



Laboratory Manual Glucarpidase

Client Services
(844) 347-2643 phone
(804)977-5041 fax
clientservices@grangergenetics.com
Monday-Friday 8am-5pm EST



What is Glucarpidase?

Glucarpidase is a carboxypeptidase recombinantly produced in bacteria. It is an enzyme that acts on Methotrexate (MTX) and quickly metabolizes it to DAMPA and glutamate. These are considered non-toxic and are quickly and easily removed by the kidneys. However, since glucarpidase can be seen by the body as foreign, an immune response may be mounted resulting in anti-glucarpidase antibodies. Some of these antibodies may be neutralizing and allow the glucarpidase to be cleared or inactivated before providing the benefit of MTX reduction.

High Dose Methotrexate Treatment and Relevance of Glucarpidase

Methotrexate is an anti-folate inhibitor and widely used drug for a variety of conditions. High Dose Methotrexate (HDMTX) is routinely used as a cancer treatment. However, HDMTX treatment can result in toxicity. Once a patient has developed renal damage, the risk of MTX toxicity becomes critical. Most methotrexate (~90%) is cleared through the kidneys. With renal damage, delayed clearance increases exposure and toxicity. Leucovorin is commonly used as a “rescue” drug after MTX treatment. Leucovorin works primarily intracellularly to counteract MTX. Glucarpidase (trade name Voraxaze), is active extracellularly in the blood stream so it can very quickly reduce the amount of MTX that is active. Typical treatment regimens include both drugs being used.

Granger Genetics offers two assays for monitoring anti-Glucarpidase antibodies. One assay is the screening assay which reports the presence or absence of anti-Glucarpidase antibodies along with the concentration antibodies present. The second is the neutralizing antibody assay which reports if a positive screening sample is either positive or negative for neutralizing antibodies. The neutralizing antibody assay is a reflex assay and is only performed on samples reported as positive in the screening assay.

Specimen Collection and Transport

Supplies

Standard phlebotomy materials and centrifugation is required at the collection site and is not provided by Granger Genetics. Upon request, we can provide the necessary collection kits to submit specimens for analysis to the laboratory. To order supplies, please contact Client Services at **844-347-2643** or <https://www.grangergenetics.com/glucarpidase/supply-order-form/>

Specimen Identification

All specimens and requisitions must be labeled at the time of collection with at least two patient identifiers, which must also be indicated on the requisition.

1. The patient's First and Last name or a unique ID code is required
2. The second patient identifier may be one of the following:
 - Date of birth
 - Other unique patient identifier, e.g. medical record number, social security number
 - Barcode labels can be used if the barcode matches the unique identifiers on the printed requisition.
3. Time and date of collection

Test Requisition

Minimum requisition requirements:

All specimen tubes must be labeled with at least a minimum of two patient identifiers. A single tube of serum (containing a minimum of 0.5 mL of sample volume) may be submitted for use for both assays.

Specimens must be labeled at the time of collection with at least two patient identifiers, which must also be indicated on the requisition.

The following items must be on the submitted requisition:

- Two patient identifiers (e.g., full name and DOB)
- Patient gender
- Patient date of birth
- Sample ID and/or MRN (for billing purposes)
- Institutional Billing Only, provide complete information for billing purposes to including address and contact information
- Ordering Physician name
- Date/Time of specimen collection
- Fax number in which to send the results or sign up for the web portal for e-delivery.

Shipping

The specimen transport bags have two pouches: place the specimen in the larger sealable pouch with absorbent material. Insert the requisition into the rear pocket.

- Specimens should be frozen for transport and shipped in an insulated container surrounded by an ample amount of dry ice or frozen cold packs to keep the specimen at proper storage condition until arrival at the laboratory.
- Specimens received internationally must be shipped using dry ice.
- It is also recommended that samples shipped during the summer months be shipped frozen on dry ice due to the potential exposure to high temperatures during shipment.

