With CMS coverage policy, NGS cancer testing goes large

Anne Paxton

July 2018—The March 16 announcement of a new Centers for Medicare and Medicaid Services coverage policy for next-generation-sequencing–based diagnostic lab tests for patients with advanced cancer did not appear out of the blue, since a draft policy was issued last fall. But the revised final national coverage determination broke away from the original draft significantly.

The new, more liberal national coverage policy of the NCD proactively lays out the reimbursement welcome mat for NGS testing, industry analysts say. “Now there is a defined FDA pathway to get an NGS test to the market and get reimbursement for Medicare patients,” says Jeff Schreier, MBA, senior director of the marketing team at Diaceutics, a company that works with pharmaceutical firms on diagnostic testing and data analytics. “Before this NCD, there was none.”

The NCD makes all NGS testing (including leukemia/lymphoma, germline, liquid biopsy tests, and more) for patients with advanced-stage cancer eligible for pathways to FDA approval and CMS coverage. It drops a requirement that the tests be backed by evidence development, and it expands the eligible patient population to patients with stage III and stage IV advanced cancer, as well as those having recurrent, relapsed, refractory, or metastatic cancer.

Foundation Medicine and Thermo Fisher’s comprehensive tumor panels (FoundationOne CDx and Oncomine Dx Target Test) will be covered immediately. So will other FDA-approved or FDA-cleared companion in vitro diagnostics when the test has an FDA-approved or FDA-cleared indication for use in a patient’s cancer. Other tests using NGS with advanced cancer will continue to have local coverage determinations made by the local Medicare administrative contractors. But the full implications of the new policy for laboratory-developed tests, medical research, payer policies, and patient care continue to be subjects for debate.

It will definitely be easier to gain approval for NGS tests. “It has provided more predictability, but some questions remain about the overall impact on the use of NGS tumor panels moving forward,” says Charles Mathews, a principal with ClearView Healthcare Partners, a worldwide health care strategy consulting firm. Still, some old assumptions will be jettisoned. His job has often involved helping people identify clinical utility evidence they can develop to secure reimbursement, “and the NCD has flipped the script a bit,” he says. “Now it says, if you get FDA approval, you don’t have to develop all of that evidence.”

Mathews

“It’s very much a conscious decision on the part of CMS to say: ‘We think this is advanced care. We want people to have access to it and we’re going to proactively support it.’” Even though there is not a lot of evidence about NGS across the board right now, Mathews sees the CMS saying, “Let’s give it a shot”—in contrast with typically cautious CMS approaches in the past. Political pressures also figure in the equation, he says, given the United Kingdom’s 100,000 Genomes Project and Germany’s recent NGS coding and payment reforms.

One result of the NCD is fairly certain, in Mathews’ view: Foundation Medicine and Thermo Fisher stand to immediately gain market share because of their approved comprehensive tumor panels. The NCD, in fact,

originated in a request by Foundation Medicine for parallel review (by CMS and FDA) of its FoundationOne CDx, which last November was the first NGS panel to win FDA approval, Mathews says. “These two companies are in a unique position where they were actually at the forefront of getting parallel approval. So now if you run a Thermo Fisher Oncomine in your lab, it has approval; the Illumina TruSight Cancer Sequencing Panel doesn’t have the same.”

“But long term, now that the pathway has been established and we know how to get approval, it’s just a matter of time for other panels to get approved,” Mathews adds. As a result, he expects that academic medical centers and community hospitals will further insource tumor panel testing, eventually eroding Foundation’s market share.

From laboratories’ perspective, tumor panel profiling makes sense, Mathews says. “The world as it was organized historically had individual tests associated with individual therapeutics; you take a piece of tissue, cut it into 15 pieces and say, ‘Let’s do the *EGFR* analysis, and now the *ALK* analysis,’ etc. And to be on label for all of these things, you have to use the FDA-approved companion diagnostic for each of them.”

“But then these NGS panels come along and say we can look at all of it at once. One sample, one workflow.” For *EGFR* and *ALK,* he adds, “we know there are certain therapies that respond well. But now you also have newer concepts such as tumor mutational burden and microsatellite instability. It appears that with the new NGS policy CMS is paying for the whole test, and that includes both the FDA-approved components of very clear value and also others that are along for the ride.”

