Ethical Framework for the Allocation of Therapeutic Drugs for Covid-19 in Wisconsin

Background

The COVID-19 pandemic has revealed the importance of developing and implementing protocols for the distribution of scarce therapeutics in possession of the state. This framework has been developed by a therapeutics allocation sub-committee of the Wisconsin State Disaster Medical Advisory Committee (SDMAC), and is based upon a foundational ethical framework already developed and adopted by the SDMAC. The Therapeutics Allocation Subcommittee consists of physicians trained in critical care, infectious disease, pediatrics, and internal medicine; hospital pharmacists, and experts in allocation frameworks and ethics.

The intention of this framework is to serve as a guide for the Department of Health Services (DHS) to readily allocate and distribute available drugs, avoiding unnecessary delays in treatment.

The design of this framework is based upon the following assumptions:

- Novel therapeutics released under an Emergency Use Authorization (EUA) may not be sufficiently researched to know with certainty which patients are most likely to benefit.
- Therapeutics may be received in quantities that are unpredictable. This may result in situations of temporary scarcity.
- No single framework will address the detailed allocation requirements of every possible therapeutic drug. A standing sub-committee of content experts from the SDMAC will meet whenever a new drug is released to apply specifics of the drug to this framework for final recommendations.

Potential Approaches for DHS distribution of the rapeutics in possession of the state.

- 1. *Distribution by geography*: Therapeutics in possession of the state could be distributed on a geographic basis (e.g., county, region) based upon size of population, burden of disease, and/or by weighting for baseline health disparities. The geographic unit of distribution may be a county (smallest) or region (largest), with subsequent distribution decisions made by receiving party.
 - a. *Example*: Please see the "Ethical Allocation Framework for Bamlanivimab Treatment of Covid-19 in Wisconsin." This drug was allocated to counties based on disease burden, with weighting for baseline health disparities.
- 2. *Targeted Geographical "Hot Spot" Approach*: Therapeutics could be directed to geographic areas of the state that are most in need of relief, due to disease burden or health care system strain. This maximizes the utility of a therapeutic drug as a public health tool, but would require strong evidence of effectiveness in the target population, which is often lacking in the EUA environment. It has the potential to be ethically complex, as some communities become "hot spots" for reasons beyond their control, and others due to intentional lack of enforcement of

mitigation strategies. The principle of equity, as outlined in the SDMAC Ethical Framework, requires a focus on objective data and the consideration that some communities may be disadvantaged in a way that makes compliance with public health recommendations more difficult. In addition, there may be sub-communities within each community that are not considered when the geographical area is labeled as a "hot spot."

- 3. Centralized Geographical Distribution Hub: Therapeutics in possession of the state could be allotted to a central distribution hub in each region of the state (i.e. county or group of counties served by a major healthcare system). Each hospital or health system can implement a weighted lottery or other allocation scheme based upon the availability and demand for the drug, and notify the hub when a medication dose is required. The drug would then be transferred from the hub to the healthcare provider. This scheme allows for a more equitable distribution of scarce medications via micro-allocation on the patient-level. Difficulties include the need for appropriate lead-time, considerations about drug transport and other logistical concerns related to not having drugs on-site, and concerns about the uniformity and execution of lottery systems at a multitude of sites. The state may have to set forth a lottery system for use by all health systems/providers in this scenario.
- 4. *Distribution by facility*: Therapeutics could be distributed to healthcare facilities or systems, local public health departments, or outpatient clinics based upon disease burden in the community or within a particular institution.
- 5. Distribution to individual patients: Therapeutics could be distributed to individual patients via random allocation for those meeting clinical criteria for treatment as defined by FDA authorization. Alternatively, therapeutics could be distributed to a subset of patients that have been identified in published research as being most likely to benefit. Note: distribution to individual patients by DHS may be impractical for large quantities of medication or if complex clinical criteria must be considered. The other major difficulty with distribution to individual patients is meeting the needs of individuals who are not part of a health system. For example, those tested at a public testing site like Miller Park or Alliant would have to be contacted with a positive test result (which may take several days) and referred to a health system or provider in order to be screened for eligibility. Depending on the route of administration and mechanism of action of the drug, the logistic delays in reaching individuals not connected with a health system may be insurmountable.
- 6. *Step-wise/Tiered approach by patient risk factors/criteria:* Please see the "Guidelines for the Implementation of an Allocation Approach" portion of the Ventilator Allocation Committee Workgroup for an example. Depending on the current supply of therapeutic drug, criteria for patient eligibility would be tightened or relaxed. Once all patients within a "tier" are treated, patients in the next (less stringent) tier would be considered. If there is not enough medication to treat all patients within a tier, then random allocation methods (random or weighted lottery) can be used. This has been the approach already used by local health-systems in Wisconsin when supply is limited i.e. remdesivir prior to FDA approval.

