COVID-19 Clinical Management

Advancing the care pathway

World Health Organization

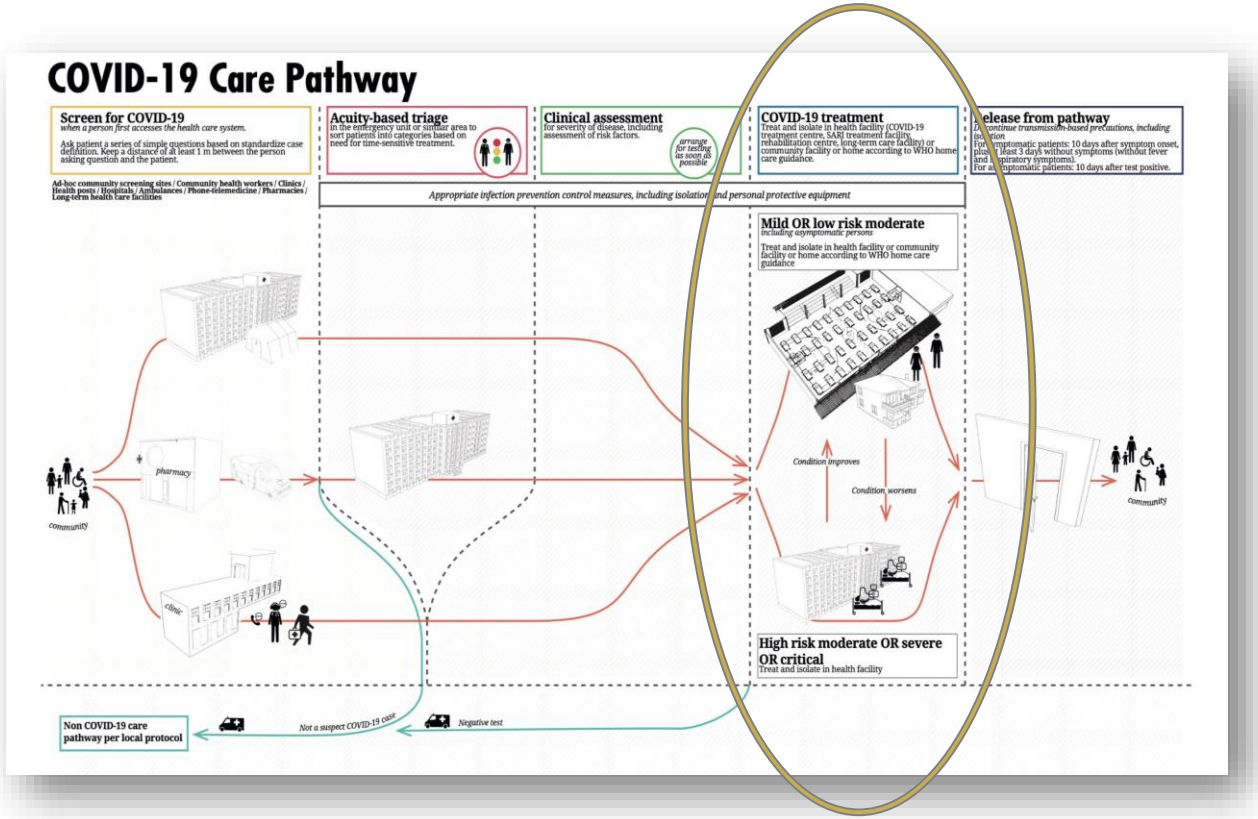
HEALTH EMERGENCIES programme

COVID-19 Care Pathway
Treatment and Intervention

Mild and Moderate Disease
Identification of patients with mild/moderate symptomology with presence of risk factors
Therapeutic Options: Oxygen monitoring (home) *and* Casirivimab and imdevimab

Severe Disease
Oxygen Support (low flow) and proning
Therapeutic Options:
Corticosteroids *and*
IL6 Receptor Blockers *and*
Casirivimab and imdevimab *(Seronegative)*

Critical Disease
Advanced Respiratory Support (CPAP, NIV, IMV) and proning
Treatment Options:
Corticosteroids *and*
IL6 Receptor Blockers *and*
Casirivimab and imdevimab *(Seronegative)*



Therapeutic Guideline Development

STEP 1 **WHO Therapeutic Steering Committee**
Scanning and prioritization

STEP 2 **Meta Analysis**

STEP 3 **Guideline Development Group Meetings**

STEP 4 **Recommendation Writing**
GRC, PRC, external review

STEP 5 **Publication**
Dissemination and development of tools

World Health Organization

Therapeutic Update: Publication date 24 September 2021
Casirivimab / Imdevimab – Neutralizing Monoclonal Antibodies

Therapeutics and COVID-19: living guideline - World Health Organization (WHO)

7. Recommendations for therapeutics

7.1 Casirivimab and imdevimab (neutralizing monoclonal antibodies)

For patients with non-severe COVID-19 (who do not meet criteria for severe or critical infection)

Conditional recommendation

New

We suggest treatment with casirivimab and imdevimab, conditional to those at highest risk of hospitalization.

