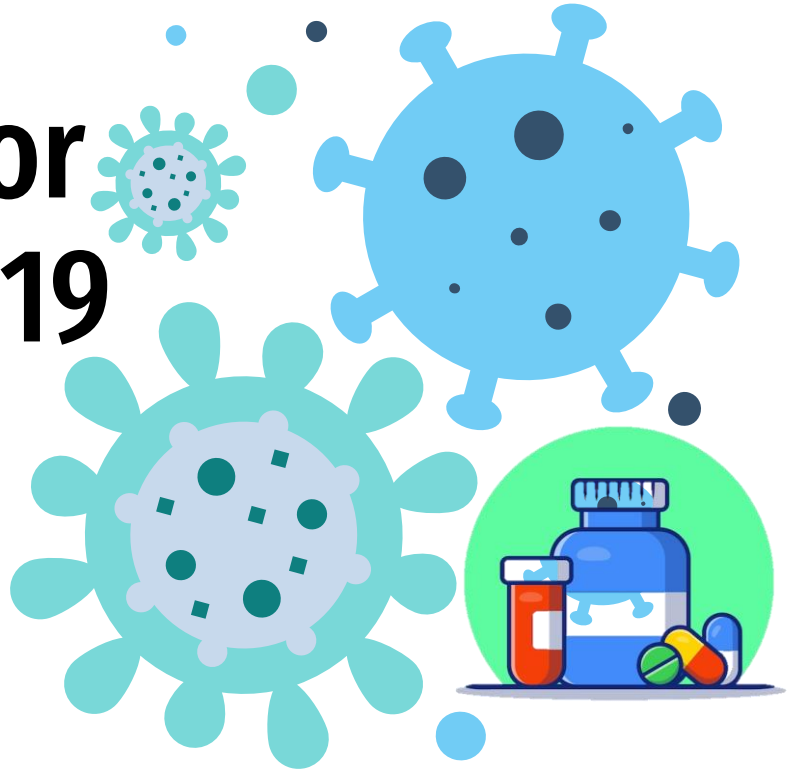
# Eligibility Criteria for Initiation of COVID-19 Oral Antiviral



FMS COVID-19 Working Group
Family Health Development Division
Ministry of Health Malaysia

*Presented by Dr Wong Ping Foo, Family Medicine Specialist, Klinik Kesihatan Cheras Baru*

