**Headline TK- Covid-19 antiviral supply lags in some states as cases continue to rise/Covid-19 antiviral supply dynamics evolve slower than infection rates**

**Dek:** An analysis of the demand for Covid-19 therapeutics and their supply has identified areas of unequal distribution and shortage

The rapid development and authorization of Covid-19 therapeutics was meant to stem the impact of the tide of cases. But a restricted supply that fails to meet the demand in certain states has meant that these therapeutics remain out of the reach of many.

Antivirals, namely molnupiravir, developed by Merck and Ridgeback Biotherapeutics, and Pfizer’s Paxlovid, have generated particular interest given that they can be taken orally. GlaxoSmithKline’s sotrovimab, the only monoclonal antibody that works against the Omicron SARS-CoV-2 variant, rounds up the list of effective authorized therapeutics.

However, as per data analysed from a Therapeutic locator dashboard run by the US Department of Health and Human Services (HHS), the supply of these therapeutics remains inadequate in comparison to the demand. And some places **like Delaware, North Dakota and Florida** face more of an acute shortage than others.

Moreover, by analysing data on the Covid-19 infection surges from the Centers for Disease Control and Prevention and HHS’ distribution, it appears that some states are going through the allocation much quicker than other states where cases have begun to reduce but continue to receive a surplus.

For example, while the national average of Paxlovid courses available to each state is **22 per 100,000 individuals, Delaware has no available Paxlovid while North Dakota has only three** for every 100,000 people. Molnupiravir is similarly **out of reach in Delaware, while North Dakota have only 13 and 18 courses** available respectively, per 100,000 individuals in each state.

Several news reports have stated the difficulty patients and providers have faced in getting access to these therapeutics. “Even resources like the therapeutic locator can point you to where a site has at least received a shipment, but it doesn't mean they have it in stock, says Michael Ganio, the director of pharmacy practice at American Society of Health Systems Pharmacists”. A prescription can be made for Paxlovid at say noon, but the center could have run out of medication even earlier in the day and not updated its stock on the dashboard till later. The patient, provider and pharmacist would then need to coordinate on either a different drug or find a location that has the original therapeutic. “Every step in that process takes time, and the longer that goes, the farther they're getting away from that five-day window in which these oral therapies and monoclonal are proven to be the most effective,” says infectious diseases clinical pharmacist Justin Moore at Northwestern Memorial Hospital.

The locator is said to be updated daily, and HHS did not respond to a request for comment.

**Supply chain disrupted**

Florida, which has some of the counties reporting the highest Covid-19 infection burden nationally, presents a particularly notable case study. It currently accounts for over 5% of all new Covid-19 cases in the US in the past seven days but only holds 3.6% of all available therapeutic courses, including just 1.1% of available courses of Paxlovid, which has emerged as the favored oral antiviral based on its safety and efficacy. The timing of the Omicron surge has been variable in different parts of the country, and Tennessee and Colorado report 3.1% and 1.4% of all cases on the national level respectively but have only 0.8% and 0.5% of all therapeutic courses.

The majority of Covid-19 cases are mild in vaccinated, in particular boosted people, but there are still hospitalizations and even intensive care admissions, says epidemiology professor Dr Luis Ostrosky, which has been overwhelming the hospital system. “It has been challenging to meet the demand, “says Ostrosky who practices at the University of Texas Health Sciences Center at Houston.

As per AmerisourceBergen, the company contracted to distribute Covid-19 therapeutics, the HHS determines weekly distribution amounts based on new Covid-19 cases and hospitalizations in each state or territory, and inventory and usage data.

However, the rapidly evolving Covid-19 burden means that some states are running through the supply faster than others. As per the latest data, Florida has only 80 available courses of either molnupiravir or Paxlovid for every 100,000 people. In comparison, Louisiana and Wisconsin – states with similar Covid-19 case levels to Florida – both have in excess of 200 available course per 100,000 people.

In practice, getting access to the antivirals requires providers or their offices to call around to different pharmacies so people can eventually get it. “It is challenging for pharmacists who are receiving phone calls asking if they have the therapies and on patients,” says Ganio.

