Clinical Policy Title:	gilteritinib
Policy Number:	RxA.317
Drug(s) Applied:	Xospata®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Gilteritinib (Xospata®) is a tyrosine kinase inhibitor. It is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
gilteritinib (Xospata®)	AML	120 mg PO once daily	120 mg/day

Dosage Forms

- Tablets: 40 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML;
2. Documentation of the presence of an FLT3 mutation;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age 18 years or older;
5. Failure of a Rydapt® (midostaurin)-containing regimen (see Appendix B), unless contraindicated or clinically significant adverse effects are experienced;
   (**Rydapt® may require prior authorization);*
6. Request meets one of the following (a or b):
   a. Dose does not exceed 120 mg (3 tablets) per day;
   b. Dose 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

B. Myeloid/Lymphoid Neoplasms with Eosinophilia and TK Fusion Genes (off Label) (must meet all)**:**
1. Diagnosis Myeloid/Lymphoid Neoplasms with Eosinophilia (MLN-Eo) and TK Fusion Genes (rearrangement of PDGFRA, PDGFRB or FGFR1);
2. Documentation of the presence of TK Fusion Genes and Hypereosinophilia (HE) eosinophil count >1.5 $x10^9$ /L;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age 18 years or older;
5. Failure of imatinib monotherapy, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 120 mg (3 tablets) per day;
   b. Dose 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. Acute Myeloid Leukemia (must meet all)**:**
1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Xospata® 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. Dose does not exceed 120 mg (3 tablets) per day;
   b. Dose 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

B. Myeloid/Lymphoid Neoplasms with Eosinophilia and TK Fusion Genes (off Label) (must meet all)**:**
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
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. Dose does not exceed 120 mg (3 tablets) per day;
   b. Dose 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

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
FLT3: FMS-like tyrosine kinase 3
MLN-Eo: Myeloid/Lymphoid Neoplasms with Eosinophilia
HE: hypereosinophilia
PDGFRA: Platelet Derived Growth Factor Receptor Alpha
PDGFRB: Platelet Derived Growth Factor Receptor Beta
FGFR1: Fibroblast Growth Factor Receptor 1

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
Rydapt® (midostaurin) + cytarabine + daunorubicin	Rydapt® 50 mg PO Q12 hours on days 8-21 + cytarabine 200 mg/m^2 IV x 7 days + daunorubicin 60 mg/m^2 IV x 3 days	Rydapt® 100 mg/day; cytarabine 200 mg/m^2/day; daunorubicin 60 mg/m^2/day

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):
  - Hypersensitivity to gilteritinib or any of the excipients.

- Boxed Warning(s):
  - Patients treated with Xospata® have experienced symptoms of differentiation syndrome, which can be fatal or life-threatening if not treated.

APPENDIX D: General Information

- Patients treated with Xospata® have experienced symptoms of differentiation syndrome, which can be fatal or life-threatening if not treated. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, or renal dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

References

1. Xospata® Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc.; May 2019. Available at: www.xospata.com. Accessed March 25,2021.
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4. Gilteritinib, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at:

http://online.lexi.com. Accessed March 25,2021.
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6. Gerds AT, Gotlib J, Bose P, et al. Myeloid/lymphoid neoplasms with eosinophilia and tk fusion genes, version 3. 2021, nccn clinical practice guidelines in oncology. Journal of the National Comprehensive Cancer Network. 2020;18(9):1248-1269. Accessed March 31,2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy was reviewed: Policy title table was updated: Clinical Policy Title was updated to ”gilteritinib". Drug(s) Applied was updated to "Xospata®". Line of Business Policy Applies to was updated to "All". 2. Dosing information was updated: “QD has been changed to once daily”. 3. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance". 4. Appendix C was updated: Boxed warning has been added. 5. Appendix D was updated: Information regarding differentiation syndrome has been added. 6. References were updated.	07/13/2020	09/14/2020
Policy was reviewed: 1. Initial and continued therapy approval criteria was created for ‘’Myeloid/Lymphoid Neoplasms with Eosinophilia and TK Fusion Genes’’ (off label use).	03/31/2021	06/10/2021

2. Approval duration for HIM was removed. 3. Appendix A: Abbreviation/ Acronym Key was updated. 4. Appendix B: Fixed header verbiage was updated as 'Below are suggested therapeutic alternatives.' 5. References were updated.		