Generic algorithm for the rapeutic distribution.

The following are branch points/questions to be asked as part of this algorithm. [Preston-I was thinking these are the types of branch points we can include in the flow diagrams, pending further discussions].

a. Eligibility Criteria (per FDA)

- i. Is this a drug for severe Covid-19 (hospitalized patients) or mild/moderate disease (outpatients)
- ii. Is this a preventive medication indicated for people not yet sick?
- iii. Is there a specific population targeted (i.e. where benefit is greatest based on existing data)?

b. Route of drug delivery

- i. Oral or IV (where can it be administered?)
- ii. Does it need preparation, or does it come ready to administer? Storage considerations?
- iii. Are there precautions with administration? (patient safety, nursing)

c. Status of Current Supply

- i. Level of scarcity
- ii. Anticipated additional supply
- iii. Current cost per dose

d. Distribution Requirements from Federal or State Government

- i. Who/where is the allocation being directed to? (i.e. health systems already administering remdesivir prioritized by ASPR for bamlanivimab)
- ii. Does the drug already exist in circulation, such that we can use current supply? (i.e. using existing therapy off label)

e. Ethical Considerations

- i. Will all those who are eligible to benefit from this drug have a chance at receiving it (even if part of a lottery system?)
 - 1. What about patients not connected to a health system?
 - 2. Patients in long-term care or nursing homes?
 - 3. People in prison?
- ii. What are the barriers to preventing all eligible individuals from having equal chance of receiving the drug?
- iii. Should someone's chance of receiving the drug be weighted depending on their anticipated barriers/social determinants of health?

f. Allocation Framework Determination: After the above questions have been considered, a general allocation framework of one (or more) of the types described above may be relevant.

Incorporating the SDMAC ethical framework into the allocation of the rapeutic drugs.

Institutions who receive a supply of therapeutics, are encouraged to develop a process of allocation to individual patients based on ethical principles.

This document outlines some initial frameworks for the allocation of therapeutics to hospitals and health systems, but these systems must develop their own treatment protocols for individual patients consistent with the ethical principles outlined in the accompanying "Ethical Principles" document.

In general, treating clinicians should not be responsible for operationalizing the allocation framework. This should be led, instead, by crisis triage officers or clinic leaders. The principle of "fairness," as outlined in the Ethics Subcommittee Ethical Framework to Guide the Allocation of COVID-19 Therapeutics and Vaccines requires that healthcare resources be allocated using criteria based **only on relevant characteristics**, using impartial procedures for allocation and distribution. This means that the team making allocation decisions should be blinded to information that is not relevant. As stated in the Ethics Subcommittee document, the following considerations should not be used to unjustly disadvantage individuals in allocation decisions, in no particular order: age, race, color, disability, gender, immigration/citizenship status, incarceration status, national origin, religion, sexual orientation and gender identity, socioeconomic status and ability to pay. Methods that should generally be avoided include "first-come, first-served" or random lottery of all Covid-19 patients. These strategies do not preserve resources to maximize the common good and may exacerbate existing health disparities.

We recommend that ethics committee representation and crisis triage teams be involved in determining a process for allocation that is equitable, fair, and reasonable.