Specimens that arrive outside of indicated storage conditions are unsuitable for analysis. The sample will be reported as not performed and a resubmission will be requested.

Note: We do not accept shipments during the weekend. Samples collected but not shipped prior to the weekend should be frozen and shipped to Granger Genetics after the weekend. Maintain the appropriate specimen temperature as indicated in the sample storage chart below. Samples should be sent via Priority Overnight Express; First AM shipping is NOT necessary.

ATTN: Clinical Accessioning

Granger Genetics

601 Biotech Dr. Suite 301

North Chesterfield, VA 23235

(844) 347-2643

Test Information for Glucarpidase

Purpose:

To assess whether a patient is producing antibodies against Glucarpidase (screening assay) and, determine if positive screening samples from the screening assay contain neutralizing antibodies.

Methodology:

Traditional antigen-capture ELISA assay. Results are reported as positive or negative for antibodies and antibody concentration in ng/mL (antibody assay).

Spectrophotometry/absorbance-based enzyme-coupled kinetic reaction. Results are reported as positive/negative (neutralizing assay).

Limitations:

Samples collected too closely to the dose of Glucarpidase cannot be assayed for neutralizing antibodies as the Glucarpidase will interfere with the assay. Samples **MUST** be collected at least two weeks after the Glucarpidase dose.

Sample Stability (Sample storage stability prior to shipping)

Temperature	Time
Refrigerated	3 days
Frozen	30 days
Freeze/thaw cycles	3 cycles

Reference Interval:

None. Physician established therapeutic range.

Special Information:

The CPT code for the screening assay is 83516. The CPT code for the neutralizing antibody assay is 83520. Indicate date and time of last injection on the submitted requisition. (This information when provided will appear on the report.).

Specimen Requirements:

Specimen:

Serum

Collection:

Venous Collection, Red-top tube or gel-barrier tube (tiger or gold top). Let the sample rest for at least 30 minutes, to allow clotting to occur, but no more than 2 hours. Then separate serum from the RBC's and collect the serum in the plastic tube for transport. Freeze serum immediately.

Volume:

0.5 – 2 mL

Storage Instructions:

Freeze prior to transport. Sample may be refrigerated at 2°C to 8°C, see stability above.

When sending out to Granger Genetics for a Glucarpidase Test with one of their kits:

1. Draw 2 mL (or as much as possible depending on the patient) in a red, gold or tiger top SS tube. Label the tube with the Patient's information. If possible, make sure the draw date and time are listed.
2. Let the sample rest for at least thirty minutes but no more than two hours, then separate serum from the RBC's and collect the serum in the plastic tube provided in our kit. Label the tube with the Patient's information. If possible, make sure the draw date and time are listed. Freeze the sample immediately after separating. We have provided shipping materials in the kit.
3. When shipping the sample: Freeze the sample and cold pack prior to packaging the sample for shipment. Using the shipping materials provided, ship the sample to Granger Genetics Monday – Thursday. Do not ship samples on Friday. The laboratory is closed on Saturday and Sunday and there are **NO WEEKEND DELIVERIES**. If the specimen is collected on a Friday, it should be separated and frozen for shipment on Monday. Include the Sample Requisition form with the specimen.

The Granger Genetics kit contains a shipping cooler inside a cardboard sleeve. There is a cold pack inside the cooler to be frozen along with the specimen for shipping. Also included in the kit: a biohazard bag, a FedEx Clinical Bag, FedEx shipping air bill, two transfer pipettes, two cryo tubes (for serum collection) and a requisition form. The transfer pipettes are used to transfer the serum to the cryo tubes. Affix a sample label to the cryo tubes and freeze the specimen. Prior to shipment, place the frozen specimen and the completed requisition form in the biohazard bag. Place the biohazard bag and **FROZEN** cold pack in the cooler. Place the cooler in the cardboard sleeve and place inside the FedEx Clinical Bag for shipping. Affix the air bill to the outside of the FedEx Bag.