Clinical Policy Title:	tucatinib
Policy Number:	RxA.647
Drug(s) Applied:	Tukysa®
Original Policy Date:	09/14/2020
Last Review Date:	07/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Tucatinib (Tukysa®) is a kinase inhibitor indicated in combination with trastuzumab and capecitabine for treatment of adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
tucatinib (Tukysa®)	Advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases.	300 mg orally twice daily in combination with trastuzumab and capecitabine Severe hepatic impairment (Child-Pugh class C): Reduce initial dose to 200 mg twice daily. Renal Impairment: CrCl <30 mL/minute: Use is not recommended	300 mg orally twice daily

Dosage Forms

- Tablets: 50 mg and 150 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. Breast Cancer (must meet all):

1. Diagnosis of advanced, unresectable, or metastatic HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;

4. Prescribed in combination with trastuzumab and capecitabine;
5. Member has received one or more prior anti-HER2-based regimens (with trastuzumab, pertuzumab, and ado-trastuzumab emtansine (TDM1) separately or in combination) in the metastatic setting;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg twice daily;
   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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Breast Cancer (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. Request meets one of the following (a or b):
   a. Dose does not exceed 300 mg twice daily;
   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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor
EBC: early breast cancer
ALT: alanine aminotransferase
AST: aspartate transaminase
NCCN: National Comprehensive Cancer Network
TDM1: ado-trastuzumab emtansine

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	Maximum Dose
Kadcyla®	3.6 mg/kg given as an intravenous infusion every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity, or a total of 14 cycles for patients with early breast cancer.	3.6 mg/kg intravenously every 3 weeks

Drug Name	Dosing Regimen	Maximum Dose
Perjeta (pertuzumab) + trastuzumab + docetaxel	Every 21 days: • Perjeta 840 mg IV day 1 followed by 420 mg IV • Herceptin 8 mg/kg IV day 1 followed by 6 mg/kg IV • Docetaxel 75-100 mg/m2 IV day 1	Perjeta 840 mg/dose Herceptin 8 mg/kg/dose Docetaxel mg/m2/dose

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

NCCN Guidelines Version 2.2022 Breast Cancer

- Added tucatinib + trastuzumab + capecitabine (category 1) as another recommended regimen for HER2-positive disease, with the following footnote: For adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.
- Embryo-Fetal Toxicity: Tukysa® can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception.
- Hepatotoxicity: Severe hepatotoxicity has been reported on Tukysa®. Monitor ALT, AST and bilirubin prior to starting Tukysa®, every 3 weeks during treatment and as clinically indicated. Interrupt dose, then dose reduce, or permanently discontinue Tukysa® based on severity.

References

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5. Seattle Genetics Announces U.S. FDA Approval of Tukysa® (tucatinib) for People with Advanced Unresectable or Metastatic HER2-Positive Breast Cancer. Seattle Genetics. 2020. Available at: https://investor.seattlegenetics.com/press-releases. Accessed July 2, 2021.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	08/11/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include generic drug name Tucatinib. 2. Dosing Information doing regimen was updated to include hepatic impairment dosing, “Severe hepatic impairment (Child-Pugh class C): Reduce initial dose to 200 mg twice daily…”. 3. Dosing Information doing regimen was updated to include renal impairment dosing, “Renal Impairment: CrCl <30 mL/minute: Use is not recommended…”. 4. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 5. Initial Approval Criteria I.A.1 was updated from “Diagnosis of recurrent, locally advanced, or metastatic breast cancer” to “Diagnosis of any one of the following (a or b)…”. 6. Initial Approval Criteria I.A.1.b was updated to include “Brain metastases related to breast cancer…”. 7. Initial Approval Criteria I.A.2 was updated to include “Documentation of advanced, unresectable, or metastatic HER2-positive breast cancer…”. 8. Initial Approval Criteria I.A.4 was updated to remove “Documentation of human	07/02/2021	09/14/2021

epidermal growth factor receptor 2 (HER2)-negative disease…". 9. Initial Approval Criteria I.A.5 was updated to include "Prescribed in combination with trastuzumab and capecitabine…". 10. Initial Approval Criteria I.A.6 was updated to include "Member has received one or more prior anti-HER2-based regimens…". 11. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 12. Continued Therapy Approval Criteria II.A.3.b was updated to include "Dose is supported by practice guidelines or peer-reviewed…". 13. Appendix A was updated to include abbreviations EBC, ALT, AST, NCCN & TDM1. 14. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 15. Appendix B: Therapeutic Alternatives was updated to include alternative drug Kadcyla® and its dosing regimen and maximum dose. 16. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 17. Appednix D was updated to include "Embryo-Fetal Toxicity…" and "Hepatotoxicity…". 18. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria I.A: Updated to remove diagnosis of breast cancer or brain metastasis related to breast cancer. 2. Appendix B: Updated to add drug name, dosing regimen and dose limit/ max dose for Perjecta. 3. References were reviewed and updated.	04/18/2022	07/18/2022