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COVID-19 Monoclonal Antibodies: Paying for Administration and Better Evidence

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This Duke-Margolis resource on COVID-19 response policies is intended to inform and help guide policy makers addressing the evolving COVID-19 pandemic in the United States and around the globe, and will be updated as the pandemic and response capabilities change over time.

It contains recommendations for a U.S. Federal response as well as steps and resources for stakeholders across the health care ecosystem. We will add further resources to address a range of related, critical policy challenges.

We thank our many collaborators, co-authors, and reviewers who have contributed significant expertise and guidance on these rapidly evolving issues. Please reach out to us with additional suggestions for resources and effective policies at dukemargolis@duke.edu - we welcome your input.

Executive Summary

The ongoing pandemic continues to result in thousands of daily hospitalizations and deaths in high-risk COVID-19 infected patients, and has been placed immense strain on the health system and its providers. Monoclonal antibodies (mAbs) for COVID-19 present an opportunity to change that impact in the near term, before vaccines are widely available. To increase access to these novel therapies, payment strategies must take into account the need for substantial modifications to the care of high-risk patients, and the associated administration costs for infusions – especially within home settings, long-term care facilities, and other temporary infusion sites that may be needed to provide access to certain patients.

In this report, we address the key payment issues for antibody administration, including the adequacy of emerging reimbursement mechanisms and potential payment models that could enhance access for patients. We also present recommendations focused on how next steps might augment the limited evidence available on monoclonal antibodies, improve patient care, and support new data collection. These include:

- Adjust payment to providers to better reflect costs associated with safe infusion in the appropriate setting for all high-risk COVID-19 patients, to support effective access to antibody treatment
- Implement CMS, HHS, and state collaboration to track access to COVID-19 treatments and identify gaps

- Consider Federal funding of deployable antibody administration capacity to hotspots and underserved areas
- Adjust COVID-19 payment rates for diagnostic tests based on return time, and increase payments for timely referral for antibody treatment by CMS and private payers
- Ensure that public and private reimbursements support a limited core data platform or registry for high-risk COVID-19 patients, to support evidence development on how to best allocate and use antibodies

Further steps on effective payment for antibodies can create a smoother path through the pandemic in the months ahead.

Introduction

The recent two Emergency Use Authorizations (EUAs) by the Food and Drug Administration (FDA) of man-made monoclonal antibodies (mAb) to the novel coronavirus (SARS-CoV2) provides a potentially valuable treatment for high-risk infected patients early in the course of illness. The EUAs apply to those 65 or over, obese, and/or with a serious chronic condition. In summarizing the available clinical trial evidence to support the EUAs, the FDA cited evidence of approximately two-thirds reduction in risk of emergency room visit or hospitalization, when the antibody treatment is given early in the course of COVID-19 – before significant breathing problems or hospitalization occur. Until vaccination is widespread, antibodies could have a substantial impact on reducing the severity of COVID-19 and alleviating the stress on the US health care system.

The Federal government has acquired supplies of both Lilly and Regeneron's antibodies and expects increased production for both products. In November, it committed to pay Lilly $375 million to provide 300,000 doses of bamlanivimab over the first two months following the EUA, and in early December it announced that it bought an additional 650,000 doses for about $803 million to be delivered through the end of January 2021. The government has also acquired the initial production of approximately 300,000 doses of Regeneron's combination casirivimab and imdevimab treatment in a $450 million contract with nearly 80,000 doses available immediately upon authorization in late November and the remainder available by the end of January. In partnership with Roche, Regeneron expects at least 2 million doses per year in 2021 and beyond. Thus, over 1.2 million doses would be available by the end of January, with the supply rising in 2021. Even if demand exceeds supply, the effective use of these therapies could have a material impact on near-term hospital surges, potentially avoiding tens of thousands of hospitalizations.

The government is allocating available antibody treatments to the states using a formula based on relative hospitalizations and case burden. States then allocate these treatments to health care providers, using a Federally-supported distribution system that can provide rapid availability at no cost to providers or patients.