# Outline

Clinical Staging of COVID-19

Oral Antiviral / Evidence

Eligibility Criteria for Initiation

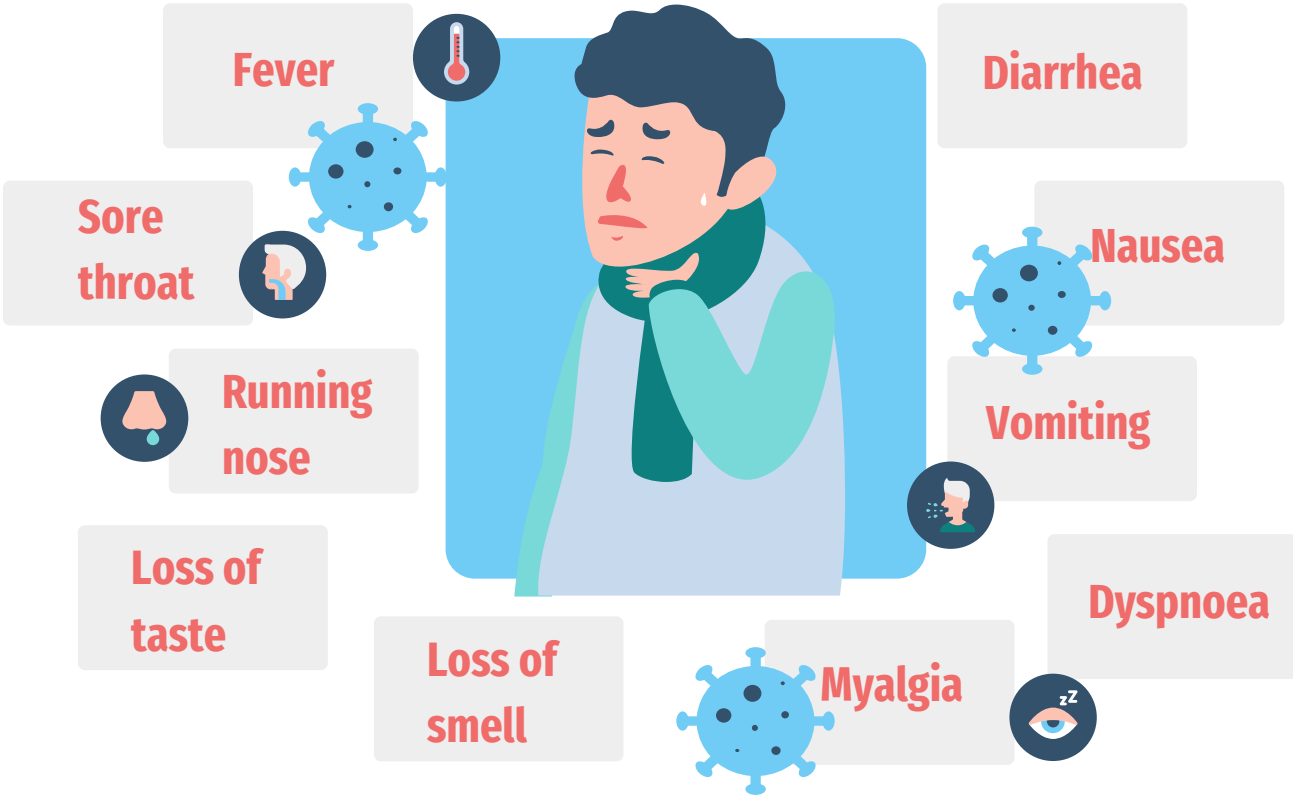
Checklist

# Clinical Staging of COVID-19

| Clinical Stage | Disease Severity |
|---|---|
| 1 | Asymptomatic |
| 2 | Symptomatic, No Pneumonia |
| 3 | Symptomatic, Pneumonia |
| 4 | Symptomatic, Pneumonia, Requiring supplemental oxygen* |
| 5 | Critically ill with multi-organ involvement |

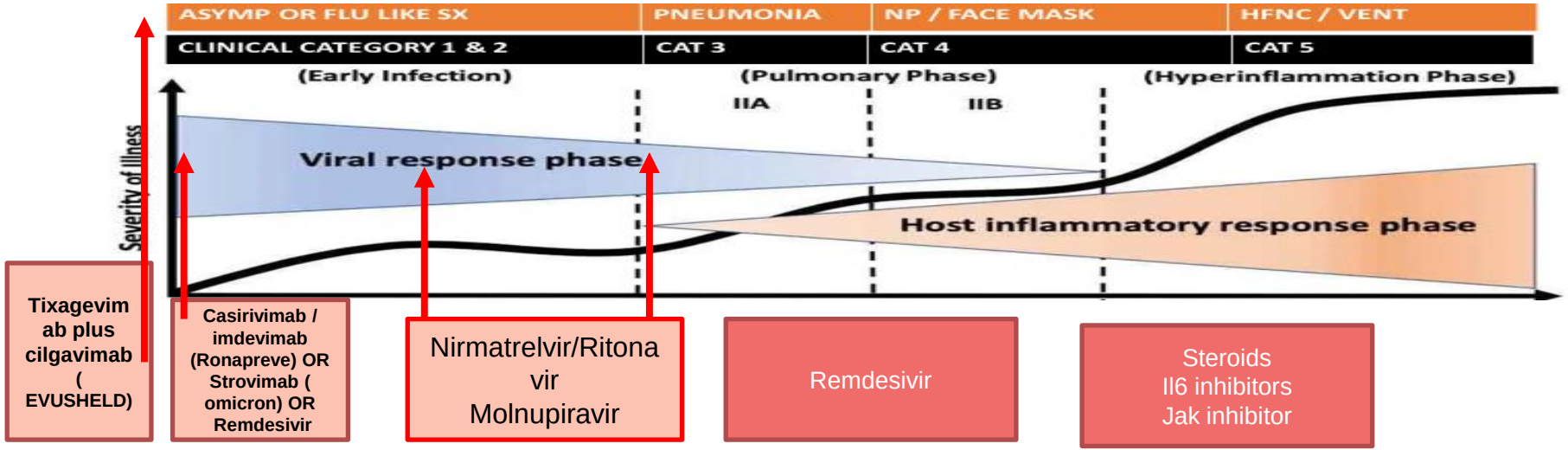
**In patients who present with hypoxia, it is important to determine if the cause is due to COVID-19 pneumonia or other causes (e.g. bronchial asthma, fluid overload and heart failure). Positive SST does not necessarily categorize the patients as category 4.*

