Washington State Health Care Authority

Oncology Agents – Phosphatidylinositol 3-Kinase (PI3K) Inhibitors

Medical policy no. 21.53.80.AA-1 Effective Date: Month, 1, Year

Related medical policies:

Policy Name
<Policy Title>
<Policy Title>
N/A

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Alpelisib (Piqray) Duvelisib (Copiktra) Idelalisib (Zydelig)	**Oncology Agents – Phosphatidylinositol 3-Kinase (PI3K) Inhibitors** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. • Non-Preferred brand name products on the Apple Health Drug List with an A-rated generic, biosimilar or interchangeable biosimilar must also meet criteria in Non-Clinical Policy No 0001 (NC-001). If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

<table>
<tr><th colspan="2">Clinical Criteria</th></tr>
<tr><td>Breast cancer, advanced or metastatic hormone receptor-positive, HER2-negative, PIK3CA-mutated
Alpelisib (Piqray)</td><td>Alpelisib (Piqray) may be approved when all of the following documented criteria are met:
1. Patient is 18 years of age or older, AND
2. Prescribed by, or in consultation with, an oncologist; AND
3. Will be used in combination with fulvestrant; AND
4. Diagnosis of advanced or metastatic breast cancer; AND
5. Documentation of all of the following:
a. Hormone receptor-positive
b. HER2-negative
c. PIK3CA-mutated confirmed; AND
6. Patient has cancer progression while on or after receiving endocrine therapy (e.g. anastrozole, letrozole, exemestane, tamoxifen).

If ALL criteria are met, the request will be authorized for 6 months.</td></tr>
<tr><td></td><td>Criteria (Reauthorization)
Alpelisib (Piqray) may be approved when all the following documented criteria are met:

1. Alpelisib will continue to be used in combination with fulvestrant; AND
2. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression].

If ALL criteria are met, the request will be authorized for 6 months.</td></tr>
<tr><td>Chronic lymphoid leukemia
Duvelisib (Copiktra)
Idelalisib (Zydelig)</td><td>Duvelisib (Copiktra) or idelalisib (Zydelig) may be approved when all the following documented criteria are met:
1. Patient is 18 years of age or older, AND
2. Prescribed by, or in consultation with, a hematologist or oncologist; AND
3. Diagnosis of chronic lymphoid leukemia; AND
a. For duvelisib: Patient has relapsed or refractory disease; OR
b. For idelalisib: Patient has relapsed disease; AND
4. Patient has not previously progressed while using another PI3K inhibitor; AND
5. For idelalisib: Request will be used in combination with rituximab; AND
6. History of failure, contraindication, or intolerance to the following:
a. For idelalisib, at least one prior chemotherapy regimen containing one of the following:
i. Bruton tyrosine kinase inhibitor (BTKi)</td></tr>
</table>

	ii. Beta cell lymphoma-2 inhibitor (BCL2i) b. For duvelisib, two prior regimens, each containing one the following; i. BTKi ii. BCL2i iii. Monoclonal antibody (e.g. obinutuzumab, rituximab) in the setting where a BTKi or BCL2i is not used. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Duvelisib (Copiktra) or idelalisib (Zydelig) may be approved when all the following documented criteria are met: 1. For idelalisib: Request will continue to be used in combination with rituximab; **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression]. If ALL criteria are met, the request will be authorized for **6 months.**
Small lymphocytic lymphoma, relapsed or refractory Duvelisib (Copiktra)	Duvelisib (Copiktra) may be approved when all the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, a hematologist or oncologist; **AND** 3. Not used in combination with other oncology therapies; **AND** 4. Diagnosis of relapsed or refractory small lymphatic lymphoma; **AND** 5. History of failure, contraindication, or intolerance to at least two prior regimens, each containing one of the following: i. BTKi ii. BCL2i iii. Monoclonal antibody (e.g. obinutuzumab, rituximab) in the setting where a BTKi or BCL2i is not used. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Duvelisib (Copiktra) may be approved when all the following documented criteria are met: 1. Not used in combination with other oncology therapies; **AND**