There are multiple obstacles to antibodies achieving their potential impact on the COVID-19 pandemic. The limited supply relative to caseloads means that there currently are not sufficient antibodies available to all patients who may benefit. Due to the substantial lead time and

specialized facilities required to manufacture the antibodies, it is difficult to increase supply in the near term. In addition, payment for treating patients with antibodies must be adequate to compensate providers for a substantial modification to the care of high-risk COVID-19 patients. Effective use of antibodies requires professional and administration services such as timely referral of appropriate patients for infusion with protections appropriate for treating actively infected patients, as well as patient assessment prior to infusion, and monitoring during and afterwards for allergic reactions or other adverse events (approximately at least three hours of nursing services to prepare, administer, and observe). Effective use of antibodies also requires pharmacist related clinical services and infusion administration supplies, as well as anaphylactic emergency kits. Consequently, special reimbursement challenges must be addressed for antibody administration to ensure adequate and equitable availability.

Finally, the drugs are coming to market with considerable uncertainty about their effects. Consequently, post-market data collection and analysis will be paramount to support provider and payer confidence. While antibodies appear to have promising overall benefits in initial clinical trials that were the basis for their emergency use authorizations, more evidence is needed on which patients benefit most so they can be targeted effectively, and to support continued reimbursement as an effective COVID-19 treatment.

In this report, we address the key payment issues for Medicare, Medicaid, and commercial payers for antibody administration, including the adequacy of emerging reimbursement rates (as well as specific considerations for various administration sites), as well as potential payment models that could enhance access for patients who will most benefit and improve the evidence available to guide effective treatment administration.

Implications of Monoclonal Antibodies for COVID-19 Care and Payment

The new antibody treatments require changing the care model for high-risk COVID-19 patients, who had previously been advised to isolate at home (or placed in isolation if they are nursing home residents) until and unless they develop serious symptoms. The new care model should enable the delivery of antibody infusion treatment within just a few days after symptoms develop to appropriate patients – which in turn requires new supporting payments.

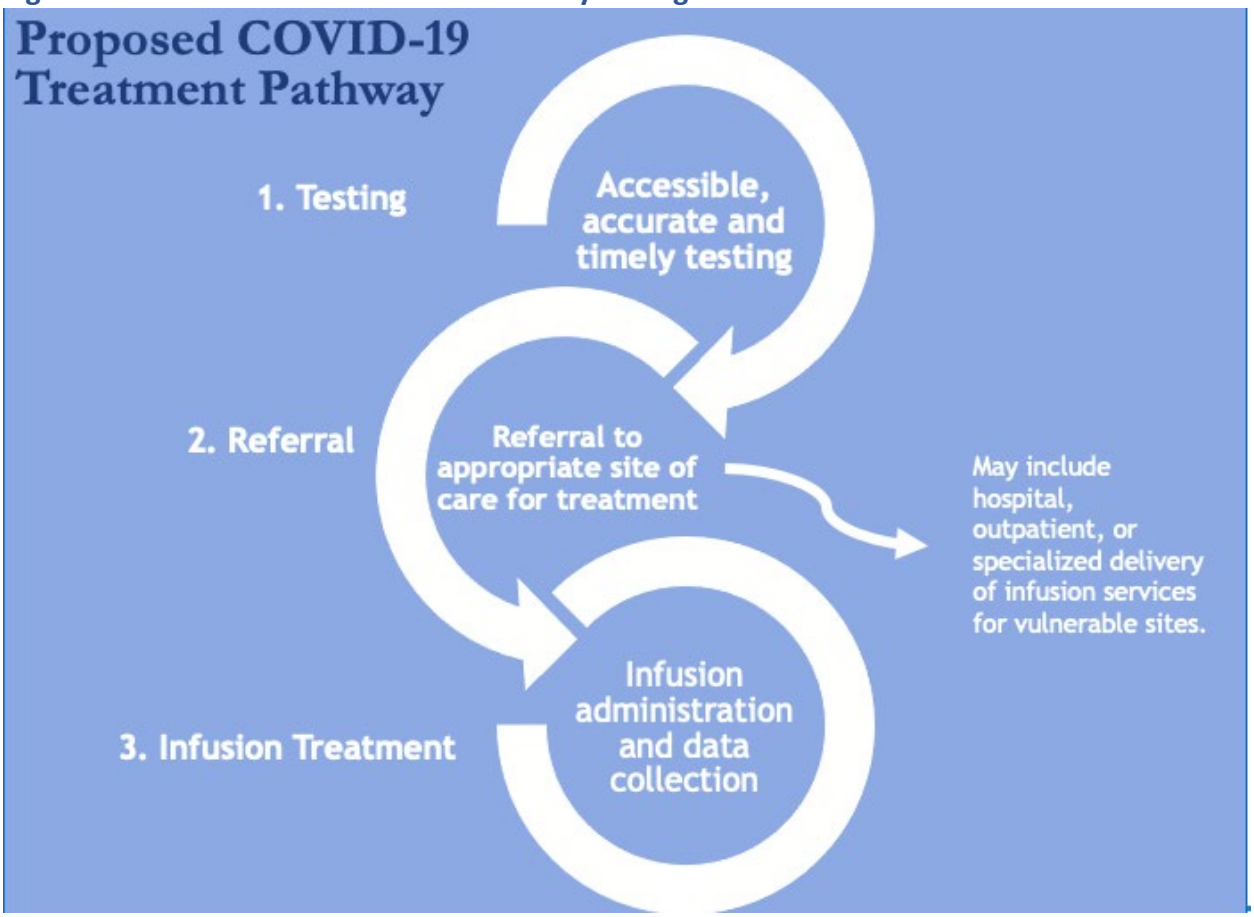
The needed care reforms are summarized in Figure 1, including:

- Accessible, accurate and timely diagnosis soon after symptoms develop
- Risk stratification with timely referral to COVID-19 treatment for appropriate patients
- Antibody infusion and monitoring, preferably with collection of key data to help improve antibody use

Many patients could be treated effectively at a specialized COVID-19 infusion clinic, located within a heath care organization or in the community, like existing outpatient or standalone infusion clinics for non-COVID patients. The repurposing and development of such infusion sites has associated costs. COVID-19 patients cannot be introduced to settings with other seriously ill

patients, such as those receiving cancer or immunotherapy treatments. A repurposed COVID-19 infusion center would have to shift existing patients to other sites, which may disrupt their care especially if there is not sufficient capacity to absorb these patients in other sites. Such a change may not be financially attractive to infusion site operators, especially if they might lose established non-COVID patients. Alternatively, if additional space is available, a new facility could be set up. But this may require additional skilled nursing staff, in short supply now, as well as additional personal protective equipment (PPE) and other isolation precautions.

Figure 1. New COVID-19 Treatment Pathway for High-Risk COVID-19 Patients



Even with such sites available, frail patients including those in nursing facilities still face access challenges, in addition to requiring costly assistance like ambulance transportation. Other patients, particularly those in rural or underserved areas, may not reside near enough to an infusion center. Home infusion services, or infusion sites set up in nursing homes, clinics, or mobile facilities, could improve access for these patients. Such services may be costlier per unit than outpatient or ambulatory infusion centers – due to fewer economies of scale and transportation time and expenses, medication delivery, and setup costs, and the potential cost of assuring medical support and supplies in the event of a serious allergic reaction or other complication. Providers may need higher reimbursement, to account for the costs associated with patient evaluation and setup, an hour for infusion, plus post-infusion monitoring with

medically-trained oversight. These services may nonetheless be critical for more equitable access and for maximizing the benefits of antibodies in preventing costly COVID-19 complications.

Finally, while predictive models of risk of COVID-19 complications are improving, evidence remains limited on many questions related to effective antibody use, such as whether certain subgroups of high-risk patients are more likely to benefit from antibody treatment, whether lower doses could be effective in some patients, whether patients with mild early symptoms can be monitored initially without increasing risk of progression, and the most effective care models for different kinds of patients. Development of better evidence on antibody treatment will benefit from additional clinical data collection. An incremental payment could support such data collection by providers.