# Symptoms of COVID-19



# Therapeutic Management of Nonhospitalized Adults With COVID-19

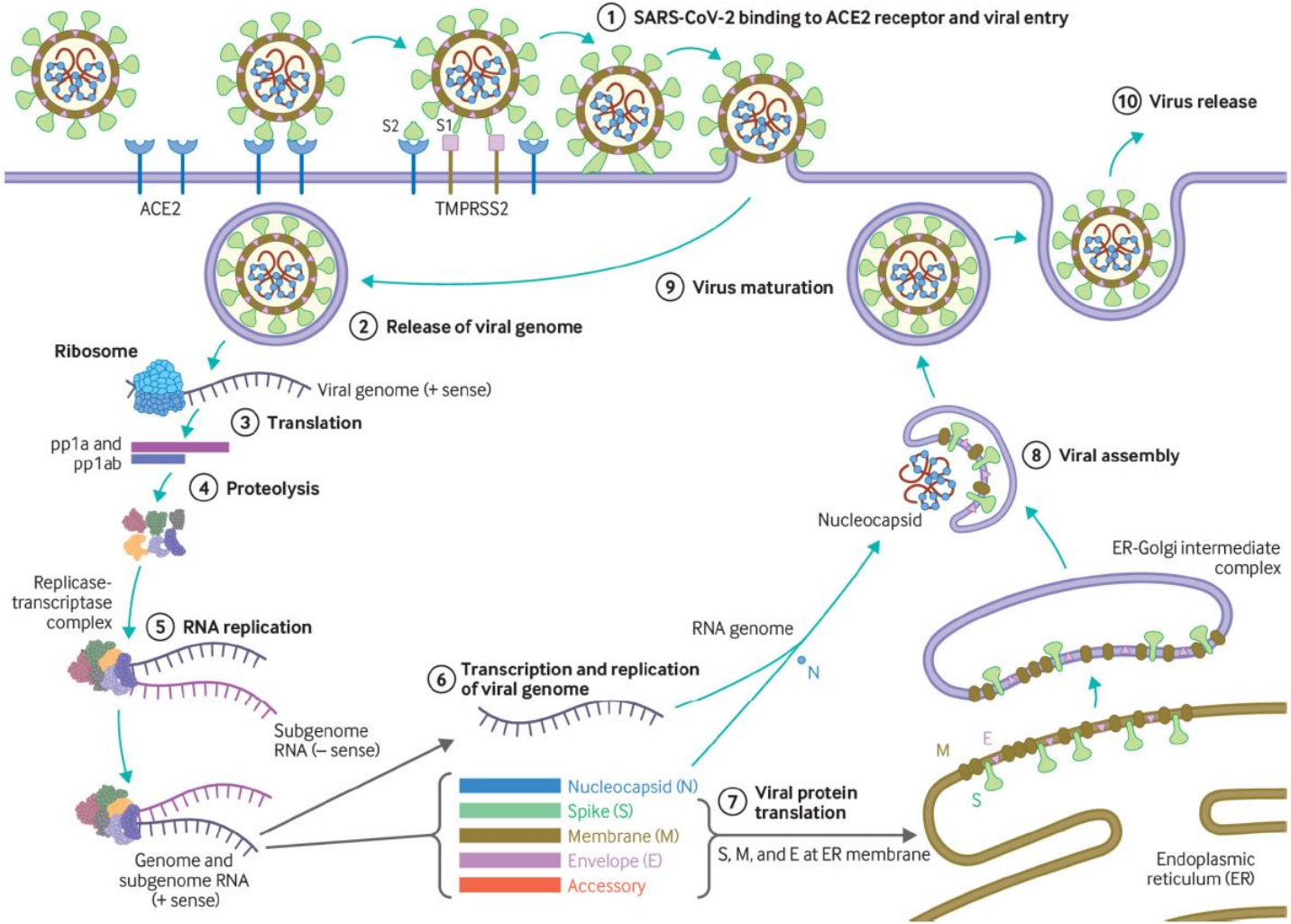
*Last Updated: April 8, 2022*



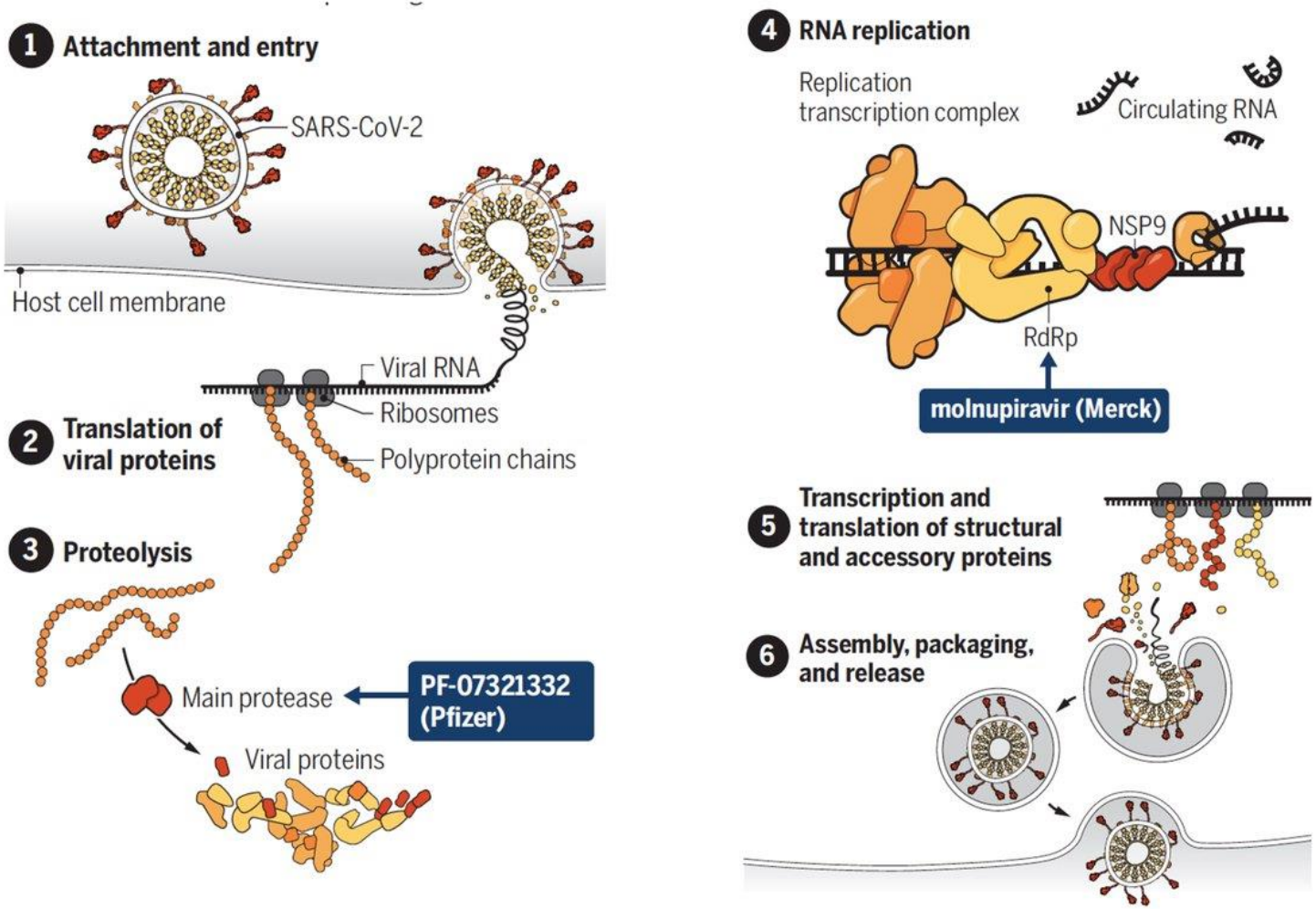
# COVID-19 Oral Antiviral Treatment

| | |
|---|---|
| First Line | **Nirmatrelvir 300mg / Ritonavir 100mg (Paxlovid) BD for 5 days** |
| Second Line | **Molnupiravir 800mg (Lagevrio) BD for 5 days** |

If the First Line Oral Antiviral is not suitable for patient, may opt for Second Line Oral Antiviral if available




Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, transmission, and pathogenesis of SARS-CoV-2. BMJ. 2020 Oct 23;371:m3862.


1 Attachment and entry
SARS-CoV-2
Host cell membrane
Viral RNA
Ribosomes
2 Translation of viral proteins
Polyprotein chains
3 Proteolysis
Main protease
PF-07321332 (Pfizer)
Viral proteins
4 RNA replication
Replication transcription complex
Circulating RNA
NSP9
RdRp
molnupiravir (Merck)
5 Transcription and translation of structural and accessory proteins
6 Assembly, packaging, and release

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 14, 2022 VOL. 386 NO. 15

# Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Jennifer Hammond, Ph.D., Heidi Leister-Tebbe, B.S.N., Annie Gardner, M.P.H., M.S.P.T., Paula Abreu, Ph.D., Weihang Bao, Ph.D., Wayne Wisemandle, M.A., MaryLynn Baniecki, Ph.D., Victoria M. Hendrick, B.Sc., Bharat Damle, Ph.D., Abraham Simón-Campos, M.D., Rienk Pypstra, M.D., and James M. Rusnak, M.D., Ph.D., for the EPIC-HR Investigators*

## ABSTRACT

### BACKGROUND

Nirmatrelvir is an orally administered severe acute respiratory syndrome coronavirus 2 main protease ($M^{pro}$) inhibitor with potent pan–human-coronavirus activity in vitro.

