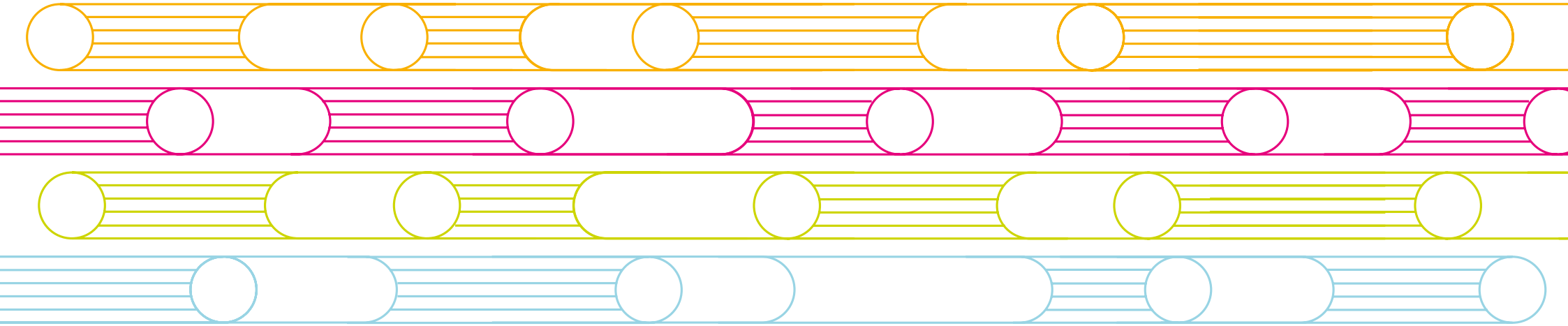
National Genomic Test Directory Guidance for Breast Cancer



For breast cancer, the relevant sections of the National Genomic Test Directory's Testing Criteria for Rare and Inherited Disease are **R208** and **R444.1**. These can be accessed on the NHS document "Rare and inherited disease eligibility criteria" on the National genomic test directory website* and is also reproduced in this document along with guidance on how to order a test.

This material has been developed by AstraZeneca
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*__Reference:__ NHS. England. National genomic test directory. Available at: https://www.england.nhs.uk/publication/national-genomic-test-directories/(Accessed June 2023).

R208 Inherited breast cancer and ovarian cancer (V5.2 June 2023)

Testing Criteria

1. Living affected individual (proband) with breast* or ovarian cancer where the individual +/- family history meets one of the criteria. The proband has:

a. Breast cancer (age <40 years), OR

b. Bilateral breast cancer (age < 50 years), OR

c. Triple negative breast cancer (age < 60 years), OR

d. Male breast cancer (any age), OR

e. Breast cancer (age <45 years) and a first degree relative with breast cancer (age <45 years), OR

f. Combined pathology-adjusted Manchester score ≥ 15 or single gene pathology adjusted score of ≥10 or BOADICEA/CanRisk score ≥10%, OR

g. Ashkenazi Jewish ancestry and breast cancer at any age

Note for living unaffected individuals: Where more than one family member may be eligible for unaffected testing, the residual probability of a causative pathogenic variant in the family should be considered, taking into account prior normal unaffected tests.

See Appendix 1 for Associated Tests with R208.

NOTES:

- *Breast cancer definition includes high grade DCIS
- The proband's cancer and majority of reported cancers in the family should have been confirmed
- The pathology adjusted Manchester score involved incorporation of pathology data for the tested proband alone, i.e. pathology need not be sought for other family members.
- Ovarian cancer: Fallopian Tube and Primary Peritoneal cancers can be included
- BRCA1/BRCA2 testing should not typically have previously been performed. Exceptions may include, for example, patients who have been tested through the Jewish Community's NHS BRCA-Testing Programme for BRCA1/BRCA2 and not received a molecular diagnosis
- Testing of unaffected and deceased individuals can only be offered by Clinical Genetics

Genetic testing may occasionally be appropriate outside these criteria following discussion at a specialist MDT with a cancer geneticist present.

Overlapping indications

- M2 Ovarian carcinoma should be used for somatic teting
- M3 Breast cancer should be used for somatic testing
- R444 NICE approved PARP inhibitor treatment

Reference: NHS. England. National genomic test directory. Available at: https://www.england.nhs.uk/publication/national-genomic-test-directories/ (Accessed June 2023).

