
SPECIALTY PHARMACY NEWS

Education, Data Are Needed on Combination Immunotherapies

Since the first of the immunotherapies came onto the U.S. market in 2011, these drugs have had a tremendous impact on the treatment of various cancers. However, these innovative therapies, which use an individual's own immune system to attack cancer cells, come at a steep price to a health care system already struggling to rein in care costs. The treatments also come with certain side effects affiliated with their mechanism of action. And while almost all the current therapies have multiple approved indications, researchers are looking at their use in combination with each other, as well as with chemotherapies. A recent survey revealed that this concurrent use is something with which payers are concerned.

The therapies currently available function by targeting specific pathways, or immune checkpoints, for inhibition: programmed cell death-1 (PD-1), PD-1 ligand (PD-L1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4).

All the drugs have annual price tags well north of \$100,000. The FDA has already given accelerated approval to the combination of Opdivo (nivolumab) and Yervoy (ipilimumab) to treat people with metastatic melanoma (*SPN 10/15, p. 10*). The first year of treatment with the two costs more than \$250,000.

Precision for Value, a company that uses payers' experiences and experts' analyses to help pharmaceutical and life sciences companies secure access and reimbursement for their products, recently conducted a survey of 20 payers representing 75 million lives and 10 integrated delivery systems on their concerns around combination immunotherapy regimens.

Among the findings are the following:

- ◆ 33% of respondents said it was either very or extremely important whether an immunotherapy was used as part of a combination treatment.
- ◆ 37% said they were more concerned about a particular combination as opposed to another. Of these, almost 75% said a combination of immunotherapies was more concerning than an immunotherapy-chemotherapy combination.
- ◆ 55% of respondents cited cost as their biggest concern around immunotherapy combinations, while the

second-highest concern, cited by 27%, was the higher adverse-event incidence in combination regimens compared with the drugs as a monotherapy.

Immunotherapies such as Yervoy and Keytruda (pembrolizumab) "have taken the cancer world by storm," maintains Jeremy Schafer, Pharm.D., senior vice president of specialty solutions at Precision for Value.

In addition, "immunotherapies are gaining in importance in terms of following science," says Janet Serluco, vice president-oncology lead at Precision for Value. She points to the Opdivo/Yervoy combination, which is "targeting two areas within the immune pathway."

Although "the survey didn't get into the granularity of adverse events," Schafer notes that because immunotherapies are so new, "there's not a lot of experience" with them. And while chemotherapies have "plenty of adverse events," physicians are "familiar with them because these products have been around a long time."

As far as immunotherapies' price tags, "these products aren't inexpensive; they come with a fair amount of costs," says Schafer, which is particularly concerning due to the large number of them in the pipeline. There will be "more and more products coming out." With combinations that "well exceed \$200,000 per year," the payer perspective is "where does it end, or does it keep going, and how do I provide access" to members?

According to Serluco, even "triple regimens are being studied."



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She points out that with the "known side effects" of chemotherapies, payers know not only what to anticipate but also what the "downstream costs" for adverse events' management are. "Typically when you have a current chemotherapy regimen," that consists of "two or three drug combinations." Side effects "are sometimes specific relative to specific agents."

With immunotherapies, "patients may present in a different way" due to adverse events, says Serluco, and there may be "specific immune-mediated side effects

that may appear," but not everyone may be familiar with those.

"An element of it comes from having predictability," says Schafer. With chemotherapy, there is a "pretty good expectation of what could happen," which enables payers and providers to "keep costs and hospitalizations as manageable as possible." In contrast, information on immunotherapy combinations is usually simply "data from clinical trials,...but real-world data" are "harder to predict."

To help with this, payers should have "engagement with the provider community" and have "policies in place for oncology patients that are very clear and are based on the most recent" data available, he asserts. But because "the space is moving so quickly," this can make it "difficult to keep policies and pathways up to date." This also addresses the potential problems of members being on a therapy when they shouldn't be and members being denied access to drugs that are appropriate for them. In addition to payers communicating with oncologists and provider networks, drug manufacturers can "keep payers up to date" on their products.

So what can payers do in terms of strategies to manage these combination treatments? Schafer says one way

is having a medical policy that requires approval for them before a physician administers them or "retroactively after they are administered." Pathway programs, which usually align with guidelines, such as those from the National Comprehensive Cancer Network (NCCN), can be effective as well.

He also points to CMS's Oncology Care Model, which launched last summer (*SPN 7/16, p. 4*), in which provider practices "take on the responsibility of a patient's health" and "manage to the best possible outcomes."

Overall, many of the survey respondents "considered themselves fairly to very knowledgeable" around immunotherapy combinations, says Serluco. But with "so many advances coming so quickly," payers are "looking for information in an efficient manner," such as from manufacturers, to keep their policies updated.

"There is always an opportunity for education," says Schafer.

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