### METHODS

We conducted a phase 2–3 double-blind, randomized, controlled trial in which symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe coronavirus disease 2019 (Covid-19) were assigned in a 1:1 ratio to receive either 300 mg of nirmatrelvir plus 100 mg of ritonavir (a pharmacokinetic enhancer) or placebo every 12 hours for 5 days. Covid-19–related hospitalization or death from any cause through day 28, viral load, and safety were evaluated.

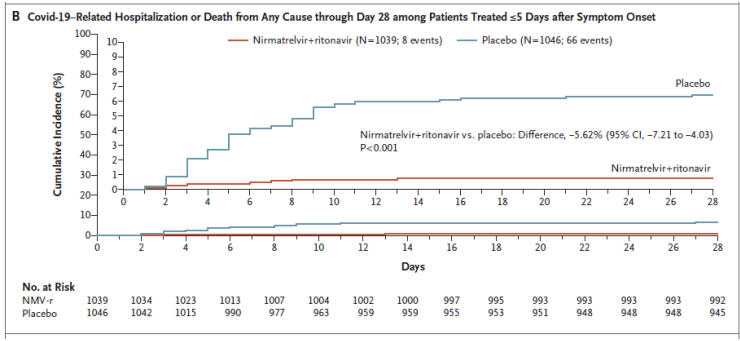
### RESULTS

A total of 2246 patients underwent randomization; 1120 patients received nirmatrelvir plus ritonavir (nirmatrelvir group) and 1126 received placebo (placebo group). In the planned interim analysis of patients treated within 3 days after symptom onset (modified intention-to treat population, comprising 774 of the 1361 patients in the full analysis population), the incidence of Covid-19–related hospitalization or death by day 28 was lower in the nirmatrelvir group than in the placebo group by 6.32

From Global Product Development, Pfizer, Collegeville, PA (J.H., H.L.-T.); Global Product Development (A.G.) and Early Clinical Development (M.L.B.), Pfizer, Cambridge, MA; Global Product Development, Pfizer, New York (P.A., W.B., B.D., R.P.); Global Product Development, Pfizer, Lake Forest, IL (W.W.); Medical and Safety, Pfizer, Sandwich, United Kingdom (V.M.H.); Köhler and Milstein Research, Mérida, Yucatan, Mexico (A.S.-C.); and Global Product Development, Pfizer, Tampa, FL (J.M.R.). Dr. Hammond can be contacted at jennifer.hammond@pfizer.com, or at Pfizer, 500 Arcola Rd., Collegeville, PA 19426.

*A list of the EPIC-HR investigators is provided in the Supplementary Appendix.

This article was published on February 16, 2022, at NEJM.org.




In the EPIC HR trial, treatment of symptomatic COVID-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe COVID-19 that was **89%** lower than the risk with placebo

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 10, 2022 VOL. 386 NO. 6

# Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients

A. Jayk Bernal, M.M. Gomes da Silva, D.B. Musungaie, E. Kovalchuk, A. Gonzalez, V. Delos Reyes, A. Martín-Quirós, Y. Caraco, A. Williams-Diaz, M.L. Brown, J. Du, A. Pedley, C. Assaid, J. Strizki, J.A. Grobler, H.H. Shamsuddin, R. Tipping, H. Wan, A. Paschke, J.R. Butterton, M.G. Johnson, and C. De Anda, for the MOVe-OUT Study Group*

## ABSTRACT

### BACKGROUND

New treatments are needed to reduce the risk of progression of coronavirus disease 2019 (Covid-19). Molnupiravir is an oral, small-molecule antiviral prodrug that is active against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

### METHODS

We conducted a phase 3, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of treatment with molnupiravir started within 5 days after the onset of signs or symptoms in nonhospitalized, unvaccinated adults with mild-to-moderate, laboratory-confirmed Covid-19 and at least one risk factor for severe Covid-19 illness. Participants in the trial were randomly assigned to receive 800 mg of molnupiravir or placebo twice daily for 5 days. The primary efficacy end point was the incidence hospitalization or death at day 29; the incidence of adverse events was the primary safety end point. A planned interim analysis was performed when 50% of 1550 participants (target enrollment) had been followed through day 29.

### RESULTS

A total of 1433 participants underwent randomization; 716 were assigned to receive

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. De Anda can be contacted at Merck, 309 Sumneytown Pike, North Wales, PA 19454.

*The members of the MOVe-OUT study group are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on December 16, 2021, and updated on February 10, 2022, at NEJM.org.

