The Impact of Payer Coverage and Reimbursement Policies on Off-Label Use of Anticancer Therapies

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Over the past two decades, the cancer community has faced a familiar drama: a physician prescribes a drug for a cancer patient only to discover that the insurer will not pay because the drug is being used for an "off-label" indication. The physician and patient point to published research to support the use of the drug, the insurer counters with the concern that the research has not been vetted by the Food and Drug Administration (FDA).

Ensuring access to medically appropriate off-label uses has been so contentious—and of such great importance to the cancer community—that federal and state laws have been enacted. These laws established off-label use as appropriate when there is a sufficiently strong body of research to have the indication listed in a national drug formulary. By law, Medicare Part B is required to reimburse for off-label uses of anticancer therapeutic regimens if they are supported by citation in at least one of three compendia: 1) the *USP DI Oncology*, a copyrighted publication of Micromedex, Inc., 2) *AHFS Drug Information*, published by the American Society of Health-System Pharmacists, and 3) the American Medical Association's *Drug Evaluation*, which is no longer published since its merger with the USP DI in 1996. The statute also allows Medicare coverage if peer-reviewed literature supports an off-label use; the decision is left to the local Medicare carriers.

The Association of Community Cancer Centers (ACCC) spearheaded efforts to make citation of a cancer drug in any of the standard reference compendia sufficient to require insurers to pay for its use outside of FDA-labeled indications. To date, 39 states have passed ACCC's off-label legislation with similar language to the Medicare rules.

Off-label use of drugs and biologicals is a critical component in cancer treatment and can include:

- Changes in the stage of cancer at which the therapy is provided
- Use of the medicine against a different tumor type based on sound clinical rationale
- Use of the medicine against a different biological target based on new research
- Changes in the medicine's use as part of a multi-drug regimen.

Just How Important Is Off-Label Use in Cancer?

To better understand the impact of payer policies on physician treatment decisions and patient access to off-label anticancer therapies, ACCC, the Biotechnology Industry Organization, and the Pharmaceutical Research and Manufacturers of America commissioned a study, which was conducted by Covance Market Access Services, Inc., a global reimbursement policy and health economics and outcomes research firm.

Despite the limitations of a small study sample size, several indications suggest that the findings may be seen in a broader sample of the oncology community. While not definitive, the findings bring attention to important issues that should be examined further. Viewed in light of the limitations, the study suggests that off-label coverage policy continues to present problems for oncologists and other specialists. Obviously, a substantially larger study would be required to confirm these results.

Interviews were conducted with a geographically diverse number of oncologists (N=28) and oncology practice managers (N=12). The interviews addressed the following issues:

- Value and importance placed on off-label use of anticancer therapies
- Perceptions of the ease of prescribing and use of anticancer therapies outside their FDA-approved indications
- Types of evidence on which physicians base off-label prescribing decisions (i.e., abstracts, unpublished data, published clinical trials data in peer-reviewed or non-peer-reviewed journal) and how, if at all, these vary from evidence sources required by CMS for national and local coverage policies
- Whether, and the degree to which, physicians and practices/offices feel constrained in their choice of anticancer therapy due to coverage policy issues and alter treatment patterns as a result
- How physicians and practices/offices are affected by local Medicare carrier policies
- Variation in off-label use by cancer type or specific patient characteristics.

The investigators also looked at local Medicare carrier and private payer coverage and reimbursement policies for off-label use of anticancer therapies. Specifically, Covance surveyed policies from 23 Medicare carriers to determine the data or evidence required by local Medicare carriers to support positive coverage decisions for off-label use.

Key Study Findings

- Oncologists place high importance on off-label use of anticancer medicines in caring for their patients.
- Oncologists draw from a wide range of evidence—primarily peer-reviewed literature and drug compendia—in making off-label treatment decisions.
- Oncologists reported that Medicare coverage policies required them to alter treatment decisions more often than private payers' coverage policies. (This statement echoed similar findings in a 1991 study by the Government Accountability Office.)
- Fifty-four percent of the interviewed oncologists reported that Medicare non-coverage "frequently" or "very frequently" caused them to alter their treatment decisions; 29 percent said that private payer policies had a similar effect.
- Oncologists generally value the option of local Medicare coverage of cancer treatments and would be concerned if this option was restricted.

What We Found

Off-label use of anticancer therapies continues to play an important role in the treatment of cancer patients, according to study results. Approximately 68 percent (19 of 28) of the interviewed oncologists reported that they placed "high importance" on their ability to use anticancer therapies for off-label diagnoses. An additional 21 percent (6 of 26) of oncologists rated off-label drug use of "medium importance."

Nearly *all* oncologists (93 percent) said that off-label use of anticancer therapies is more commonly reserved for advanced stages of cancer. However, some oncologists note that for some cancer types, such as pancreatic cancer, off-label use of anticancer therapies is necessary independent of cancer stage.

