

As we dive into talking about the newly-approved fractionable carbidopa/levodopa 25-100 in the form of Dhivy, I think it's important to acknowledge that there's a plethora of Parkinson's medication options. And, as I said earlier, I think these options are a double-edged sword in many ways. They both present us with an opportunity to fine-tune medications for our patients but also a challenge of how we select it.

And no one patient will respond to one medication or another. We may have to use a trial and error method to optimize it. And sometimes the beauty of managing Parkinson's is that you really use a combination therapy, which I mentioned, a polypharmacy approach of different classes of medications, and each class of medications adds in its own component to it.

And levodopa certainly being the dominant class in terms of giving you the most reduction in motor symptoms-- what's called the gold-standard class of medications-- it's important to understand that we must be aware of all the different formulations of levodopa, from the fractionable formulation, to the immediate-release, to the extended-release, to the surgical option, and the inhaled option because, really, this becomes the mainstay of Parkinson's management.

Many times individuals will ask, once I started one class of medications, how long will I be on this class? And I'll say, we'll add a second class or a third class. When we start levodopa, many times patients will ask that question and say, how long before I add another medication? No, we don't add additional medications. We may add some, but this class of medications has a large pool in terms of the dosing from the smallest amount of dose to the highest dose. So, really, once you start levodopa, you have a lot of options. And now, with a variety of different formulations, we have even more options.

So having a fractionable option is interesting because at first blush many of us might look at it and say, well, why do we need a fractionable option? Well, if you look at a 25-100 immediate-release, it has a line through the center, which means patients, if they cut it diligently, can cut it into a perfect half. Many times I've seen individuals when they pull out their half a tablet usually it's more like a half-plus or half-less, so it's more like a 40% of a tablet or 65% of a tablet because they're not able to get an even-scored cut in that sense. So there's a challenge right up there.

Even with the score, sometimes the cutting is a little bit more of a challenge, and many times patients will say that when they cut tablet, half the tablet retains and the other half powderizes and they can't take it. So having something that is scored and can be reliably cut into halves, quarters, or 3/4 is an important, unmet need for individuals. With that said, we typically may dose individuals with the immediate-release formulation at one tablet, one and a half, two, or even two and a half tablets. For the most part, we're leaving gaps in between where they may need that fine-tuning.

And sometimes we learn that patients don't always need the same dose of Levodopa throughout the day. They may start with the higher dose in the morning and have a middle of the day dose that's lower dosage. And they may take even a lower dose at nighttime because maybe taking a higher dose in the evening time may result in more vivid dreams or they may simply not need that and they have more dyskinesias towards the end of the day. So having that fractionable precision may be helpful for individuals in taking the dose they want whether for individuals that may take one tablet might be a little too little but one and a half might be too much.

Well, let's define "too much." Too much might be something along the lines of, I'm having dyskinesias at that point, or I'm having more nausea at one and a half, or I'm having more lightheadedness at that point. And as I earlier mentioned that we have a carbidopa formulation of 25 milligrams, we don't tend to use that as much because it's more user-intense having to take a carbidopa tablet 30 minutes before you take the actual levodopa and all of that has to be taken apart from food, whereas having to take a lower dosage of it might be more helpful. So in that fractionable population, the obvious population that is at need for this as well, the individuals that find half a tablet cannot be reliably cut-- that's an obvious one.

The second are individuals that may need to start with a lower than half because of nausea even though they take half a tablet. And sometimes I encourage them to even take it with a little bit of a snack to settle their stomach-- nothing with protein, nothing with fat, so a little bit of fruit, a banana, a piece of bread or so, or crackers to be able to settle their stomach. They still have that challenge of being able to manage the nausea, so starting with something that gives me a reliable quarter, 25 milligrams of levodopa, it may be helpful in that population.

So individuals that are sensitive to the nausea, unable to cut in an exact half, individuals that may be stuck in a dosage in between, where they may not quite need a half but they may not need a full, they really need a 3/4-- that's a population-- or somebody that needs a 1 and 1/4, 1 and 3/4 dosing. So those fine-tuning allows me to be able to give them this dosage with a fractionable levodopa.

And then there's, of course, the individuals that do not have a consistent need throughout the day. They may start their dosage off at 1 and 1/2 or 1 and 3/4, have the middle of their day and add 1 and 1/4, and end their day off at 3/4. Well, there's no one formulation that's going to work with them, but they can really adjust their dosing with fractionable levodopa to exactly what they need throughout the day.