N Engl J Med 2022;386:509-20.
DOI: 10.1056/NEJMoa2116044

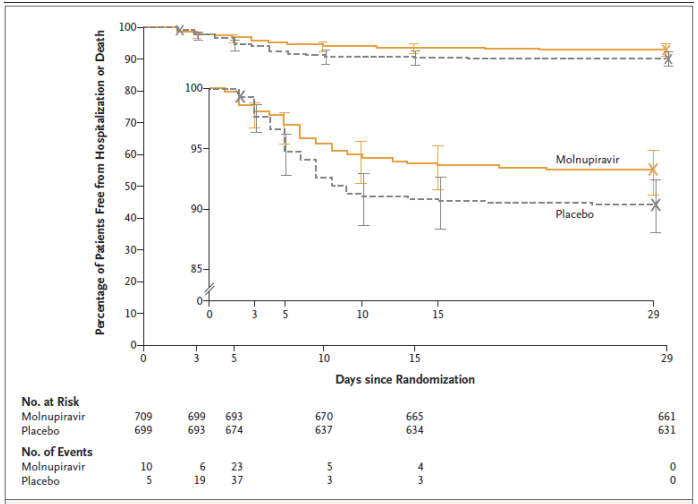




**Figure 2. Time-to-Event Analysis of Hospitalization or Death through Day 29 in the Modified Intention-to-Treat Population.**

Shown are Kaplan–Meier curves with 95% confidence intervals (I bars). X indicates censored values. Data for the single participant with unknown survival status and no hospitalization reported were censored on the day when the participant was last known to be alive. The inset shows the same data on an expanded y axis.

In the MOVe-OUT trial, molnupiravir reduced the rate of hospitalization or death by **31%** compared to placebo

# COVID-19 Oral Antiviral Treatment

| | |
|---|---|
| First Line | **Nirmatrelvir 300mg / Ritonavir 100mg (Paxlovid) BD for 5 days** |
| Second Line | **Molnupiravir 800mg (Lagevrio) BD for 5 days** |

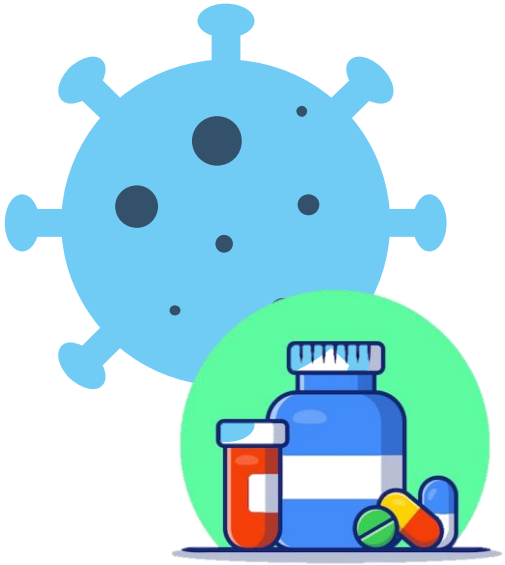
If the First Line Oral Antiviral is not suitable for patient, may opt for Second Line Oral Antiviral if available

# Non Indications/Contraindications

01 Age < 18 years old

02 Symptoms onset > 5 days

03 Patients on oxygen



Drug-drug interaction

Liver failure 04

End stage renal failure 05

Pregnancy/ Breastfeeding 06

https://www.covid19-druginteractions.org/checker

# The initiation of oral antiviral therapy in mild disease (Category 2-3) is based on the Eligibility Criteria

| ELIGIBILITY CRITERIA | Yes | No |
|---|---|---|
| Age ≥ 60 years old | | |
| Immunocompromised | | |
| Any co-morbidity | | |
| Obesity | | |
| Current or ex-smoker | | |
| Unvaccinated or Incomplete vaccination | | |

# Checklist

## CRITERIA FOR COVID-19 ORAL ANTIVIRAL THERAPY

Name: _____

IC/ID No.: _____ D.O.B.: _____ Age: _____

| NON-INDICATION / CONTRAINDICATION CHECKLIST | Tick ☑ |
|---|---|
| 1. Age < 18 years old | ☐ YES ☐ NO |
| 2. Symptoms onset > 5 days | ☐ YES ☐ NO |
| 3. Patient requires oxygen | ☐ YES ☐ NO |
| 4. Pregnant/breastfeeding | ☐ YES ☐ NO |
| 5. Drug-drug interactions, refer to; https://www.covid19-druginteractions.org/checker | ☐ YES ☐ NO |
| 6. Severe liver disease | ☐ YES ☐ NO |
| 7. Severe renal disease | ☐ YES ☐ NO |

| ELIGIBILITY CRITERIA (for Cat. 2 & Cat. 3) | Yes | No |
|---|---|---|
| 1. Age ≥ 60 years old | | |
| 2. Immunocompromised | | |
| 3. Any co-morbidity | | |
| 4. Obesity | | |
| 5. Current or ex-smoker | | |
| 6. Unvaccinated or incomplete vaccination | | |