Initial Payment Policies for COVID-19 Monoclonal Antibody Infusions

CMS recently released an Interim Final Rule with Request for Comments (IFC) and a Medicare COVID-19 Monoclonal Antibody program instruction, intended to reflect the significant costs related to effective antibody infusion services. In the program instruction, CMS stated that antibody infusion would be covered using its reimbursement authority for COVID-19 vaccine administration, that is directly through the Medicare Administrative Contractors (MAC), with the reimbursement rate applicable to all infusion sites based on the reimbursement rate for complex infusion and monitoring in the hospital outpatient setting. The corresponding reimbursement amount is $309.60. Like COVID-19 vaccines, no Medicare copayments will be imposed on Fee-for-Service (FFS) and Medicare Advantage beneficiaries for antibody administration while under the EUA.

However, it remains unclear if this policy will continue after the antibodies get FDA approval. If so, pilots or single provider models for the Medicare population as a whole could be an efficient way to manage treatment allocation, workforce challenges, and system pressures while helping to centralize data on outcomes. CMS could also structure these payments as a fixed-rate contract based off of an FFS rate and an administration fee and have the MAC perform against it as a value-based contract.

The CMS payment approach uses public health emergency authorities. However, there are outstanding issues that will need to be addressed if and when the Federal government moves away from controlled purchasing and distribution. During the public health emergency (PHE), antibody payments are reimbursed separately from all other services bundled into outpatient payment groups or nursing home per diem payments. After the PHE, this process may change.

Private insurers are generally following Medicare's approach basing payment on complex outpatient infusion with no copays. Some are using the Medicare rate. Many are using higher rates based on contract terms that use a multiple of the Medicare rate, which on average may mean about twice the Medicare rate, or approximately $700 or slightly higher. Commercial payers also generally intend to adopt the CMS base approach for coding.

Medicaid coverage without copayments was also required by CMS during the PHE, based on the CARES Act Maintenance of Effort requirements for states to receive enhanced Federal Medicaid funding. Coverage for uninsured patients is also required under the current treatment and testing fund being administered by the Health Services Resource Administration (HRSA). Beyond these requirements, CMS has provided limited guidance on reimbursement rates for Medicaid providers. Treatments authorized through emergency use are ineligible for Federal rebates under the Medicaid Drug Rebate Program, with potential implications for states.

While experience is limited, early steps by hospitals and infusion centers to set up COVID-19 infusion programs suggests that the $309.60 Medicare infusion rate and corresponding private insurance rates may be adequate for supporting infusion programs in these settings. However, such a reimbursement level may not be sufficient to result in substantial access in nursing homes and other patients who cannot easily get access to infusion centers. Moreover, uncertainty about antibody availability may also reduce provider willingness to invest in alternatives to infusion center access.

On December 2, the Department of Health and Human Services announced a contract with Coram, the CVS home infusion service, to pilot a program to infuse antibodies at home and in residential settings like nursing homes in seven metropolitan areas. This bundled contract for a specified capacity of infusion services – initially specified as 1,000 treatments through March – addresses the distinct payment challenges for home and on-site infusion. However, the scale of the pilot project is too small to have a substantial impact on access and outcomes.

Other early initiatives to provide home or nursing home infusion include delivery platforms such as Option Care Health, which provides home infusion of other monoclonal antibodies in coordination with a patients' care team and payers, and initiatives of some states, including Indiana in partnership with Eli Lilly, to create infusion sites with a relatively limited capacity of approximately 100 infusions per day. In addition, on December 4, 2020, Eli Lilly and United Healthcare Group (UHG) announced a partnership to conduct a pragmatic study of bamlanivimab for UHG's Medicare Advantage enrollees. The study, which will enroll up to 500,000 people, with at least 5,000 people expected to receive bamlanivimab, will include delivery through home infusions. Private payers have not yet set up such contracts, which may require higher payment rates to support greater home and on-site access.

Depending on early experience with antibody infusion availability, use, and costs, and rather than changing the home infusion payment rate, additional payments that reflect the increased cost of PPE and the costs associated with administering the therapies in different geographies may be needed for patients with inadequate access to infusion centers. Alternative regional contracts like the CVS pilot could also be helpful. Table 1 summarizes the care and evidence considerations that may require further payment refinements for each potential administration site.

