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| Clinical Policy Title: | trifluridine/tipiracil |
| Policy Number: | RxA.396 |
| Drug(s) Applied: | Lonsurf® |
| Original Policy Date: | 03/06/2020 |
| Last Review Date: | 12/11/2025 |
| Line of Business Policy Applies to: | All lines of business (except Medicare) |

Criteria

I. Initial Approval Criteria

A. Colorectal Cancer (must meet all):

1. Diagnosis of metastatic, advanced or unresectable CRC;
2. Documentation of RAS (KRAS or NRAS) wild-type gene status;
3. Trial and failure of the following agents, *(a, b, c or d) unless contraindicated or clinically significant adverse effects are experienced:
 - a. 5-fluorouracil or capecitabine;
 - b. Oxaliplatin and irinotecan;
 - c. An anti-VEGF agent: Avastin®, Cyramza®, Stivarga®, Zaltrap®, Mvasi® or Zirabev™;
 - d. If tumor expresses the RAS wild-type gene, an anti-EGFR agent: Erbitux® or Vectibix®;

*Prior authorization may be required.
4. Prescribed as a single agent or in combination with bevacizumab*;

*Prior authorization may be required.

Approval duration

All lines of business (except Medicare): 12 months, Split-fill

B. Gastric Cancer or Gastroesophageal Junction Adenocarcinoma (must meet all):

1. Diagnosis of metastatic, unresectable, or recurrent gastric cancer (GC) or GEJ adenocarcinoma;
2. Documentation of HER2/neu gene status;
3. Trial and failure of at least two (2) of the following agents,* unless contraindicated or clinically significant adverse effects are experienced.
 - a. 5-fluorouracil or capecitabine;
 - b. Cisplatin, carboplatin, or oxaliplatin;
 - c. Docetaxel, paclitaxel, or irinotecan;

*Prior authorization may be required.
4. If tumor is HER2/neu-positive (i.e., HER2-overexpressing): Trial and failure of at least one (1) of the following agents* (Herceptin®, Herzuma®, Kanjinti™, Ogivri®, Ontruzant, Trazimera™), unless contraindicated or clinically significant adverse effects are experienced;

*Prior authorization may be required.
5. Prescribed as a single agent;

Approval duration

All lines of business (except Medicare): 12 months, Split-fill

II. Continued Therapy Approval

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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

1. Auto approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval duration

All lines of business (except Medicare): 12 months

References

1. National Comprehensive Cancer Network. Colon Cancer Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 14, 2024.
2. National Comprehensive Cancer Network. Rectal Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf. Accessed June 14, 2024.
3. National Comprehensive Cancer Network. Gastric Cancer Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed June 14, 2024.
4. National Comprehensive Cancer Network. Esophageal and Esophagogastric Junction Cancers Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed June 14, 2024.

| Review/Revision History | Review/Revised Date | P&T Approval Date |
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| Policy established | 01/2020 | 03/06/2020 |
| Policy was reviewed: <ol style="list-style-type: none"> 1. Policy title was updated. 2. Indications were updated. 3. Initial Approval criteria updated. 4. Continued Therapy Approval criteria I.A.1 was rephrased. 5. References were updated. | 07/29/2020 | 09/14/2020 |
| Policy was reviewed: <ol style="list-style-type: none"> 1. References were reviewed and updated. | 06/03/2021 | 09/14/2021 |
| Policy was reviewed: <ol style="list-style-type: none"> 1. Initial Approval Criteria, I.A.4: Updated to remove prior diagnostic criteria "Documentation of RAS (KRAS or NRAS) wild-type gene status". 2. Initial Approval Criteria, I.A.4.c: Updated trial and failure criteria from An anti-VEGF agent: Avastin®, Cyramza®, Stivarga® or Zaltrap® to An anti-VEGF agent: Avastin®, Cyramza®, Stivarga®, Zaltrap®, Mvasi® or ZirabevTM. 3. Initial Approval Criteria, I.A.6: Updated to remove prior diagnostic criteria "Attestation of obtaining complete blood counts prior to and on Day 15 of each cycle and more frequently as clinically indicated". 4. Initial Approval Criteria, I.B.5: Updated to remove prior diagnostic criteria "Attestation of obtaining complete blood counts prior to and on Day 15 of each | 03/23/2022 | 07/18/2022 |

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| <p>cycle and more frequently as clinically indicated".</p> <p>5. Initial Approval Criteria, I.B.6: Updated trial and failure criteria from If tumor is HER2/neu-positive (i.e., HER2-overexpressing): Failure of Herceptin®, unless contraindicated or clinically significant adverse effects are experienced; to 6. If tumor is HER2/neu-positive (i.e., HER2-overexpressing): Trial and failure of at least one (1) of the following agents* (Herceptin®, Herzuma®, Kanjinti™, Ogivri®, Ontruzant, Trazimera™), unless contraindicated or clinically significant adverse effects are experienced.</p> <p>6. Continued Therapy Approval, II.A.3: Updated to remove prior diagnostic criteria "Attestation of obtaining complete blood counts prior to and on Day 15 of each cycle and more frequently as clinically indicated".</p> <p>7. References were reviewed and updated.</p> | | |
| <p>Policy was reviewed:</p> <p>1. Initial Approval Criteria, I.A.4: Updated to include new Documentation criteria Documentation of RAS (KRAS or NRAS) wild-type gene status.</p> <p>2. Initial Approval Criteria, I.A.6: Updated to include new prescribing criteria prescribed as a single agent or in combination with bevacizumab*.</p> <p>3. Initial Approval Criteria, I.A.7: Updated to include new Documentation criteria Documentation of member's body surface area (m2).</p> <p>4. Initial Approval Criteria, I.B.7: Updated to include new prescribing criteria prescribed as a single agent.</p> <p>5. Initial Approval Criteria, I.B.8: Updated to include new Documentation criteria Documentation of member's body surface area (m2).</p> <p>6. References were reviewed and updated.</p> | <p>04/25/2023</p> | <p>07/13/2023</p> |
| <p>Policy was reviewed.</p> | <p>10/19/2023</p> | <p>10/19/2023</p> |
| <p>Policy was reviewed:</p> <p>1. Age Criteria Removed.</p> <p>2. Dose criteria Removed.</p> | <p>6/14/2024</p> | <p>6/14/2024</p> |

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| 3. Approval Duration Updated. 4. Continuation Criteria updated. 5. References were reviewed and updated. | | |
| Policy was reviewed. | 12/05/2024 | N/A |
| Policy was reviewed. | 12/11/2025 | 12/11/2025 |