Topics for ethics committee and crisis triage teams to <u>consider</u> in the development of hospital/health system level allocation frameworks:

- Use of additional clinical criteria for treatment eligibility beyond those specified in the EUA, in order to maximize benefit, for example:
 - Prioritizing persons who have a higher number of qualifying comorbidities.
 - Prioritizing older adults in congregate/overcrowded living situations.
- Patient care responsibility for patients tested outside the hospital/health system
 - Health systems that participate in community testing supported by the state should include all those tested as possible recipients of allocation if they meet criteria
- Evaluation of a lottery system. After risk-based criteria and ethical principles are applied and there are still not enough resources for each person who meets the criteria, lotteries can be ethically appropriate strategies to use in decision making. In this way, lotteries allow for each eligible patient to have an equitable chance of receiving the drug. One approach is to randomly allocate among eligible patients. Another is to weight the lottery based on relevant factors in order to advance fairness and health equity.

For an example of a policy that aligns with the ethical allocation goals outlined in this document and makes use of a weighted lottery, please refer to **Appendix A**. This is

one example from the state of Pennsylvania, but there are many other possible methods that meet ethical goals stated here.

The following are member of the Therapeutics Allocation Sub-Committee of the SDMAC who provided valuable expertise for the creation of this framework:

Committee Members

Alyson Capp, PhD (co-chair) Director of Ethics Advocate Aurora Health

Sarah Sorum, PharmD (co-chair) Executive Vice President & CEO Pharmacy Society of Wisconsin

Dennis Brierton, Pharm D, BCPS, FASHP System Director, Clinical Pharmacy Advocate Aurora Health

Gina Dennik-Champion, MSN, RN, MSHA Executive Director Wisconsin Nursing Association

Helen Marks Dicks, JD State Issues Advocacy Director AARP Wisconsin

J. Paul Kelleher, PhD Associate Professor UW-Madison

Mohammad (Mo) Kharbat - MBA, BPharm, R.Ph., BCPS Regional VP of Pharmacy Services SSM Health

Elizabeth (Liz) Laubach, PharmD, BCPS Regional Director of Pharmacy Ascension Wisconsin

Steven R Leuthner, MD, MA Neonatal-Perinatal Medicine and Center for Bioethics MCW & Children's Wisconsin

Eric Marty, MD Director of Palliative Care Agrace

Sridevi Mohan, MPH, MA Epidemiologist Public Health Madison & Dane County

Carlo Nevicosi, APSW Deputy Director Walworth County Health & Human Services **Underlying Principles to Guide Equitable Vaccine and Therapeutics Allocation** Please refer to Ethics Subcommittee Ethical Framework to Guide the Allocation of COVID-19 Therapeutics and Vaccines for a review of underlying principles influencing this document.

Ethical Justification for Proactively Mitigating Health Disparities in Covid-19 Outcomes COVID-19 has had a disproportionate impact on low-income communities and certain racial/ ethnic minorities in the United States. Equity calls attention to the systematic differences in health outcomes and opportunities to be healthy that adversely affect socially discounted and/or marginalized groups. For Covid-19, these inequities may arise from higher burdens of pre-existing comorbid disease, poor health care access, or not having the option for social distancing due to living in densely-populated neighborhoods or households. There are also more economically disadvantaged individuals working essential jobs during the pandemic, and many are unable to perform job functions from the safety of their home. This puts them at greater risk of interacting with others who may transmit Covid-19. Public health interventions may be used to attempt to mitigate these disparities in Covid-19 by recognizing the structural inequities that underlie them. One way to do this is to account for a level of social vulnerability in the allocation guidelines used by the state to alleviate disease burden, such as novel therapeutics. The CDC's Social Vulnerability Index (SVI) is one measure that uses 15 US census variables (such as poverty and crowded housing) to measure a community's resilience to stressors, including disasters like the Covid-19 pandemic (https://www.atsdr.cdc.gov/placeandhealth/svi/at-a-glance svi.html). SVI has been used by other states, such as Pennsylvania, in their therapeutic allocation protocols. It is preferred over other measures like the Area Deprivation Index (ADI) due to its increased number of variables included. Considering SVI may increase the allocation of a scarce resource to areas most heavily impacted by both Covid-19 and structural inequities, recognizing that those inequities may independently increase the risk of poor outcomes from Covid-19.