- *Whereas casirivimab and imdevimab achieves a substantial reduction in the relative risk of hospitalization, the absolute benefit will be trivial or unimportant in absolute terms for all but those at highest risk for which the intervention should be reserved.*
- *The panel identified a risk beyond 10% of being hospitalized for COVID-19 to represent a threshold at which most people would want to be treated with casirivimab and imdevimab.*
- *In the absence of credible tools to predict risk for hospitalization in people infected with COVID-19, typical characteristics of people at highest risk include lack of vaccination, older people, or those with immunodeficiencies and/or chronic diseases (e.g. diabetes).*

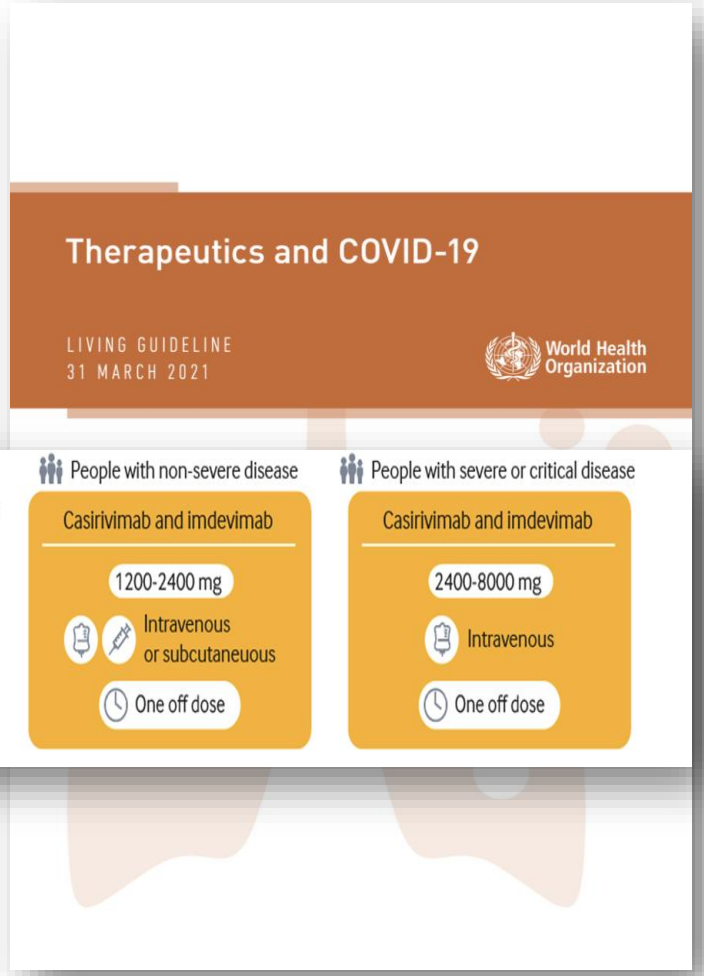
For patients with severe or critical COVID-19

Conditional recommendation

New

We suggest treatment with casirivimab and imdevimab, under the condition that the patient has seronegative status.

- *With benefits of casirivimab and imdevimab observed only in patients with seronegative status, clinicians will need to identify these patients by credible tests available at the point of care to appropriately apply this recommendation (see Evidence to Decision section).*
- *Treatment with casirivimab and imdevimab is in addition to the current standard of care, which includes corticosteroids and IL-6 receptor blockers.*