*Patients with **ANY** of the above criteria will be eligible for oral antiviral therapy*

*FMS COVID-19 Working Group (Version3.0)*

## CRITERIA FOR COVID-19 ORAL ANTIVIRAL THERAPY

| TREATMENT [Tick ☑] | NOTES |
|---|---|
| ☐ Tab. Nirmatrelvir 300mg + Ritonavir 100mg (PAXLOVID®) BD for 5 days. | Preferred. |
| ☐ Tab. Nirmatrelvir 150mg + Ritonavir 100mg (PAXLOVID®) BD for 5 days. | Renal adjustment dose. **eGFR 30 – 60 mL/min.** |
| ☐ Cap. Molnupiravir 800mg BD for 5 days. | If contraindicated to **Nirmatrelvir** or **Ritonavir**. Female of childbearing potential should use reliable contraception during treatment and 4 days after the last dose. |
| ☐ Not started on oral antiviral | Reason: |

**NOTES:**

**Seen by:**

**.....** **Name of FMS discussed with**

**Name:**

**Designation:**

**Time & Date:**

*FMS COVID-19 Working Group (Version 3.0)*

# Take Home Message

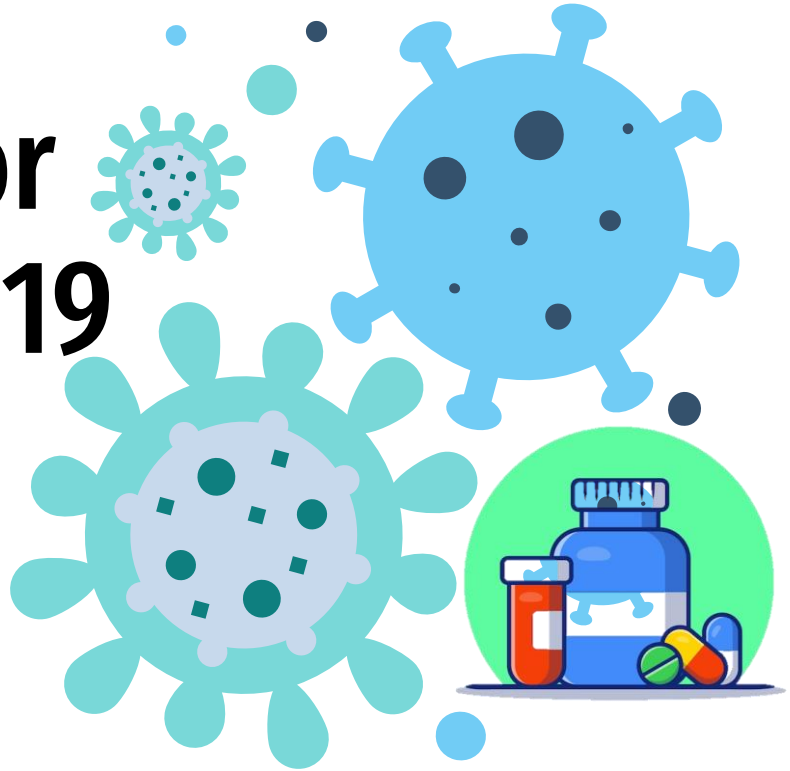
Oral Antiviral is not to replace vaccination and preventive measures

Oral Antiviral is only effective if initiated within 5 days of symptoms

Initiation of Oral Antiviral according to the current Eligibility Criteria

Continue routine Home Assessment Tool and management as per current guideline

# Application of Eligibilty Criteria for Initiation of COVID-19 Oral Antiviral (Case Studies)



*Presented by Dr Wong Ping Foo, Family Medicine Specialist, Klinik Kesihatan Cheras Baru*

# Assessment Steps in Prescribing

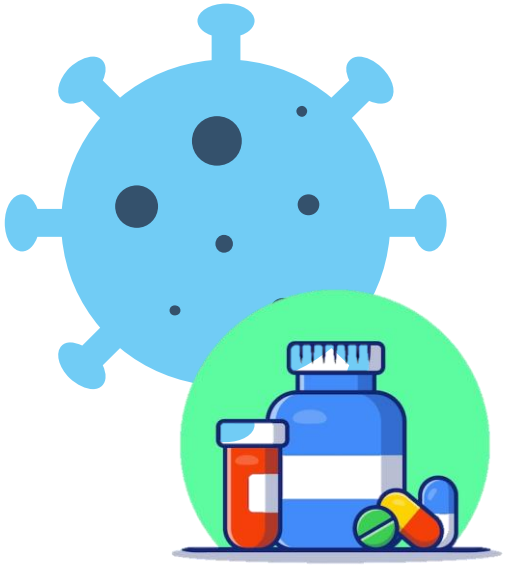
1. Check Indications / Contraindications
2. Check Eligibility Criterias