R444 NICE approved PARP inhibitor treatment (V5.2 June 2023)

Testing Criteria

Testing Criteria only applies to patients not meeting R208/R430 criteria AND with current cancer diagnosis for treatment decisions.

R444.1 Breast Cancer

1. For people with triple negative breast cancer who have received neo-adjuvant chemotherapy:
   - residual invasive cancer in the breast, the resected lymph nodes (non-pathological complete response) or both at the time of surgery
2. For people with triple-negative breast cancer having adjuvant chemotherapy:
   - node-positive OR
   - node-negative cancer with a primary tumour ≥ 2 cm
3. For people with hormone receptor-positive, HER2-negative breast cancer who have received neoadjuvant chemotherapy:
   - residual invasive cancer in the breast, the resected lymph nodes (non-pathologic complete response) or both at the time of surgery, AND a CPS + EG score of ≥3 based on pre-treatment clinical and posttreatment pathological stage, receptor status and histological grade
4. For people with hormone receptor-positive, HER2-negative breast cancer having adjuvant chemotherapy:
   - 4 or more pathologically confirmed positive lymph nodes.

See Appendix 2 for Associated Tests with R444.1.

Overlapping indications (for breast cancer)

- R208 Inherited breast cancer and ovarian cancer
- M3 Breast cancer should be used for somatic testing

Please consult the Test Directory Rare & Inherited disease criteria for complete list of overlapping indications

Reference: NHS. England. National genomic test directory. Available at: https://www.england.nhs.uk/publication/national-genomic-test-directories/ (Accessed June 2023).

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How do I order a test?

Request the clinical indication (breast cancer R208 or R444.1). Test request forms and sample requirements can be found on your local Genomic Laboratory Hub (GLH) website www.england.nhs.uk/genomics/genomic-laboratory-hubs.

Referrals for testing will be triaged by the local GLH to ensure the most appropriate test is performed. For your local GLH, please consult the regional map.

Central and South GLH
https://centralsouthgenomics.nhs.uk/

East GLH
www.eastgenomics.nhs.uk

North East and Yorkshire GLH
www.ney-genomics.org.uk

North Thames GLH
www.norththamesglh.nhs.uk

North West GLH
www.mft.nhs.uk/nwglh

South East GLH
www.southeastgenomics.nhs.uk

South West GLH
www.nbt.nhs.uk/south-west-genomic-laboratory-hub

Image adapted from https://www.genomicseducation.hee.nhs.uk/genotes/knowledge-hub/genomic-laboratory-hubs/

Please note: In some areas there may be local testing hubs in addition to GLHs where you can order tests. Please check locally for test request forms.

Contact us

If you have any questions on the R208 and/or R444.1 testing criteria and would like to talk to someone in the AstraZeneca UK oncology team, please contact us at:

sharon.keeling@astrazeneca.com or
miguel.garcia1@astrazeneca.com

Reference: NHS England. Genomic Laboratory Hubs. Available at: https://www.england.nhs.uk/genomics/genomic-laboratory-hubs/ (Accessed June 2023).

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Appendix 1

Associated Tests: Please note all the tests below will be undertaken for R208 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R208.1	BRCA1; BRCA2; PALB2; RAD51C; RAD51D; ATM; CHEK2	Singleton	Small variants	Small panel of genes	BRCA1; BRCA2; PALB2; RAD51C; RAD51D; ATM; CHEK2	Small panel
R208.2	BRCA1; BRCA2; PALB2; RAD51C; RAD51D; ATM; CHEK2 MLPA or equivalent	Singleton	Exon level CNVs	Single gene(s)	BRCA1; BRCA2; PALB2; RAD51C; RAD51D; ATM; CHEK2	MLPA or equivalent

Appendix 2

Associated Tests: Please note all the tests below will be undertaken for R444.1 Clinical Indication requests, unless clinical presentation and/or initial results indicate all tests are not necessary.

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R444.1	NICE approved PARP inhibitor treatment	Singleton	Small variants	Small panel of genes	BRCA1; BRCA2; PALB2; RAD51C; RAD51D; ATM; CHEK2	Small panel