At the other end of the spectrum, Illinois and Mayland’s shares of all available courses (5.1% and 2.2%) far exceed their share of new Covid-19 cases (2.7% and 0.5%). Maryland, where cases levels started to decline earlier than in most other states, currently appears to be one of the states with the most plentiful stock of allocated courses, with just 1.4 Covid-19 cases for each available antiviral course. Maine stands out as one of the few states not to experience a dramatic increase in case rates during the recent Omicron surge, and yet it too has high stocks of available courses – currently 3 for every new case. Both Tennessee and North Dakota have over 20 new Covid-19 cases for each available antiviral course.

“My understanding of this system is that they do take into account sort of the size of the population and the sort of caseload that they did experiencing,” says Ostrosky. While the supply has been limited, he said access to the medications have been accessible in Texas. But he adds, colleagues in other parts of the country that have had a high case burden, had had a different experience in prescription and availability of drugs.

**Omicron impact**

The Delta surge from earlier in 2021 affected the distribution system by leaving a lasting impact. “The Delta variant meant severe disease but had lower transmissibility, so the demand for monoclonal antibodies was much lower than what we've seen recently,” says Moore. In early 2021, the government had stopped distribution and allocation, and through open access individual pharmacies could order the treatments, says Ganio. But, in order to maintain an equitable distribution, not just in terms of location and patient populations but also to ensure that there are enough supplies over time, the government took over the system again and this has continued over the most recent surge as well, he explains. “It was the right move was to place the oral antivirals in retail pharmacies which are very widely distributed in both urban and suburban areas,” says Ostrosky. But the rate limiting factor is actual number of courses each pharmacy is getting.

Having an oral therapeutic for me was a game changer. Because it would pretty much assure me that somebody who's at high risk of going through this complicated pathway, who would have a 90% chance of not going down that route.”

Omicron changed the supply dynamics significantly, because of its infectivity rate. Also, once it rendered other authorized mAbs by Eli Lilly and Regeneron ineffective, that reduced the number of effective treatments. “When there was a reliable supply of the mAbs by Eli Lilly or Regeneron, there were no issues in getting it for patients, but now supply [of effective antivirals] is the rate-limiting factor,” says Ostrosky.

Details on [sotrovimab](https://www.pharmaceutical-technology.com/news/gsk-vir-sotrovimab-eua/), the only mAb treatment that is [effective against Omicron](https://www.pharmaceutical-technology.com/special-focus/covid-19/covid-19-gsk-sotrovimab-activity-omicron-variant/), currently the most dominant variant in most parts of the world, are not included in the therapeutic locator. A separate database maintained by the HHS that is updated weekly does include information on sotrovimab. A GSK spokesperson said the company did not have any information to provide on sotrovimab’s supply since the HHS was controlling the allocation and distribution. The HHS did not respond to a request for additional comment.

The therapeutic locator also includes information on Evusheld, AstraZeneca’s long-acting monoclonal antibody combination that is FDA authorized as a pre-exposure prophylactic. However, this mAb combination is specifically meant to prevent Covid-19 in individuals who are not currently infected or exposed to the virus.

Still, while limited, sotrovimab’s supply appears to be equitable in places like Florida. The state, which is home to approximately 7% of Americans, has received 6% of total doses of sotrovimab. However, there are not enough doses of sotrovimab to make up for Florida’s low allocation of the other antivirals – nationally, distributed doses of molnupiravir and Paxlovid have outnumbered sotrovimab doses three-to-one in recent weeks."

Several weeks ago, Moore says his hospital saw the highest number of patients its ever seen, even before the availability of vaccines, but there has been a downward trend since. “But the point of these drugs is to keep people out of the hospital, so the high demand will not be going to go away anytime soon, especially with the Omicron variant’s transmissibility,” he adds. “We have such a high demand that we're not able to supply them… and it’s frustrating for patients. It's frustrating for a clinician”.

“It is important to ramp up production and increase distribution, because while Omicron is peaking in some places, it is barely starting in others,” Ostrosky says. “Even if a place hits the peak in infections, it will take four to six weeks to go down to pre-Omicron levels, so we're going to be in the situation of a high caseload in the US for at least the next 2-3 months”.