Kyle Fetter, executive vice president and general manager of diagnostic services for Xifin, a health care IT company that provides lab information systems and revenue cycle management systems and services for diagnostic companies, views the NCD as a step in the right direction. “It’s a validation of technology that’s very important in diagnosing cancer patients.”

Fetter believes many laboratories will now take the route of developing their own tests and then apply for coverage through an individual MAC or Palmetto GBA’s MolDX program, which decides genetic testing coverage for most of the Medicare contractors.

Most recently, MolDX approved NGS coverage for gene testing for familial adenomatous polyposis, *BRCA1* and *BRCA2,* myeloproliferative disease, and Lynch syndrome, and more tests are on deck. “Right now there are three specific NGS tests being considered by the MolDX program for coverage,” Diaceutics’ Schreier says. The tests are comprehensive genomic profiles to guide treatment in patients with advanced primary fallopian tube and ovarian cancer, metastatic colorectal cancer, and metastatic melanoma. MolDX revisited these panels two weeks after the NCD was issued, Schreier notes.

Fetter

Fetter says more FDA approvals of NGS sequencing technologies are likely over time. “But we actually feel that if CMS is covering laboratory-developed tests, many labs will continue to do LDTs in sequencing and simply go through the Medicare contractors” to win approval for reimbursement. Fetter hopes that labs will continue to push to get coverage for their specific NGS-based LDTs to supplement the FDA-approved tests, as well as push for expanded indications for coverage beyond those in the current NCD.

But a big problem for laboratories, Fetter says, is that the price point for testing with some of the genetic panels is way too low—$500 to $700. “When these prices were first released, it was well understood within the industry that they were too low, and people over time have become sort of passively accepting of it, but there are very few labs,

if any, that can perform that testing at such a low cost. The specimens are very expensive, the logistical support and testing are very expensive, and the development is very expensive."

People seeking approval of LDTs, he notes, appear to be seeking a new CPT code to get reimbursed at an appropriate rate, rather than be tied to the very low price for the established CPT codes. Xifin is encouraging more laboratories to work to get their LDTs approved through their MACs and to provide comments to the CMS on pricing and expanding their coverage indications for the NCD.

It was recently announced, Mathews says, that Foundation Medicine received a novel advanced diagnostic laboratory test, or ADLT, designation. "For a nine-month period starting July 1, CMS will reimburse FoundationOne CDx at a rate of $3,500 per test, which interestingly is less than their $5,800 list price," Mathews says. The other assays do not have this designation, he adds, and will go through a process in which each individual carrier will set its own price before a final national price is established (gap-filling).

The coverage of evidence requirement, mandating that LDT developers demonstrate clinical utility of their NGS test, was a concern for many when it was part of the original draft of the NCD, though there was surprise when the CMS removed it in the final draft, Fetter says. "I do think it would be prohibitive for many laboratories trying to get into performing NGS for particular patients. So when CMS removed that requirement, most laboratories would have agreed that that removes a barrier to their performing that type of testing." The laboratory community in general, he notes, believes approval should be based on just making sure there is clinical validation for the NGS tests they are running.

The laboratories in contact with Schreier have been positive about the NCD, and so are Diaceutics' pharmaceutical clients. "The pharmaceutical companies are very keen to the need to understand what patient access there will be for NGS," Schreier says, "because their drug pipelines are so dependent on the testing. And that access will depend on reimbursement, and the NCD is a step forward in getting NGS testing covered and reimbursed." Since the NCD was announced, he has seen an uptick in drug companies' announcements of collaborations with Foundation Medicine to develop companion diagnostic tests for their therapeutic assets.

Only four NGS tests have FDA-approved companion diagnostic indications in advanced cancer: Illumina's Praxis, Thermo Fisher's Oncomine Dx Target test, and Foundation Medicine's F1CDx and FoundationFocus CDx BRCA. "Those three companies are automatically receiving coverage under the final NCD, provided that the other coverage criteria are met, which gives them a sizable advantage," Schreier says. More uncertain, in his view, is what will happen with tests like the MSK-IMPACT, developed by Memorial Sloan Kettering Cancer Center's pathology department, which has marketing rights because the test was 510(k) cleared but does not have FDA approval. Because the FDA did not indicate the MSK-IMPACT test as a companion diagnostic test, MSK-IMPACT is not included as having automatic coverage under the final NCD, Schreier notes.