Table 1. Payment and Implementation Considerations for COVID-19 Treatment and Infusion across Different Sites of Care

Site of Care	Implementation Considerations	Payment Rate Considerations*
Hospital outpatient and standalone infusion centers	• Health care organizations will likely have to hire or repurpose existing staff to provide additional infusion capacity; and may face challenges with meeting the safety needs of non-COVID patients. • Large infusion systems and hospital systems may be well suited to participate in data collection and sharing, as well as registries; many systems are doing so already.	• Unlike chemotherapy drugs, these antibodies are one-time infusions and the drugs are provided at no costs. • Given the potential number of volume of patients requiring counseling services in outpatient settings, current Medicare E/M rates may not be entirely sufficient to effectively coordinate care. • Current Medicare reimbursement may not reflect all efforts associated with safe and effective infusion delivery, such as hiring staff or purchasing PPE; developing new infusion centers; and providing infusion services for both COVID and non-COVID patients. • Workforce eligible to administer antibodies will also be in high demand for vaccine administration, leading to additional burden
Home Infusion, Temporary Standing Infusion Sites and Administration in Long-term Care Facilities	• In existing home-infusion models, a home infusion company obtains orders from the physician; acquires, prepares, and delivers the drug to the home; and arranges skilled staff to administer the drug and monitor for adverse events. • May provide less costly, safer access for patients who might face complications, delays, or high costs from transport to an outpatient infusion center. • May be a strategy to provide infusions to rural and other underserved locations. • Will require specialized nurses and transportation of equipment and personnel to the site of care. • Could potentially be done in partnership with a health system, home infusion providers/specialty pharmacy, or community infusion centers. • Would need to have sufficient medical backup to manage allergic reactions or other serious complications.	• Current Medicare reimbursement may not reflect all efforts associated with safe and effective infusion delivery, such as hiring staff, and transportation costs for staff and medication, especially since economies of scale may be limited. • This model is primarily used for other monoclonal antibodies by commercial and Medicare Advantage insurance plans, because of greater payment flexibility compared to traditional Medicare. *Medicare's $309.60 rate is equal to existing outpatient reimbursement rates of more complex chemotherapy drugs. Private insurers will likely follow Medicare's approach, using the Medicare rate or a multiple of the Medicare rate, approximately $700 or slightly higher.

Refining Payment Policies to Support Effective Treatment for High-Risk COVID-19 Patients

Adequate payment for infusion is only part of an effective model of care for high-risk COVID-19 patients. Further payment reforms could support more rapid and substantial adoption of more effective care models. Especially as antibody supply increases, such policies could substantially improve outcomes and reduce the hospitalization burden for COVID-19. Effective therapy for

high-risk patients now starts "upstream": timely testing, results reporting, and appropriate referral to infusion can substantially impact patient outcomes. CMS has established a range of billing codes for services in FFS Medicare (see Table 2) that precede antibody infusion and influence upstream care.

To encourage timely testing and results reporting, as of January 1, CMS will adjust payments for diagnostic testing based on use of high-throughput tests and reporting times. CMS and private payers should consider enhancing such incentives. Second, CMS provides a counseling and management payment to clinicians who conduct testing. The payment reflects the effort required to counsel the patient about isolation and contact tracing if results are positive; it does not necessarily account for the effort required for assessment for antibody infusion and timely referral. CMS should consider an adjustment, potentially linked to antibody use, if gaps or inequities in timely referral emerge in the early experience of antibody use.

Table 2. Billing Codes Created by CMS for Medicare

Types of Testing Billing Codes	Referral and Counselling Services	Treatment
• Administration of a COVID-19 diagnostic test • Collection of testing samples • Narrow range of testing-related services (e.g. some select imaging of patient lungs and chest) • The diagnostic technology itself • As of 1/1, CMS will adjust payment amount based on whether a high-throughput platform is used and based on a measure of usual time to return for a test.	• Education and management counselling for COVID-19 diagnosis (approximately $30-$50 depending on the patient and modality of counselling).	• Administration and post-administration monitoring ($309.60) • Technology [reimbursed to providers at 95% of the average wholesale price (AWP) when the product is no longer provided for free]

Especially for patients receiving services from integrated providers or accountable care organizations, fragmentation of payment for each individual COVID-19 service may not provide enough flexibility to encourage the most efficient, coordinated care models for antibody use. Instead, providers could receive one bundled case rate payment for their "upstream" COVID-19 services, such as testing, testing services and diagnosis and referral, and another bundled case rate payment for infusion and infusion services performed by providers that would be available across a range of sites of care, building on the CMS infusion payment model but potentially including adjustments for patient mix, such as a greater share of complex patients who need access at sites other than infusion centers.