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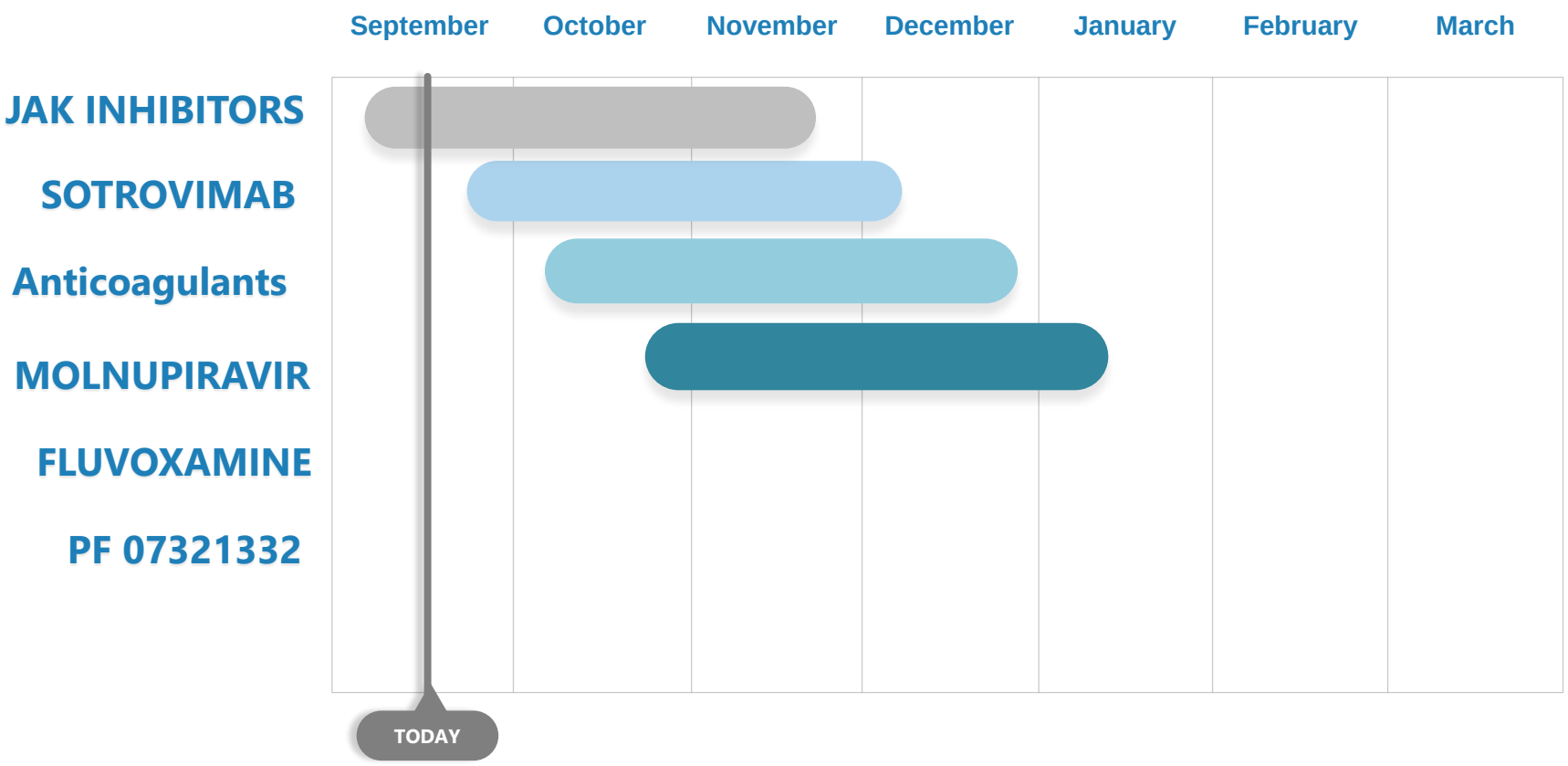
Current therapeutics under assessment (for all use cases)



Considerations:
For molecules to be considered by the *WHO Therapeutic Steering Committee* – there must be significant available data to be shared.

Timeline from initial data sharing to publishing of guideline is 8-10 weeks.

Critical Reflections

- ✓ Positive progress seen in **Oxygen scale up**
- ✓ **Effective therapeutics** recommended and in pipeline
- ✓ **Fast and reliable process** to synthesize evidence and publish therapeutic guidelines
- ✓ **Expanding dissemination** opportunities of living guidelines through MAGICapp, BMJ