The survey also revealed that the frequency of off-label use has changed over the past five years. About 42 percent of oncologists and office practice managers said that off-label use of cancer medicines appears to be increasing for a number of reasons, including more aggressive treatment of many cancers and, in some cases, narrower FDA-approved labeling on new cancer drugs. Both oncologists and office practice managers attributed this increase to greater availability of and access to new drugs. Interestingly enough, 30 percent of respondents reported a decreased use of off-label drug use for reasons such as broadened product labeling on older medicines and reimbursement challenges.

Overall, oncologists and office practice managers identified more than 50 physician-administered anticancer therapies used for a variety of off-label diagnoses, with the top five

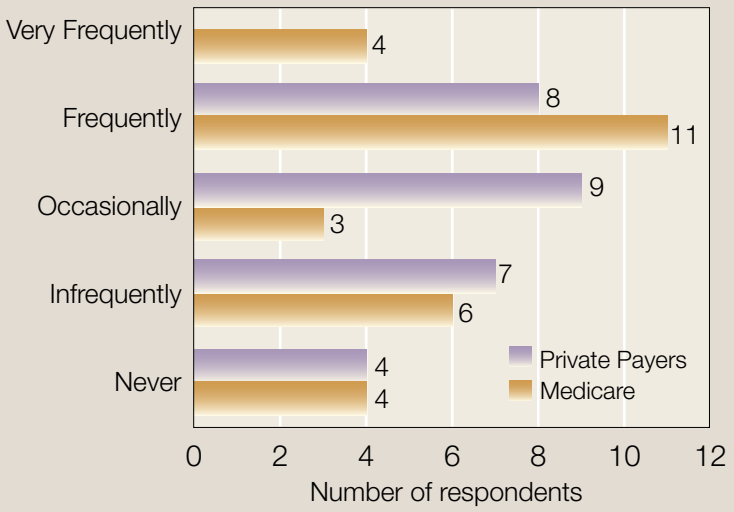
"I find it hard, because Medicare will deny every off-label indication that is not listed in one of the two compendia. So, at this point, I am only using those products off-label for those indications that are listed in the compendia." —*Oncologist 9*

physician-administered anticancer therapies representing nearly 50 percent of the identified off-label uses. Oral drugs accounted for 87 percent of the anticancer therapies being used for off-label indications. The top two oral drugs represented 31 percent and 16 percent, respectively.

Oncologists who participated in the study reported that they rely on a "wide range" of evidence sources for clinical decision-making, including peer-reviewed literature (89 percent), drug compendia (60 percent), drug manufacturer hotlines (25 percent), and case reports (25 percent). Phase II and Phase III clinical trial data and unpublished trial data were mentioned a combined total of 13 times during the interviews.

Perhaps of greatest concern is the finding that reimbursement challenges appear to be affecting treatment decisions—particularly for Medicare beneficiaries. More than half (54 percent) of the oncologists said that Medicare non-coverage "frequently" or "very frequently" caused them to alter their treatment decisions. About 28 percent reported that private payer policies have a similar effect.

Figure 1: Extent to Which Medicare and Private Payer Policies for Off-Label Use of Anticancer Medicines Interfere With Oncologists' Clinical Decision-making



About 32 percent of oncologists said that "they will only prescribe an anticancer therapy to Medicare beneficiaries for an off-label use if they know it will be covered" (i.e., either accepted by drug compendia or listed in a local Medicare carrier policy as covered). The majority of oncologists anticipated that anticancer therapies that are *not* listed in drug compendia or in a drug-specific coverage policy would result in payment denials and increased administrative and financial burden on their practice. Therefore, to avoid potential payment denials, some oncologists avoid other off-label therapies that may be eligible for coverage but lack an affirmative policy (e.g., an off-label use supported by peer-reviewed medical literature but not listed in recognized compendia).

In instances where coverage for an off-label use of a medicine is denied by Medicare, patients can appeal the denial to the carrier and higher levels if necessary; however, examination of coverage appeals was outside the scope of this study.

Policy Implications

First, policymakers should recognize the wide range of medically appropriate off-label uses, and the wide range of evidence sources oncologists rely on to support such uses. In particular, policymakers should accept peer-reviewed medical literature and other clinical sources in addition to the specified drug compendia as bases for coverage of off-label use, particularly for new cancer therapies, advanced stages of cancer, and rare cancer types. Compendia listings represent an important but incomplete subset of medically appropriate off-label uses. Listings in recognized compendia are often outdated, incomplete, and may not include references to potential off-label uses of new drugs that are supported by other published clinical evidence.

Second, future coverage policies should seek to *improve*—rather than constrain—provider and patient access to off-label drug uses. This would reduce the administrative burden on providers seeking to verify patient eligibility for therapies routinely deemed medically necessary by oncology specialists.

In addition, Medicare carriers should provide clear guidance on the data or evidence required to support positive coverage decisions for individual off-label drug uses. Medicare carriers should consider streamlining or minimizing their documentation requirements—and thus reducing the provider administrative burden—for those anticancer therapies used regularly for rare cancer types.

Finally, additional research—including a larger sample size of oncology practices—should be undertaken to further examine the extent of coverage/reimbursement policy impact on patients' ability to receive cancer therapy for off-label uses.

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