But with the NCD, there's a set pathway to go through FDA approval and a set pathway for clearance under the 510(k) process. "Very few diagnostic tests have gotten FDA clearance through the 510(k) pathway, depending on test indication," Schreier says, noting that MRDx BCR-ABL by MolecularMD was the most recent one, in December 2017. (Robert Feeney, PhD, director of the global lab team at Diaceutics, points out that the MRDx test is different than other companion diagnostics in that it's used as a monitoring aid for treatment discontinuation, not initiation, suggesting to him that the FDA may view it as lower risk.) "The FDA is attempting to reinvent the ways in which these labs can have easier and more realistic pathways to get approval. That policy is still evolving, and it's tied in with FDA's broader goal of overseeing from a regulatory aspect the development of lab tests," Schreier says. In line with this agenda, he adds, the FDA is providing technical assistance to a congressional committee that has drafted the Diagnostic Accuracy and Innovation Act to reframe some of these regulatory issues.

However, every NGS company can now pursue a regulatory path through the FDA or elect to go through its local Medicare administrative contractor. Many may choose the latter because of the cost, effort, and time required to go through the FDA, Schreier says. Seeking approval from a local Medicare contractor is not a shortcut, he emphasizes, because the MAC, unlike the FDA, will still base its decision on clinical utility, which is difficult to

prove. But MolDX approval, if granted, would span the geographic jurisdiction of four MACs.

In response to concerns that the NCD could inhibit the development of oncology NGS for other clinical applications, Schreier agrees that the NCD is tilted heavily in favor of companies that are FDA approved, like Foundation Medicine. “The NCD could inhibit the development of newer and better tests by disincentivizing labs that don’t have the budget or the resources to go through the FDA.”

On the other hand, Schreier says, test developers could have a greater financial incentive to innovate and go down the FDA path. “It is now a new development that by obtaining FDA approval as a companion diagnostic test, an NGS test developer obtains greater reimbursement for the test. What remains to be seen is the level of reimbursement that is set by CMS for tests that go the route of the MACs and obtain positive local coverage decisions as a result.”

The various pathways to NGS test approval laid out in the NCD could have unexpected consequences for payment, Schreier believes. As a Diaceutics blog noted shortly after the NCD was announced: “The question now is, how much will the MACs reimburse the labs that are running NGS panels as LDTs? The payment amount could be a fraction of the rate that CMS pays for an FDA-approved or -cleared test. This is a way for CMS to reconcile both LDT and IVD pathways, but push commercialization through the FDA path, with the carrot of assured and likely higher reimbursement, given the expense of FDA review.”

The proper role of evidence in making the case for approving NGS tests is still under discussion. “On April 12, a few weeks after the NCD was rendered, the FDA came out with guidance on what public clinical databases could be used as a vehicle to obtain FDA approval, to support the clinical validation of NGS—databases such as ClinGen, which is maintained by the National Institutes of Health,” Schreier explains. “There’s also been publicized apprehension about the FDA dropping the coverage of evidence requirement, because if you don’t continue to amass evidence, and labs that get CMS coverage are able to go forward with testing in the absence of evidence, there could ultimately be blowback if a lot of money is being spent on these tests and one day it’s determined there is no clear benefit.”

Insurers look at the dropping of the coverage of evidence requirement with a lot of skepticism, Schreier says, because they want solid clinical utility evidence of patient benefit from a test. “They are just looking at it in terms of direct diagnostic expenditure. How many patients get tested before you have a patient with a clinical benefit? For how many patients is there no clinical benefit? That’s the issue when you have a 324-gene panel that is run, even when it’s run on an advanced stage III or IV metastatic cancer. With the majority of patients, a result comes up that can’t help; it doesn’t result in the therapy that’s on label.” But the results of NGS tests often point to genomic alterations for which there are companion diagnostics for other tumors. So there’s a concern that the rate of off-label prescribing could increase, Schreier says, but the likelihood of that is unknown.

Mathews expects that the new coverage of evidence policy will have a negative effect on needed research. “CMS’ rationale for dropping the coverage of evidence development was that people are developing evidence anyway. But they were developing this evidence because they thought it was a requirement for coverage. If you give people payment without waiting for the evidence, you lose that tailwind.”

As for laboratory-developed tests, there is debate over whether they will benefit or suffer from the NCD. Mathews splits the LDT world into academic medical centers, where pathologists are developing the tests, and proprietary companies like Guardant Health. “The companies are going to try to get FDA approval for their products and then compete. At the medical centers, depending on what instrument you have, you can decide to run the FDA-approved tumor panel locally and get paid for it now, without having to go through the thought process of generating all of your own evidence to document clinical utility.” Mathews anticipates that the NCD will make it easier for medical center laboratories to get paid for testing they may want to do internally.

