Clinical Policy: Talazoparib (Talzenna)

Reference Number: CP.PHAR.409
Effective Date: 03.01.19
Last Review Date: 02.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Talazoparib (Talzenna™) is a poly (ADP-ribose) polymerase (PARP) inhibitor.

FDA Approved Indication(s)

Talzenna is indicated for the treatment of adult patients with
Deleterious or suspected deleterious germline *BRCA*-mutated (gBRCAm) human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer, as a single agent. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna.

- Homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), in combination with enzalutamide.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Talzenna is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Diagnosis of recurrent, locally advanced, or metastatic breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For brand Talzenna requests, member must use generic talazoparib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Prescribed as a single agent;
6. Documentation of HER2-negative disease;
7. Mutations in the *BRCA* genes;
8. Member has not previously received a PARP inhibitor (e.g., Lynparza®, Rubraca®, Zejula®);
9. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i or ii):
      i. 1 mg per day;
      ii. 1 capsule per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Prostate Cancer (must meet all)**:**
1. Diagnosis of metastatic CRPC, as evidenced by disease progression despite bilateral orchiectomy or other androgen deprivation therapy (ADT) (*see Appendix D*);
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. For brand Talzenna requests, member must use generic talazoparib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Documentation of a HRR gene mutation;
6. Prescribed concurrently with Xtandi®;
7. Member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy (*see Appendix D*);
8. Member has not previously received a PARP inhibitor (e.g., Lynparza®, Rubraca®, Zejula®);
9. Request meets one of the following (a or b):*
   a. Dose does not exceed any of the following (i or ii):
      i. 0.5 mg per day;
      ii. 1 capsule per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Talzenna for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Talzenna requests, member must use generic talazoparib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For breast cancer: New does not exceed any of the following (i or ii):
      i. 1 mg per day;
      ii. 1 capsule per day;
   b. For mCRPC: New dose does not exceed any of the following (i or ii):
      i. 0.5 mg per day;
      ii. 1 capsule per day;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADP: adenosine diphosphate
ADT: androgen deprivation therapy
BRCA: breast cancer gene
gBRCAm: mutations in the germline BRCA genes
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
HRR: homologous recombination repair
mCRPC: metastatic castration-resistant prostate cancer
NCCN: National Comprehensive Cancer Network
PARP: poly (ADP-ribose) polymerase

Appendix B; Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- The FDA approved indication for talazoparib includes using the diagnostic tool BRACAnalysis CDx™ by Myriad Genetic Laboratories. It is available at http://www.fda.gov/companiondiagnostics.
- There is insufficient data regarding the use of consecutive PARP inhibitors. Most PARP inhibitor pivotal trials excluded prior PARP inhibitor use, the NCCN does not make any explicit recommendations (other than for ovarian cancer, where they state data is limited), and there are no randomized controlled trials evaluating such use.
- NCCN recommended use: Single agent therapy (preferred regimen) for patients with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) human epidermal growth factor receptor 2 (HER2)-negative, BRCA 1/2-germline mutated disease that is:
  - Hormone receptor-negative
  - Hormone receptor-positive
  - Hormone receptor-positive with visceral crisis or endocrine therapy refractory
- Examples of ADT include:
  - Bilateral orchiectomy (surgical castration)
  - Luteinizing hormone-releasing hormone (LHRH) given with or without an anti-androgen
    - LHRH (or GnRH) agonists: Zoladex® (goserelin), Supprelin® (histrelin), leuprolide (Lupron Depot®, Eligard®), and Trelstar® (triptorelin)
    - Anti-androgens: bicalutamide (Casodex®), flutamide, nilutamide (Nilandron®)
  - LHRH antagonist: Firmagon® (degarelix), Orgovyx™ (relugolix)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	1 mg PO QD	1 mg/day

Indication	Dosing Regimen	Maximum Dose
	For patients with moderate renal impairment (CrCl 30 – 59 mL/min): 0.75 mg PO QD For patients with severe renal impairment (CrCl 15 – 29 mL/min): 0.5 mg PO QD	
mCRPC	0.5 mg PO QD in combination with enzalutamide For patients with moderate renal impairment (CrCl 30 – 59 mL/min): 0.35 mg PO QD For patients with severe renal impairment (CrCl 15 – 29 mL/min): 0.25 mg PO QD	0.5 mg/day

VI. Product Availability

- Hard hypromellose capsules: 0.1 mg, 0.25 mg, 0.35 mg, 0.5 mg, 0.75 mg, 1 mg
- Soft gelatin capsules: 0.1 mg, 0.25 mg, 0.35 mg, 0.5 mg, 0.75 mg, 1 mg

VII. References

1. Talzenna Prescribing Information. New York NY: Pfizer; February 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/211651s012lbl.pdf. Accessed March 25, 2024.
2. Talzenna (Soft Gelatin) Prescribing Information. New York NY: Pfizer; March 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217439s000lbl.pdf. Accessed March 25, 2024.
3. Litton JK, Rugo HS, Ettl J, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. *N Engl J Med*. 2018; 379:753-763.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 24, 2023.
5. National Comprehensive Cancer Network. Breast Cancer Version 4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 24, 2023.
6. National Comprehensive Cancer Network. Prostate Cancer Version 4.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 25, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; added recurrent or locally advanced breast cancer to align with NCCN and FDA-approved indication; references reviewed and updated.	10.29.19	02.20
Added requirement for no prior PARP inhibitor use; added off-label dosing language.	06.23.20	08.20
1Q 2021 annual review: updated dose limits given renal impairment adjustments would exceed 1 capsule per day; added new template	10.15.20	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
language regarding redirection to generic if available for oral oncology agents; references reviewed and updated; references to HIM.PHAR.21 revised to HIM.PA.154.		
1Q 2022 annual review: no significant changes; RT4: added new strengths (0.5 mg and 0.75 mg) and removed dose optimization language for renal impairment; references reviewed and updated.	10.04.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.23.22	
1Q 2023 annual review: no significant changes; revised "medical justification" to "member must use" language per updated template; updated Appendix D; references reviewed and updated.	10.17.22	02.23
RT4: new indication of mCRPC added in addition to new strength capsules.	07.11.23	
1Q 2024 annual review: for prostate cancer, added "member will use a gonadotropin-releasing hormone (GnRH) analog concurrently or has had a bilateral orchiectomy" per NCCN compendium; for breast cancer, added "prescribed as a single agent" to align with FDA indication and NCCN compendium; updated Appendix D to align with current NCCN compendium; references reviewed and updated.	10.24.23	02.24
RT4: added new soft gelatin capsule formulation; for continued therapy, changed maximum dosing criteria from "does not exceed both of the following" to "does not exceed any of the following" to allow variability in maximum daily dose reduction per prescriber information.	03.25.24	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.