	2. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g., stabilization of disease, decrease in tumor size or tumor spread, lack of disease progression]. If ALL criteria are met, the request will be authorized for **6 months.**

Dosage and quantity limits

Drug	Indication	Approved Dose	Dosage Form and Quantity Limit
Alpelisib (Piqray)	Breast cancer, advanced or metastatic hormone receptor-positive, HER2-negative, PIK3CA-mutated	Up to 300 mg once daily	• Piqray 200 mg daily dose: 28 therapy packs (each pack contains one 200 mg tablet) per 28 days • Piqray 250 mg daily dose: 28 therapy packs (each pack contains one 200 mg tablet and one 50 mg tablet) per 28 days • Piqray 300 mg daily dose: 28 therapy packs (each pack contains two 150 mg tablets) per 28 days
Duvelisib (Copiktra)	Chronic lymphoid leukemia	Standard dosing: Up to 25 mg twice daily Dose adjustment with moderate CYP3A4 inducers: Up to 40 mg twice daily	• 15 mg tablets: 56 tablets per 28 days • 25 mg tablets: 56 tablets per 28 days
	Small lymphocytic lymphoma, relapsed or refractory	Standard dosing: Up to 25 mg twice daily Dose adjustment with moderate CYP3A4 inducers: Up to 40 mg twice daily	• 15 mg tablets: 56 tablets per 28 days • 25 mg tablets: 56 tablets per 28 days
Idelalisib (Zydelig)	Chronic lymphoid leukemia	Up to 150 mg twice daily	• 100 mg tablets: 60 tablets per 30 days • 150 mg tablets: 60 tablets per 30 days

Background:

Patients with advanced or metastatic breast cancer with hormone receptor-positive, HER2-negative and PIK3CA-mutated characteristics following endocrine therapy represent a treatment population that can be managed with alpelisib and fulvestrant. The safety and efficacy of alpelisib was established in the SOLAR-1 clinical trial. The number of progression free survival (PFS) events and overall response rate (ORR), defined as percentage of patients with confirmed complete response or partial response with measurable disease at baseline, was 61% and %35.7 in the alpelisib + fulvestrant group, respectively. The number of PFS events and ORR in the placebo + fulvestrant group was 75% and %16.2, respectively. The median PFS months was 11.0 in the alpelisib + fulvestrant group and 5.7 in the placebo + fulvestrant group. There was no significant difference in the overall survival between the alpelisib + fuvlestrant treatment group compared to the placebo + fulvestrant treatment group. Serious adverse reactions occurred in 35% of participants with serious reactions >2% occurrence including hyperglycemia, rash, diarrhea, acute kidney injury, abdominal pain, anemia and osteonecrosis of the

jaw. There are a significant number of adverse reactions and laboratory abnormalities that occurred with alpelisib + fulvestrant (please see prescribing information for full details).[1]

Patients with chronic lymphoid leukemia who have failed at least 1 or 2 lines of systemic therapy may be treated with idelalisib or duvelisib, respectively. Patients with small lymphocytic lymphoma who have failed at least 2 lines of systemic therapy may be treated with duvelisib. First and second lines of systemic therapy typically consist of regimens containing a Bruton tyrosine kinase inhibitor (BTKi) or a beta cell lymphoma-2 inhibitor (BCL2i).[4] The safety and efficacy of duvelisib was established in the DUO study which contained 319 adult patients with chronic lymphoid leukemia and 7 patients with small lymphocytic lymphoma. The efficacy outcome of progression free survival was median 16.4 months and 9.1 months for duvelisib vs ofatumumab, respectively. The overall response rate was 78% and 39% for duvelisib and ofatumumab, respectively. There was a 0% complete response rate in both the duvelisib and ofatumumab groups. Serious adverse reactions occurred in 65% of participants with the most frequent serious reactions including infection, diarrhea/colitis, pneumonia, rash, and pneumonitis. There are a significant number of adverse reactions and laboratory abnormalities that occurred with duvelisib (please see the prescribing information for full details).[2] The safety and efficacy of idelalisib was established in the GS-US-312-0116 study. The efficacy outcome of progression free survival was a median of 19.4 months vs 6.5 months for the idelalisib + rituximab vs placebo + rituximab, respectively. The overall response rate, defined as percentage of patients with confirmed complete response or partial response, was 83.6% and 15.5% in the idelalisib + rituximab vs placebo + rituximab. Serious adverse reactions occurred in 59% of participants with the most frequent serious reactions including pneumonia, diarrhea, pryexia, sepsis, and febrile neutropenia. There are a significant number of adverse reactions and laboratory abnormalities that occurred with idelalisib + rituximab (please see the prescribing information for full details).[3]