# Non Indications/Contraindications

01 Age < 18 years old

02 Symptoms onset > 5 days

03 Patients on oxygen



Drug-drug interaction

Liver failure 04

End stage renal failure 05

Pregnancy/ Breastfeeding 06

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| ELIGIBILITY CRITERIA | Yes | No |
|---|---|---|
| Age ≥ 60 years old | | |
| Immunocompromised | | |
| Any co-morbidity | | |
| Obesity | | |
| Current or ex-smoker | | |
| Unvaccinated or Incomplete vaccination | | |

# Checklist

## CRITERIA FOR COVID-19 ORAL ANTIVIRAL THERAPY

Name: _____

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| 5. Drug-drug interactions, refer to; https://www.covid19-druginteractions.org/checker | ☐ YES ☐ NO |
| 6. Severe liver disease | ☐ YES ☐ NO |
| 7. Severe renal disease | ☐ YES ☐ NO |

| ELIGIBILITY CRITERIA (for Cat. 2 & Cat. 3) | Yes | No |
|---|---|---|
| 1. Age ≥ 60 years old | | |
| 2. Immunocompromised | | |
| 3. Any co-morbidity | | |
| 4. Obesity | | |
| 5. Current or ex-smoker | | |
| 6. Unvaccinated or incomplete vaccination | | |

*Patients with **ANY** of the above criteria will be eligible for oral antiviral therapy*

*FMS COVID-19 Working Group (Version3.0)*

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**NOTES:**

**Seen by:**

**.....** **Name of FMS discussed with**

**Name:**

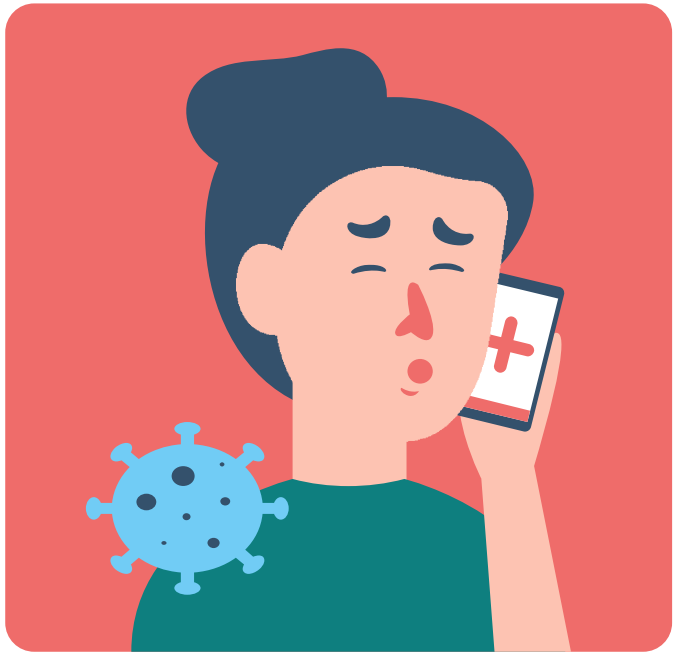
**Designation:**

**Time & Date:**

*FMS COVID-19 Working Group (Version 3.0)*

# Case Study 1

**Not Indicated**



- 34 years old, smoker
- No known medical illness
- Self RTK Saliva Test is positive
- Not having any symptoms

# Case Study 2 Contraindicated

16 years old

Bronchial Asthma

Self RTK Saliva Test is positive

Fever and sorethroat for 1 day

# Case Study 3 Eligible

- 65 years old
- Hypertension on T.Perindopril 4mg OD
- Self RTK Saliva Test is positive
- Having fever and headache
  (Day 2 of symptoms)

# Case Study 4 Eligible


50 years old,
incomplete vaccination, has diabetes with morbid obesity

Self RTK Saliva Test is positive

Has fever for 2 days and sore throat for 3 days

# Case Study 5 Eligible

- 72 years old
- Diabetes, CKD Stage 1
- Self RTK Saliva Test is positive
- Fever and diarrhea for 2 days

# Case Study 6 Not Indicated

60 years old

Diabetes, Hypertension

PCR SARS CoV-2 is negative

Fever and sorethroat for 2 days

# Thank you

# Any questions?