COVID-19 Therapies in Pediatrics: Monoclonal Antibodies and Antivirals

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IDPH
Disclosures

• None
Objectives

• Increase awareness of guidelines for outpatient Covid-19 treatments in children
• Improve knowledge of clinical considerations in prescribing therapeutics
• Enhance understanding of the logistical and practical considerations in providing therapeutics
COVID-19 hospitalization rates among children ages 4 and younger were 5x as high during the peak of Omicron compared with Delta.*

Hospitalizations per 100,000 children

- Delta: 2.9
- Omicron: 14.5

Get vaccinated to help protect yourself and those too young to be vaccinated.

*Week ending September 11, 2021 (Delta peak) compared with week ending January 8, 2022 (Omicron peak)

bit.ly/MMWR7111
In April 2022 0-4 yo have a HIGHER hospitalization rate than 18-49 yo!
Breakthrough hospitalizations: Risk of hospitalization among unvaccinated remains significantly higher across all age groups in Illinois

COVID-19 admissions per 100K (IL), Mar 6, 2022 – Apr 2, 2022

For Official Use Only (FOUO)

Breakthrough data as of Apr 26, 2022

1. Per Illinois Department of Public Health - represents 253 breakthrough admissions between Mar 6, 2022 - Apr 2, 2022 for 4.26M boostered individuals in IL (average over time period)
2. Represents 216 breakthrough admissions in IL for 4.08M fully vaccinated, no booster individuals (average over time period)
3. Represents 1,433 non-breakthrough admissions for 4.39M unvaccinated or partially vaccinated individuals in IL (average over time period)

Source: I-CARE, CDC Hospitalization Trackers, REDCap reports, INEDSS, IDPH data team, Census estimates (2018, 2019 American Community Survey - 1 year estimates)
COVID-19 Outpatient Therapeutics
Clinical Decision Aid for Ages 12+

Adult or pediatric patient (ages 12 and older weighing at least 40 kg) with mild to moderate COVID-19 and at high risk for progression to severe disease

Is patient:
- Hospitalized for COVID-19
- Requiring O₂
- Requiring an increase in baseline home O₂ due to COVID-19?

- NO
- YES

Symptom onset within the past 5–7 days?

- NO
- YES

Treatment of symptoms, management per NIH & CDC Guidelines

Consider one of the following therapeutics, if available, feasible, and clinically appropriate:

Paxlovid within 5 days of symptom onset: If patient does not have severe renal impairment (eGFR <30 mL/min OR severe hepatic impairment (Child-Pugh Class C))
- eGFR ≥ 60 mL/min: 300 mg nirmatrelvir taken with 100 mg ritonavir twice daily for 5 days
- eGFR 30 to < 60: 150 mg nirmatrelvir taken together with 100 mg ritonavir twice daily for 5 days
- Evaluate concomitant use of CYP3A inducers and medications with high dependency on CYP3A for clearance as these may be contraindicated

OR

Veklury (remdesivir): 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3 begun ASAP within 7 days of symptom onset

If Paxlovid and Veklury (remdesivir) are not available, feasible or clinically appropriate consider one of the following therapeutics:

beteleovimab ASAP within 7 days of symptom onset
175 mg single IV injection

OR

Lagevrio (molnupiravir): If patient age 18 or older AND possibility of pregnancy, if applicable, ruled out:
800 mg by mouth every 12h for 5 days begun ASAP within 5 days of symptom onset

Prescribers must review and comply with the mandatory requirements outlined in the Lagevrio (molnupiravir) EUA.

References:
2. Paxlovid EUA: https://www.fda.gov/media/155050/download
5. Beteleovimab EUA: https://www.fda.gov/media/164152/download
6. Lagevrio EUA: https://www.fda.gov/media/155054/download

April 18, 2022
“Breaking News” for Week of April 25
Veklury EUA Update

- April 25 – The FDA expanded the use of the COVID-19 treatment Veklury (remdesivir) to include pediatric patients 28 days of age and older weighing at least 3 kilograms (about 7 pounds) with positive results of direct SARS-CoV-2 viral testing, who are:
  - Hospitalized, or
  - Not hospitalized and have mild-to-moderate COVID-19 and are at high risk for progression to severe COVID-19, including hospitalization or death.

- Veklury is the first approved COVID-19 treatment for children less than 12 years of age. As a result of the expanded approval, the FDA also revoked the EUA for Veklury that previously covered this pediatric population.
  - Previously, Veklury was only approved to treat certain adults and pediatric patients (12 years of age and older who weigh at least 40 kilograms) with COVID-19.

ASPR’s Response to COVID-19 website (https://aspr.hhs.gov/COVID-19/Pages/default.aspx)
New and Notable: COVID-19 Therapeutics Announcements (https://aspr.hhs.gov/COVID-19/Therapeutics/Pages/default.aspx)
Clinical Decision Aid for Pediatric Patients

Outpatient 3.5 kg to less than 40 kg or younger than 12 years of age weighing at least 3.5 kg, with mild to moderate COVID-19 and at high risk for progression to severe disease

1. **Symptom onset within the past 7 days?**
   - **YES**
     - Pediatric patient (greater than 28 days old) with severe renal impairment (eGFR <30 mL/min)
     - OR
     - