RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	vemurafenib
Policy Number:	RxA.571
Drug(s) Applied:	Zelboraf®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Vemurafenib (Zelboraf®) is a kinase inhibitor. It is indicated for the treatment of:

- Patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test
- Patients with Erdheim-Chester Disease with BRAF V600 mutation

Limitation(s) of use: Vemurafenib is not indicated for treatment of patients with wild-type BRAF melanoma.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
vemurafenib (Zelboraf®)	Melanoma	960 mg PO BID	1920 mg/day
vemurafenib (Zelboraf®)	Erdheim-Chester disease	960 mg PO BID	1920 mg/day

Dosage Forms

- Tablet: 240 mg

Clinical Policy

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

I. Initial Approval Criteria

A. Melanoma (must meet all):

1. Diagnosis of unresectable or metastatic melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. One of the following (a or b):
   a. Positive for a BRAF V600 mutation;
   b. Brain metastasis with a primary diagnosis of melanoma against which Zelboraf® was active;
5. Dose does not exceed 1920 mg per day (8 tablets per day).

Approval Duration

Commercial: 6 months

Medicaid: 6 months

B. Erdheim-Chester Disease (must meet all):
1. Diagnosis of Erdheim-Chester Disease;
2. Prescribed by or in consultation with a hematologist or oncologist;
3. Age 18 years of age or older;
4. Positive for a BRAF V600 mutation;
5. Dose is does not exceed 1920 mg per day (8 tablets per day).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Non-Small Cell Lung Cancer (off-label) (must meet all):
1. Diagnosis of non-small cell lung cancer (NSCLC);
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. Positive for a BRAF V600E mutation;
5. Failure of Tafinlar® and Mekinist® unless contraindicated or clinically significant adverse effects are experienced;*
   *Prior authorization may be required.
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Hairy Cell Leukemia (off-label) (must meet all:
1. Diagnosis of hairy cell leukemia;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age 18 years of age or older;
4. Prescribed as subsequent therapy for relapsed or refractory disease;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

E. Thyroid Carcinoma (off-label) (must meet all):
1. Diagnosis of differentiated thyroid carcinoma (i.e., papillary, follicular or Hurthle cell carcinoma);
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. Positive for a BRAF mutation;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

F. Central Nervous System Cancers - Low-Grade (WHO Grade II) Infiltrative Supratentorial Astrocytoma/Oligodendroglioma(off-label) (must meet all):

1. Diagnosis of Low-Grade (WHO Grade II) Infiltrative Supratentorial Astrocytoma/Oligodendroglioma;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
4. Positive for a BRAF V600E mutation;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy, or documentation supports that member is currently receiving Zelboraf® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 1920 mg per day (8 tablets per day);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
CRC: colorectal cancer
FDA: Food and Drug Administration
NSCLC: non-small cell lung cancer

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Tafinlar® (dabrafenib)	NSCLC: 150 mg orally twice daily	300 mg/day
Mekinist (trametinib)	NSCLC: 2 mg orally once daily	2 mg/day

irinotecan (Camptosar®)	CRC: Varies	Varies
Erbitux® (cetuximab)	CRC: Varies	Varies
Vectibix®(panitumumab)	CRC: Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information

- Meningioma is classified into 1 of 3 grades
  - WHO Grade I = Benign meningioma
  - WHO Grade II = Atypical meningioma
  - WHO Grade III = Malignant (anaplastic) meningioma.

References

1. Zelboraf® Prescribing information. South San Francisco, CA: Genentech USA, Inc.; May 2020. Available at: https://www.gene.com/download/pdf/zelboraf_prescribing.pdf . Accessed October 07, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/. Accessed October 07, 2020.
3. National Comprehensive Cancer Network. Cutaneous Melanoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf . Accessed October 07, 2020.
4. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer Version 8.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf Accessed October 07, 2020.
5. National Comprehensive Cancer Network. Hairy Cell Leukemia Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed October 07, 2020.
6. National Comprehensive Cancer Network. Thyroid Carcinoma Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf Accessed October 07, 2020.
7. National Comprehensive Cancer Network. Central Nervous System Cancers Version 3.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf . Accessed October 07, 2020.
8. National Comprehensive Cancer Network. Rectal Cancer Version 6.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf Accessed October 07, 2020.
9. National Comprehensive Cancer Network. Colon Cancer Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf Accessed October 07, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title table updated. 2. Line of Business Policy Applies to was updated to all line of	10/07/2020	12/07/2020

business. 3. Initial Approval criteria updated: Off label indication (Central Nervous System Cancers - Low-Grade (WHO Grade II) Infiltrative Supratentorial Astrocytoma/Oligodendroglioma) and its criteria was added. Colorectal cancer criteria was removed. 4. Commercial approval duration was updated for initial approval criteria from length of benefit to 6 months. 5. Commercial approval duration was updated for Continued approval criteria from length of benefit to 12 months. 6. HIM approval duration removed. 7. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by Rxadvance. 8. APPENDIX B: Therapeutic Alternatives statement was rephrased to “Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements”. 9. APPENDIX B: Dosing regimen updated for Tafinlar® from PO QD to orally twice daily. 10. APPENDIX D updated to include Meningioma classification. 11. References were updated.		