References

1. Piqray [Prescribing Information]. East Hanover, NJ: Novartis. January 2024.
2. Copiktra [Prescribing Information]. Las Vegas, NV: Secura Bio: July 2024.
3. Zydelig [Prescribing Information]. Foster City, CA: Gilead Sciences: February 2022.
4. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymhoma, version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf.

History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	New policy created

Washington State Health Care Authority

Oncology Agents – Phosphatidylinositol 3-Kinase (PI3K) Inhibitors

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation of a positive clinical response? ☐ Yes ☐ No

2. What is the patient's diagnosis?
   ☐ Breast cancer, advanced or metastatic hormone receptor-positive, HER2-negative, PIK3CA- mutated
   ☐ Chronic lymphoid leukemia
   ☐ Small lymphocytic lymphoma, relapsed or refractory
   ☐ Other Specify: _____

3. Provide the following for the patient:
   Indicate disease stage:
   Indicate disease type (i.e. New onset, refractory, etc.):

4. Indicate if prescribed by or in consultation with:
   ☐ Oncologist ☐ Hematologist ☐ Other Specify: _____

For diagnosis of Breast cancer, advanced or metastatic hormone receptor-positive, HER2-negative, PIK3CA- mutated:

5. Will the prescribed medication be used in combination with fulvestrant? ☐ Yes ☐ No

6. Provide documentation of all of the following:
   a. Hormone receptor-positive
   b. HER2-negative
   c. PIK3CA-mutated confirmed

7. Has cancer progressed while on or after receiving endocrine therapy (e.g. anastrozole, letrozole, exemestane, tamoxifen)? ☐ Yes ☐ No

For diagnosis of Chronic lymphoid leukemia:

8. For duvelisib:
   Has patient relapsed? ☐ Yes ☐ No

   Is disease refractory? ☐ Yes ☐ No

Does patient have a history of failure, contraindication, or intolerance to one of the following?

At least two prior chemotherapy regimen containing:

☐ Bruton tyrosine kinase inhibitor (BTKi)
☐ Beta cell lymphoma-2 inhibitor (BCL2i)
☐ Monoclonal antibody (e.g. obinutuzumab, rituximab)
☐ Other Specify: _____

9. For idelalisib:

Has patient relapsed? ☐ Yes ☐ No

Has patient not previously progressed while using another PI3K inhibitor? ☐ Yes ☐ No

Will the prescribed medication be used in combination with rituximab? ☐ Yes ☐ No

Does patient have a history of failure, contraindication, or intolerance to one of the following?

At least one prior chemotherapy regimen containing:

☐ Bruton tyrosine kinase inhibitor (BTKi)
☐ Beta cell lymphoma-2 inhibitor (BCL2i)
☐ Other Specify: _____

For diagnosis of Small lymphocytic lymphoma, relapsed or refractory:

10. Is this being used in combination with other chemotherapeutic, radiotherapeutic, or adjuvant agents?
☐ Yes ☐ No
If yes, list all therapies:

11. Does patient have a history of failure, contraindication, or intolerance to one of the following?

At least two prior chemotherapy regimen containing:

☐ Bruton tyrosine kinase inhibitor (BTKi)
☐ Beta cell lymphoma-2 inhibitor (BCL2i)
☐ Monoclonal antibody (e.g. obinutuzumab, rituximab)
☐ Other Specify: _____

12. Indicate for patient:
Height (cm): **Date taken:**
Weight (kg): **Date taken:**
Body surface area (m^2): **Date taken:**

CHART NOTES ARE REQUIRED WITH THIS REQUEST

Prescriber signature	Prescriber specialty	Date