SmartPA Criteria Proposal

Drug/Drug Class:	Mitogen-activated Extracellular Kinase Inhibitors (MEKi) & B-raf Kinase Inhibitors (BRAFi) PDL Edit
First Implementation Date:	April 6, 2023
Revised Date:	N/A
Prepared For:	MO HealthNet
Prepared By:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: The MO HealthNet Pharmacy Program will implement a state-specific preferred drug list.

Why Issue Selected: Melanoma is a form of skin cancer; in 2018 approximately 84,000 new cases were diagnosed in the United States. When caught in the early stages, melanoma can normally be treated via surgical intervention. If it progresses to an advanced stage and becomes metastatic, surgery becomes a less viable option and systemic therapies are warranted.

Advances in genetic sequencing have identified certain gene mutations responsible for metastases, the most common being a mutation involving the B-Raf (BRAF) gene; this mutation has been identified in 40 to 60% of patients with melanoma. The BRAF gene is responsible for a protein in the RAS/MAPK pathway regulating proliferation, differentiation, migration, and apoptosis of cells. Inhibition of mutated BRAF impedes tumor cell growth. Mitogen-activated extracellular kinase (MEK) is a downstream effector of BRAF. Inhibition of MEK1 and MEK2 causes decreased cellular proliferation, cell cycle arrest, and increased apoptosis. Two medication classes have been developed for the purposes of inhibiting these pathways and halting metastasis – mitogen-activated extracellular kinase inhibitors (MEKi) and B-Raf kinase inhibitors (BRAFi). The MEKis regulate the extracellular signal-related kinase pathway and phosphorylation of the BRAF mutant cell lines. MEKis potentiate BRAFi inhibitory effects, delay development of resistance to treatment, and reduce some toxicities directly associated with BRAF inhibition.

There are currently three MEKi plus BRAFi combinations used in patients with BRAF-mutated advanced melanoma. Mektovi® (binimetinib), Cotellic® (cobimetinib), and Mekinist® (trametinib) are MEKis approved for use in combination with the BRAFis Braftovi® (encorafenib), Zelboraf® (vemurafenib), and Tafinlar® (dabrafenib), respectively. All combinations are approved for advanced melanoma. The combination of Tafinlar + Mekinist is also indicated for numerous other malignancies. Other potential uses of MEK or BRAF inhibitors include: encorafenib in combination with cetuximab for the treatment of metastatic colorectal cancer, vemurafenib for Erdheim-Chester Disease (ECD), and cobimetinib was very recently approved for histiocytic neoplasms, a family of blood diseases that includes ECD.

Total program savings for the PDL classes will be regularly reviewed.

Program-Specific Information:	Preferred Agents		Non-Preferred Agents	
	BRAFi	**MEKi**	**BRAFi**	**MEKi**
	• Tafinlar® • Zelboraf®	• Mekinist® • Cotellic®	• Braftovi®	• Mektovi®

Type of Criteria: ☐ **Increased risk of ADE** ☒ **Preferred Drug List**
☐ **Appropriate Indications** ☐ **Clinical Edit**

Data Sources: ☐ **Only Administrative Databases** ☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Mitogen-activated extracellular kinase inhibitors (MEKi) and B-Raf kinase inhibitors (BRAFi)
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Documented compliance on current therapy regimen **OR**
- For non-preferred agents:
  - Failure to achieve desired therapeutic outcomes with trial on 2 or more preferred agents:
    - Documented trial period for preferred agents **OR**
    - Documented ADE/ADR to preferred agents **OR**
  - Documented reason of medical necessity for use of a non-preferred agent without required trial of preferred agents (e.g., contraindication, drug interaction with existing therapy that cannot be modified/ameliorated, preferred agents are not indicated or NCCN/ASCO guideline-recommended)

Denial Criteria

- Lack of adequate trial on required preferred agents
- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:	☐	Progress Notes:	☐
MedWatch Form:	☐	Other:	☐

Disposition of Edit

Denial: Exception Code “0160” (Preferred Drug List)
Rule Type: PDL

Default Approval Period

1 year

References

- Evidence-Based Medicine and Fiscal Analysis: “Therapeutic Class Review: MEK1/MEK2-BRAF Kinase Inhibitors, Differentiating Characteristics”, Gainwell Technologies; Last updated November 11, 2022.
- Flaherty KT, Puzanov I, Kim KB, Ribas A, McArthur GA, Sosman JA, O'Dwyer PJ, Lee RJ, Grippo JF, Nolop K, Chapman PB. Inhibition of mutated, activated BRAF in metastatic melanoma. N Engl J Med. 2010 Aug 26;363(9):809-19. doi: 10.1056/NEJMoa1002011. PMID: 20818844; PMCID: PMC3724529.
- Centers for Disease Control and Prevention. *United States Cancer Statistics: Incidence of Malignant Melanoma of the Skin—United States, 2009–2018.* USCS Data Brief, no. 28. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2022.
- USPDI, Micromedex; 2022.
- Facts and Comparisons eAnswers (online); 2022 Clinical Drug Information, LLC.