There is room for a possible increase in coverage for liquid biopsies, Schreier says, because the CMS did not specify tissue type in the NCD. In fact, the NCD does not limit coverage according to how samples are prepared for performing a diagnostic laboratory test using NGS. This point is stated in a CMS clarification issued in response to

comments. “So liquid biopsies can be included in the approval or clearance pathway to get national coverage by CMS,” Schreier says. “But tissue is still the gold standard. If a liquid biopsy result is negative for a mutation or a genetic abnormality, then you still need to try to get tissue.” In addition, the FDA has defined the newly created New York State Department of Health/510(k) accelerated pathway as being currently suitable only for tissue tests, not liquid biopsy tests.

Schreier

A classic CMS pattern complicates payment policy, Mathews points out, and here, it is that “this policy was propagated by the coverage group at CMS, and the coding and payment group is different.” To his thinking, there is a question about whether Medicare, when it comes down to it, will actually execute payment for NGS diagnostic lab tests. “Foundation One has gotten regulatory approval only for the smaller panel within the bigger panel of the genes they associate with particular therapies. There’s a lot of other stuff that’s kind of along for the ride.” So coverage management, or what Medicare says it will pay for, is not yet clear.

For example, as ClearView points out in a summary it prepared on the expected impact of the NCD, FoundationOne CDx includes an assessment of not only genes relevant for selection of 17 different on-label targeted therapies, but also information on 324 genes, microsatellite instability, and tumor mutational burden. “Will Medicare pay for all of this or just the FDA-approved part? If only the latter, then how will they tease out the value of that component? Will they enforce a limitation to just indicated solid tumors with CDx indication, or pay for it for all solid tumors?” Mathews asks.

The impact of the NGS NCD on commercial payers is one of the bigger unknowns as the new coverage policy evolves, and measuring commercial payers’ views was one goal of a survey that ClearView conducted earlier this year. Commercial payers have not yet embraced NGS technology for broad tumor panel profiling, Mathews says. Forty-five percent of payers do not cover these tests at all, and the remaining 55 percent approve coverage on an exceptions-only basis. ClearView’s survey tapped the opinion of 12 commercial payer medical directors, whose companies collectively represent 44 million covered lives in the U.S., or 14 percent of the population.

“Commercial payers view the CMS decision with caution and concern,” Mathews says the survey showed. Many of them question whether NGS has demonstrated clinical utility; comments expressed skepticism about whether the CMS decision was evidence based, concern that the NCD was put together too hastily, suspicion that the NCD was capitulation to political pressure, and certainty that they would not change their current coverage policy.

However, fully half of respondents expect to cover FDA-approved NGS tests for companion diagnostic indications, with two plans going the further step of saying they would also cover laboratory-developed tests for NGS, and one plan saying it would cover testing done in accordance with clinical trials such as NCI-MATCH (Molecular Analysis for Therapy Choice) or TAPUR (Targeted Agent and Profiling Utilization Registry). Within one or two years, however, the majority of payers expect that their commercial coverage of NGS in oncology will fall in line with the Medicare NCD, the ClearView survey revealed.

Whichever direction payment takes, Mathews hopes people will keep in mind the continuing need to demonstrate clinical utility of NGS diagnostic tests. “The important thing for local pathologists is to definitely know and understand what’s going on with the NGS coverage and monitor what rolls out over time and be prepared to adjust,” he says. He has had conversations with people in multiple labs in academic medical centers who say they are using the NCD now to go upstairs to administration with new plans about the tests they plan to use. “You may want to wait until tests you are using get FDA approved. But at least now we know there’s an approval pathway for

NGS. So we know the clock is ticking on that."

Given the resource constraints in health care, Mathews says, "What I hate to see is a situation where NGS flourishes temporarily because of the national coverage determination, and then the financial administration of the hospital or oncology group says, 'We did all of this and it didn't move the needle on patient care,' or 'We don't know what it did. Do we need to keep doing this?'" So Mathews urges pathologists, when setting up their programs, to pay ongoing attention to the need for evidence on how NGS is working and how it's affecting care. "It's just better for care overall if we understand the impact and whether or not a test is useful."

Anne Paxton is a writer and attorney in Seattle.