MAYO CLINIC LABORATORIES

Test Definition: HERMB

HER2, Breast, Semi-Quantitative Immunohistochemistry, Manual with HER2 FISH Reflex

Overview

Useful For

Determining overexpression of HER2 protein on formalin-fixed, paraffin-embedded tissue sections

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
HERBN	HER Breast IHC Automated NO Reflex	Yes	No
H2BR	HER2, Breast Tumor, FISH, Tissue	Yes	No

Testing Algorithm

Cases that are equivocal (2+) by immunohistochemical stain will reflex to *HER2* amplification by fluorescence in situ hybridization at an additional charge.

Special Instructions

- Pathology/Cytology Information

Method Name

Immunoperoxidase Stain with Manual Quantitative Immunohistochemistry (IHC)

NY State Available

Yes

Specimen

Specimen Type

Special

Ordering Guidance

For gastroesophageal cancer, order HERGM / HER2, Gastric/Esophageal, Semi-Quantitative Immunohistochemistry, Manual or HERGN / HER2, Gastric/Esophageal, Semi-Quantitative Immunohistochemistry, Manual, No Reflex.

Shipping Instructions

Attach the green "Attention Pathology" address label (T498) to the outside of the transport container before putting into the courier mailer.

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HER2, Breast, Semi-Quantitative Immunohistochemistry, Manual with HER2 FISH Reflex

Necessary Information

1. **An accompanying pathology report stating the final diagnosis is required.** If not available, a preliminary diagnosis is acceptable **only** if it refers to invasive or metastatic breast carcinoma.

2. Information regarding fixative used, time to fixation, and duration of fixation as well as tumor type and classification is required.

The following questions, as stated on the Pathology/Cytology Information (T707) form or presented electronically, must be answered:

a. "Was specimen fixed in 10% neutral buffered formalin within 1 hour from surgical collection time? Yes, No, or Unknown."

b. "Has specimen been fixed in 10% neutral buffered formalin for 6 to 72 hours? Yes, No, or Unknown."

c. "Was tissue decalcified? Yes, No or Unknown."

d. "Tumor type? Primary invasive breast carcinoma or metastatic breast carcinoma."

e. "Tumor classification? Invasive breast carcinoma, metastatic breast carcinoma, or micro-invasive breast carcinoma."

Specimen Required

Supplies: Pathology Packaging Kit (T554)

Specimen Type:

Preferred: A paraffin-embedded tissue block containing breast cancer tissue that has been fixed in 10% neutral buffered formalin within 1 hour from surgical collection time and for a total of 6 to 72 hours.

Acceptable: 5 Unstained sections containing breast carcinoma on charged slides cut at 4 microns less than 1 month ago. Tissue on the slides should have been fixed in 10% neutral buffered formalin within 1 hour from surgical collection time and for a total of 6 to 72 hours.

Container/Tube: Pathology Packaging Kit

Collection Instructions: Submit paraffin-embedded invasive or metastatic breast carcinoma tissue.

Additional Information:

1. According to the American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines, HER2 protein immunohistochemical test results are only valid for nondecalcified, paraffin-embedded specimens fixed in 10% neutral buffered formalin within 1 hour from surgical collection time and for a total time of 6 to 72 hours. Delay to fixation, or under- or over-fixation may affect these results.(1)
2. HER2 immunohistochemistry testing on intracystic papillary carcinoma and solid papillary carcinoma, without clearly stating invasive carcinoma, is not appropriate and will be reported as indeterminate.
3. Paraffin blocks will be returned with final report.

Forms

If not ordering electronically, complete, print, and send with the specimen:

1. Pathology/Cytology Information (T707) is required if not ordering electronically.

2. Immunohistochemical (IHC)/In Situ Hybridization (ISH) Stains Request (T763)

Reject Due To

No specimen should be rejected.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container

Special	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

The *HER2* (official gene name *ERBB2*) proto-oncogene encodes a membrane receptor with tyrosine kinase activity and homology to the epidermal growth factor receptor. Amplification and overexpression of the *HER2* gene in human breast, endometrial, ovarian, and other epithelial cancers have been associated with a shorter disease-free interval and shorter overall survival. Overexpression of HER2 protein is an indication for Herceptin (trastuzumab) therapy in patients with breast cancer.