Further, building on the CMS regional pilot for home and on-site antibody infusion, payers and providers could partner to commit to using a certain supply of antibody infusion capacity at the regional level. Such a population-level payment, linked to upstream payments that support effective testing and referral, would encourage a greater level of coordination and planning to

enable more effective care for high-risk COVID-19 patients, with a limited but predictable and increasing supply of antibodies. States could encourage such efforts by committing to advance allocations of expected antibody supplies.

In addition, CMS and private payers should consider a small incremental payment on top of base reimbursement rates for providers who collect key data or participate in practical clinical studies needed to improve models for predicting benefit from antibody use and to inform better care models for referral and infusion. Payers can also support these efforts by requiring product-specific reporting for payment. In its antibody reimbursement instruction, CMS created specific billing codes for the Lilly antibody as well as its infusion and post-administration monitoring, providing data on which antibody product is used. Providers will only bill for administration using the product-specific code during the period when it is distributed to health care providers from the government advance purchase; the specific billing code for the product would be used when it is no longer supplied for free. Continuing to assign antibody-specific codes, for the Regeneron antibody combination as well as each product authorized in the future, will help ensure appropriate antibody tracking.

Next Steps

There are several short-term principles and recommendations that should inform next steps to augment the limited evidence available on monoclonal antibodies, improve patient care, and support new data collection. These include:

- **Payment to antibody infusion providers needs to be adequate to build new capacity in the short-term quickly.** Payment to providers should adjust to better reflect all costs associated with infusion delivery, especially when administered in non-conventional infusion sites, to support effective access to antibody treatment for all high-risk COVID-19 patients**.** As CMS and other payers continue to monitor utilization and access based on Medicare's payment rates, it will be critical to monitor utilization at the potential alternative sites of care for identified in Table 1 for payment challenges.
- **Federal and state partners should monitor access to treatments**. CMS should collaborate with states and HHS to track access to COVID-19 treatments and identify gaps. Tracking state distribution and claims data from multiple sources can start to identify areas where access to COVID-19 treatments lags. CMS, HHS and states, to the extent possible, should also determine closely monitor the data of certain patient groups, such as those in nursing homes or LTC facilities, rural settings, dually-eligible beneficiaries, and patients from historically marginalized populations.
- **The Federal government should consider expanding direct support for infusion capacity high-risk patients with inadequate access.** The Federal government should consider funding deployable antibody administration capacity to hotspots and underserved areas. Funding should be used to either fill gaps in personnel or operational capacity where high-risk patients cannot easily be treated at available COVID-19 antibody infusion facilities. This quickly deployable funding would be an extension of the small HHS pilot for home- and site-based infusion capacity, and could reflect insights from similar approaches used

by the Federal government to support "surge" community testing facilities and vaccination services for nursing homes.

- **CMS and private payments should encourage faster testing and referral for antibody treatment.** CMS and private payers should consider whether there should be further adjusting of payment rates for test return time. CMS should also adjust the description of reimbursable test counseling services to include referral for antibody testing and counselling to receive further care, and consider adjustments in counseling payments to support referrals.
- **Evidence on high-risk patients should be developed and available to all stakeholders.** Public and private reimbursement should support a limited core data platform or registry for high-risk COVID-19 patients, to improve evidence on how to best allocate and use antibodies. Some health systems, such as Providence Health, Mayo Clinic, Intermountain and HCA have developed early COVID-19 registry systems and incorporated key data on dosing and patient characteristics. Such existing registries could potentially be adapted to support evidence generation on effective antibody use. The additional data collection costs should be modest, to limit burden on providers.

Payment strategies for antibody treatments will likely need to evolve based on early experience with access and use. This will help providers build more effective care pathways, avoid inequities in access and outcomes, and reduce the burden of surging COVID-19 cases. With effective payment strategies, antibody treatments can be an important bridge to greater use of vaccinations in high-risk patients, and become a key element of preventing further health impacts and disruptions from COVID-19.