BRCA1 AND *BRCA2* SEQUENCING AND/OR DELETION/DUPLICATION ANALYSIS

I. *BRCA1* and *BRCA2* (81162, 81163, 81164, 81165, 81166, 81167, 81216) sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **medically necessary** when**:**

A. The member is 18 years or older, **AND**

B. The member has a personal history of any of the following:

1. Male (sex assigned at birth) breast cancer, **OR**
2. Triple-negative breast cancer, **OR**
3. Breast cancer diagnosed at age 65 or younger, **OR**
4. Epithelial ovarian cancer (including fallopian tube cancer or peritoneal cancer), **OR**
5. Exocrine pancreatic or ampullary cancer, **OR**
6. Metastatic prostate cancer, **OR**
7. High- or very-high-risk group prostate cancer, **OR**
8. Multiple primary breast cancers (diagnosed synchronously or metachronously), **OR**

C. The member has a personal history of breast cancer **AND** <u>any</u> of the following:

1. Ashkenazi Jewish ancestry, **OR**
2. One or more close relatives with <u>any</u> of the following:

a) Female (sex assigned at birth) breast cancer diagnosed at age 50 years or younger, **OR**

b) Male (sex assigned at birth) breast cancer, **OR**

c) Ovarian cancer, **OR**

d) Pancreatic cancer, **OR**

e) Prostate cancer that is either metastatic, intermediate-risk with intraductal/cribriform histology, or high- or very-high-risk group, **OR**

3. Three or more total diagnoses of breast cancer and/or prostate cancer (any grade) on the same side of the family including the member with breast cancer, **OR**

D. The member has a first- or second-degree relative meeting any of the above criteria, **OR**

E. The member has metastatic breast cancer and is being considered for systemic treatment using PARP inhibitors, **OR**

F. The member has high-risk, HER2-negative breast cancer and is being considered for adjuvant treatment with olaparib, **OR**

G. The member's probability of having a *BRCA1* or *BRCA2* pathogenic variant is greater than 2.5% based on prior probability models (examples: Tyrer-Cuzick, BRCApro, CanRisk).

II. *BRCA1* and *BRCA2* (81162, 81163, 81164, 81165, 81166, 81167, 81216) sequencing and/or deletion/duplication analysis for hereditary breast and/or ovarian cancer susceptibility is considered **investigational** for all other indications.

III. *BRCA1/BRCA2* mRNA sequencing analysis for the interpretation of variants of unknown significance (0138U), when billed in addition, is considered **investigational** because it is typically either considered an existing component of the genetic testing process for quality assurance or follow up testing without proven utility.

DEFINITIONS

1. **Close relatives** include first, second, and third degree <u>blood</u> relatives on the same side of the family:

a. **First-degree relatives** are parents, siblings, and children

b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings

c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

2. **Breast cancer**: Term that applies to patients with invasive cancer or ductal carcinoma in situ (DCIS).

3. **High-risk breast cancer for olaparib therapy:** Defined as

    a. Triple negative breast cancer treated with either:

        i. Adjuvant chemotherapy with axillary node-positive disease or an invasive primary tumor greater than or equal to 2 cm on pathology analysis, **OR**

        ii. Neoadjuvant chemotherapy with residual invasive breast cancer in the breast or resected lymph nodes, **OR**

    b. Hormone receptor positive disease treated with either:

        i. Adjuvant chemotherapy with four or more positive pathologically confirmed lymph nodes, OR

        ii. Neoadjuvant chemotherapy which did not have a complete pathologic response, with a CPS+CG score [pre-treatment clinical (CS) and post-treatment pathological stage (PS), estrogen-receptor status (E) and grade (G)] of 3 or higher

4. **High-risk prostate cancer:** Defined by NCCN as an individual who has no very-high-risk features but has exactly one of the following high-risk features:
    a. cT3a, OR
    b. Grade Group 4 or Grade Group 5, **OR**
    c. PSA > 20ng/ml

5. **Very-high-risk prostate cancer:** Defined by NCCN as an individual who has at least one of the following:
    a. CT3b-cT4
    b. Primary Gleason pattern 5
    c. 2 or 3 high-risk features

d. >4 cores with Grade Group 4 or 5

REFERENCES

1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. Version 3.2024. https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf.
2. Owens DK, Davidson KW, Krist AH, et al. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA -Related Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA - J Am Med Assoc*. 2019;322(7):652-665. doi:10.1001/jama.2019.10987
3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Ampullary Adenocarcinoma. Version 2.2024.
4. Bedrosian I, Somerfield MR, Achatz MI, et al. Germline Testing in Patients With Breast Cancer: ASCO-Society of Surgical Oncology Guideline. J Clin Oncol. 2024;42(5):584-604. doi:10.1200/JCO.23.02225