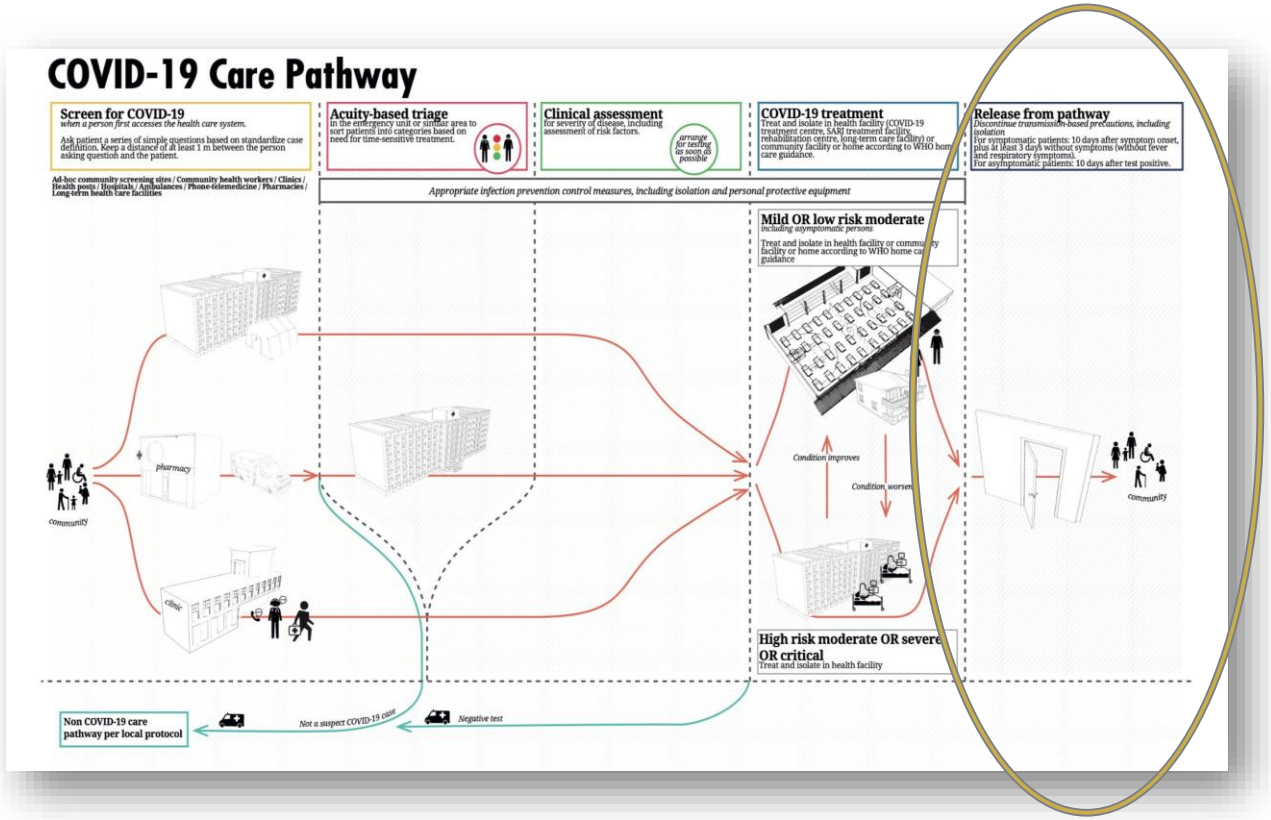
- Significant challenges remain with **equitable access** to COVID-19 therapeutics (e.g. IL6 Receptor Blockers)
- **Revised approach needed** with industry to seek better access, pricing and timeline to meet patient and clinical demand

Annex

COVID-19 Care Pathway

Discharge, Recovery and Post COVID-19 Condition Management

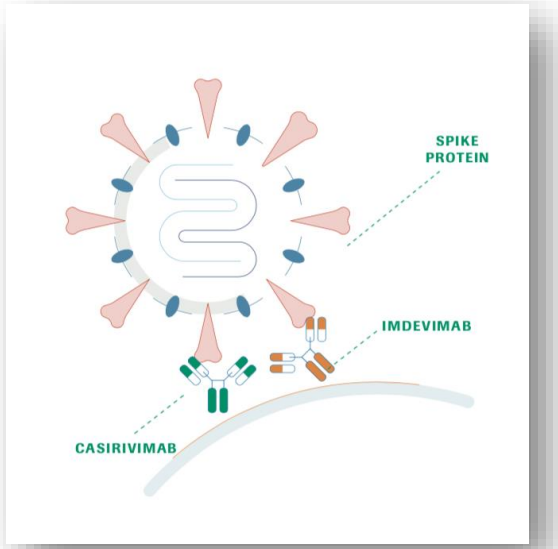
After care and Follow up



Casirivimab / Imdevimab - Neutralizing Monoclonal Antibodies

Mechanism of Action:
Casirivimab and imdevimab are a combination of 2 recombinant human antibodies (immunoglobulin G1 monoclonal antibodies) that are unmodified in the Fc regions, where each antibody targets a different, non-overlapping epitope of the spike protein of SARS-CoV-2.

The blockage of the spike protein interaction with angiotensin-converting enzyme 2 (ACE2) leads to inhibition of infection of host cells.



Administration:
Single dose IV (SC possible at lowest dose)
(dose range depending on case use)
2-8 degree storage, co packaged formulation (1 vial of each antibody, must be used with inline or add on 0.2 micron filter

Serological Testing for Hospitalized
Exploring testing options, that could be scaled for patient cohort

Implementation and Access Challenges
Single manufacturer – Roche Regeneron
FDA approval, WHO EOI launched, pending PQ
New to market
Cost and production capacity