Consideration of a Weighted Lottery

A weighted lottery can be used as a way to

• Should a weighted lottery occur at the state, regional, or site level?

- Can there be a standardized lottery determined by the state?
 - Provide a statement regarding clinical judgement and when to apply the lottery
 - Provide a list of factors to consider if the site is creating the lottery criteria
 - Ethical arguments may change with each drug
 - Could there be ethical parameters a site may be working under that are not congruent with the state's predetermined lottery?

Underlying Principles to Guide Equitable Vaccine and Therapeutics Allocation

Please refer to Ethics Subcommittee Ethical Framework to Guide the Allocation of COVID-19 Therapeutics and Vaccines for a review of underlying principles influencing this document.

Ethical Justification for Proactively Mitigating Health Disparities in Covid-19 Outcomes

COVID-19 has had a disproportionate impact on low income communities and certain racial/ ethnic minorities in the United States. Equity calls attention to the systematic differences in health outcomes and opportunities to be healthy that adversely affect socially discounted and/or marginalized groups. For Covid-19, these inequities may arise from higher burdens of preexisting comorbid disease, poor health care access, or not having the option for social distancing due to living in densely-populated neighborhoods or households. There are also more economically disadvantaged individuals working essential jobs during the pandemic, and many are unable to perform job functions from the safety of their home. This puts them at greater risk of interacting with others who may transmit Covid-19. Public health interventions may be used to attempt to mitigate these disparities in Covid-19 by recognizing the structural inequities that underlie them. One way to do this is to account for a level of social vulnerability in the allocation guidelines used by the state to alleviate disease burden, such as novel therapeutics. The CDC's Social Vulnerability Index (SVI) is one measure that uses 15 US census variables (such as poverty and crowded housing) to measure a community's resilience to stressors, including disasters like the Covid-19 pandemic (https://www.atsdr.cdc.gov/placeandhealth/svi/at-aglance svi.html). SVI has been used by other states, such as Pennsylvania, in their therapeutic allocation protocols. It is preferred over other measures like the Area Deprivation Index (ADI) due to its increased number of variables included. Considering SVI may increase the allocation of a scarce resource to areas most heavily impacted by both Covid-19 and structural inequities, recognizing that those inequities may independently increase the risk of poor outcomes from Covid-19.

The framework for the state allocation of bamlanivimab consists of three main steps:

1) Determine the proportion of doses allocated based on county level data.

Allocation is based on county Covid-19 burden (number of cases among individuals ≥ 65 years in past 7 days) AND county Social Vulnerability Index (SVI). Rather than allocate proportionally based on raw case counts across counties, the state will adjust each county's case

count to reflect the background social vulnerabilities of residents in each county. Counties are divided into four quartiles based upon SVI, and case counts are weighted appropriately by quartile.

- Case counts in the 1st quartile SVI counties (highest SVI counties, most disadvantaged) will be increased by 25% before determining their proportional allocation.
- Case counts in 2nd quartile SVI counties will be increased by 12.5%.
- Case counts in 3rd quartile SVI counties will be increased by 6.25%.
- Case counts in 4th quartile SVI counties will not be altered prior to determining proportional allocation.

2) Distribute bamlanivimab to hospitals/health systems based on total proportion calculated in step 1.

- For counties with only one hospital, the entire allocation will go to that hospital.
- For counties with more than one hospital, treatment courses will be allocated proportionally based on the average daily Covid-19 hospital admissions through the hospital's Emergency Department (ED) over the past 7-days.
- For counties without hospitals, the allocation will be made to a neighboring county where residents can receive the drug based on input from that county's public health officials.
- For health systems that serve multiple counties, they will receive the total number of treatment courses from all counties served.
- If a hospital opts out, the drug will be reallocated among other sites within that county according to methodology explained above.

Bamlanivimab will be distributed with the intent that it is to be used to serve local communities. To promote access, hospitals/health systems are allowed to move the drug between sites of care in order to maximize benefit to patients and best serve the common good by alleviating stress on health care resources.

