepore M, Pampanelli S, Fanelli C, et al. Pharmacokinetics and pharmacodynamics of subcutaneous injection of long-acting human insulin analog glargine, NPH insulin, and ultralente human insulin and continuous subcutaneous infusion of insulin lispro. Diabetes. 2000;49(12):2142-2148. doi:10.2337/diabetes.49.12.2142
7. Lutz Heinemann. Variability of insulin action: Does it matter?. Insulin. 2008;3(1):37-45. doi:10.1016/S1557-0843(08)80010-3
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10. Nedelkov D, Niederkofler EE, Oran PE, Peterman S, Nelson RW. Top-down mass spectrometric immunoassay for human insulin and its therapeutic analogs. J Proteomics. 2018;175:27-33. doi:10.1016/j.jprot.2017.08.001

Performance

Method Description

Insulin analogs are extracted from serum using an immunopurification followed by liquid chromatography separation and mass analysis using a high-resolution accurate mass-mass spectrometer.(Egan AM, Galior KD, Maus AD, et al. Pitfalls in diagnosing hypoglycemia due to exogenous insulin: Validation and utility of an insulin analog assay. Mayo Clin Proc.

2022;97(11):1994-2004. doi:10.1016/j.mayocp.2022.07.021)

PDF Report
No

Report Available
10 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
G0480
80375 (if appropriate for select payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
INSAL	Insulin Analogs, S	In Process

Result ID	Test Result Name	Result LOINC® Value
624133	Human	In Process
624134	Glargine M1	In Process
624135	Glargine M2	In Process
624136	Lispro	In Process
624137	Glulisine	In Process
624138	Aspart	In Process