

A Review of Evidence Supporting NCCN Category 2B Off-Label Recommendations for Determination of Medicare Reimbursement Eligibility

TEMPUS

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INTRODUCTION

Antineoplastic indications that are “off-label” but supported by a category 1 or 2A NCCN guideline recommendation are generally reimbursed by private insurance and Medicare. While initial coverage requests for off-label NCCN category 2B indications may be denied, Medicare will consider reimbursement for 2B indications supported by clinical trial evidence published in one of 26 peer-reviewed journals.

Herein, we evaluated the published clinical evidence supporting off-label drug indications in 10 common solid tumor types that are supported only by NCCN category 2B evidence.

METHODS

Category 2B drug indications for the 10 most common solid tumors were identified in the NCCN compendium (n=104).

These were then filtered to remove the 2B indications associated with concurrent category 1 or 2A indication(s) in the same tumor type (n=90), as the higher category indications could offer an alternate pathway to reimbursement and/or lower payer scrutiny.

Next, drugs with an FDA approval in the tumor of interest, but supported by only category 2B evidence at NCCN, were excluded from the study (n=6). This resulted in eight indications supported by only an NCCN category 2B recommendation.

Published clinical studies supporting these indications were assessed for study type (clinical trial Y/N, phase of clinical trial, randomization Y/N) and journal name in PubMed. Journal names were cross-referenced with the Centers for Medicare & Medicaid Services (CMS)-endorsed journal list.

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SUMMARY

Among the **non-FDA-approved drug indications** for the **10 most common solid tumor types** with only **category 2B recommendations**, 87% had at least one clinical trial publication in a designated CMS journal.

These results suggest clinicians should consider pursuing the appeals process and provide supporting evidence in cases of claim denial. While coverage is not guaranteed, the **evidence supporting 2B indications frequently meets** the criteria identified in the **Medicare statute**.

Evaluation of other 2B indications is in progress and may support expanded coverage of these indications.

RESULTS

Table. Non-FDA-approved Drug Indications with Only Category 2B Recommendations

| Drug(s) | Cancer Type | PubMed ID | Journal Name | Type of Study | Evidence Supported by CMS? |
|--|-------------------------------------|-----------|-------------------------------------|--|----------------------------|
| Vandetanib | Non-small cell lung cancer | 27803005 | <i>Annals of Oncology</i> | Phase 2 RCT | Y |
| | | 27825616 | <i>Lancet Oncology</i> | Non-randomized, Phase 2 Clinical Trial | Y |
| | | 25881079 | <i>BMC Cancer (Biomed Central)</i> | Phase 3 RCT | N |
| | | 25366691 | <i>Journal of Clinical Oncology</i> | Case report | N |
| Eribulin | Uterine neoplasms - uterine sarcoma | 21937277 | <i>Lancet Oncology</i> | Non-randomized, Phase 2 Clinical Trial | Y |
| Cisplatin, Vinblastine, and Dacarbazine | Cutaneous melanoma | 19001327 | <i>Journal of Clinical Oncology</i> | Phase 3 RCT | Y |
| | | 25332243 | <i>Journal of Clinical Oncology</i> | Phase 3 RCT | Y |
| Talimogene laherparepvec and Ipilimumab | Cutaneous melanoma | 26014293 | <i>Journal of Clinical Oncology</i> | Phase 3 RCT | Y |
| | | 28981385 | <i>Journal of Clinical Oncology</i> | Phase 2 RCT | Y |
| Binimetinib | Cutaneous melanoma | 28284557 | <i>Lancet Oncology</i> | Phase 3 RCT | Y |
| Docetaxel | Uterine neoplasms | 16234823 | <i>British Journal of Cancer</i> | Non-randomized Phase 2 Clinical Trial | Y |
| Gemcitabine | Bladder | N/A | N/A | N/A | N |
| Gemcitabine, Docetaxel, and Capecitabine | Pancreatic | 25492104 | <i>Cancer</i> | Non-Randomized, Phase 2 Clinical Trial | Y |

Table: Seven out of 8 indications (87%) supported exclusively by a category 2B NCCN recommendation had at least one publication that met the evidentiary requirements for Medicare reimbursement, with 5 supported by a randomized clinical trial. *RCT, Randomized Controlled Trial; Y/N, Yes/No; N/A, Not Available.*

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