This test is most frequently used to evaluate HER2 overexpression in breast cancer.

Reference Values

Reported as negative (0, 1+), equivocal (2+), and strongly positive (3+) according to the interpretation guidelines for the US Food and Drug Administration-approved Ventana Pathway HER2 (4B5) antibody.

Interpretation

Results are reported as negative (0, 1+), equivocal (2+), and strongly positive (3+) according to the published American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) interpretation guidelines.(1)

Cautions

The performance and quality of immunohistochemical stains in formalin-fixed, paraffin-embedded tissue depends critically on proper fixation.

Clinical Reference

1. Wolff AC, Hammond ME, Hicks DG, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol. 2018;36(20):2105-2122 doi:10.1200/JCO.2018.77.8738
2. Riber-Hansen R, Vainer B, Steiniche T. Digital image analysis: a review of reproducibility, stability and basic requirements for optimal results. Apmis. 2012;120(4):276-289
3. Gavrielides MA, Gallas BD, Lenz P, Badano A, Hewitt SM.: Observer variability in the interpretation of HER2/neu immunohistochemical expression with unaided and computer-aided digital microscopy. Arch Pathol Lab Med. 2011;135(2):233-242
4. Cuadros M, Villegas R. Systematic review of HER2 breast cancer testing. Appl Immunohistochem Mol Morphol. 2009;17(1):1-7
5. Nassar A, Cohen C, Agersborg SS, et al. Trainable immunohistochemical HER2/neu image analysis: a multisite performance study using 260 breast tissue specimens. Arch Pathol Lab Med. 2011;135(7):896-902

Performance

Method Description

Testing is performed using US Food and Drug Administration-approved Ventana Pathway HER2 (4B5) rabbit monoclonal primary antibody and a proprietary detection system, using modified manufacturer's instructions.(Package insert: PATHWAY anti-HER-2/neu (4B5) Rabbit Monoclonal Primary Antibody. Ventana Medical Systems, Inc; 09/2022)

Scoring is performed according to American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guidelines as follows:
Score of 3+ is defined as circumferential membrane staining that is complete, intense and in greater than 10% of invasive tumor cells.
Score of 2+ is defined as weak to moderate complete membrane staining observed and in greater than 10% of the invasive tumor cells; or circumferential membrane staining that is complete, intense and in less than or equal to 10% of invasive tumor cells.
Score of 1+ is defined as incomplete membrane staining that is faint or barely perceptible and in greater than 10% of the invasive tumor cells; or weak to moderate complete membrane staining observed and less than 10% of the invasive tumor cells.
Score of 0 is defined as no staining observed or membrane staining that is incomplete and is faint or barely perceptible and in less than or equal to 10% of the invasive tumor cells.(Wolff AC, Hammond ME, Hicks DG, et al. Human Epidermal Growth Factor Receptor 2 Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Clinical Practice Guideline Focused Update. J Clin Oncol. 2018;36(20):2105-2122 doi:10.1200/JCO.2018.77.8738)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

5 to 15 days

Specimen Retention Time

Until 1 week after results are reported. Materials made at Mayo Clinic may be retained at Mayo Clinic indefinitely.

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

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 has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

88360

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HERMB	HER Breast SemiQuant IHC + Reflex	85319-2

Result ID	Test Result Name	Result LOINC® Value
620801	Interpretation	50595-8
620802	Participated in the Interpretation	No LOINC Needed
620803	Report electronically signed by	19139-5
620804	Material Received	81178-6
MA058	Fixed in 10% NB formalin w/in 1 hr	8100-0
MA059	Fixed in 10% NB formalin 6-72 hrs	8100-0
MA060	Tumor type	44638-5
MA061	Tumor classification	21918-8
MA062	Tissue was decalcified	8100-0
620805	Disclaimer	62364-5
620806	Case Number	80398-1