3) Hospitals follow EUA eligibility criteria to develop a process of allocation to individual patients based on ethical principles.

The Wisconsin DHS has developed an initial framework for the allocation of bamlanivimab to hospitals and health systems, but these systems must develop their own treatment protocols for individual patients consistent with the ethical principles outlined in the accompanying "Principles" document.

In general, treating clinicians should not be responsible for operationalizing the allocation framework. This should be led, instead, by crisis triage officers or clinic leaders. The principle of "fairness," as outlined in the Ethics Subcommittee Ethical Framework to Guide the Allocation of COVID-19 Therapeutics and Vaccines requires that healthcare resources be allocated using criteria based **only on relevant characteristics**, using impartial procedures for allocation and distribution. This means that the team making allocation decisions should be blinded to information that is not relevant. As stated in the Ethics Subcommittee document, the following considerations should not be used to unjustly disadvantage individuals in allocation decisions, in

no particular order: age, race, color, disability, gender, immigration/citizenship status, incarceration status, national origin, religion, sexual orientation and gender identity, socioeconomic status and ability to pay. Methods that should generally be avoided include "first-come, first-served" or random lottery of all Covid-19 patients. These strategies do not preserve resources to maximize the common good and may exacerbate existing health disparities.

We recommend that ethics committee representation and crisis triage teams be involved in determining a process for allocation that is equitable, fair, and reasonable.

Topics for ethics committee and crisis triage teams to <u>consider</u> in the development of hospital/health system level allocation frameworks:

- Use of additional clinical criteria for treatment eligibility beyond those specified in the EUA, in order to maximize benefit, for example:
 - Prioritizing persons who have a higher number of qualifying comorbidities.
 - o Prioritizing older adults in congregate/overcrowded living situations.
- Patient care responsibility for patients tested outside the hospital/health system
 - Health systems that participate in community testing supported by the state should include all those tested as possible recipients of allocation if they meet criteria
- Evaluation of a lottery system. After risk-based criteria and ethical principles are applied and there are still not enough resources for each person who meets the criteria, lotteries can be ethically appropriate strategies to use in decision making. In this way, lotteries allow for each eligible patient to have an equitable chance of receiving the drug. One approach is to randomly allocate among eligible patients. Another is to weight the lottery based on relevant factors in order to advance fairness and health equity.

For an example of a policy that aligns with the ethical allocation goals outlined in this document and makes use of a weighted lottery, please refer to **Appendix A**. This is one example from the state of Pennsylvania, but there are many other possible methods that meet ethical goals stated here.

The following are member of the Therapeutics Allocation Sub-Committee of the SDMAC who provided valuable expertise for the creation of this framework:

Committee Members

Alyson Capp, PhD (co-chair) Director of Ethics Advocate Aurora Health

Sarah Sorum, PharmD (co-chair) Executive Vice President & CEO Pharmacy Society of Wisconsin

Dennis Brierton, Pharm D, BCPS, FASHP System Director, Clinical Pharmacy Advocate Aurora Health **Gina Dennik-Champion, MSN, RN, MSHA** Executive Director

Wisconsin Nursing Association

Helen Marks Dicks, JD

State Issues Advocacy Director AARP Wisconsin

J. Paul Kelleher, PhD

Associate Professor UW-Madison

Mohammad (Mo) Kharbat - MBA, BPharm, R.Ph., BCPS Regional VP of Pharmacy Services SSM Health

Elizabeth (Liz) Laubach, PharmD, BCPS Regional Director of Pharmacy

Ascension Wisconsin

Steven R Leuthner, MD, MA Neonatal-Perinatal Medicine and Center for Bioethics MCW & Children's Wisconsin

Eric Marty, MD Director of Palliative Care Agrace

Sridevi Mohan, MPH, MA Epidemiologist Public Health Madison & Dane County

Carlo Nevicosi, APSW Deputy Director Walworth County Health & Human Services

References

 News Release. Lilly announces agreement with U.S. government to supply 300,000 vials of investigational neutralizing antibody bamlanivimab (LY-CoV555) in an effort to fight COVID-19. October 28, 2020.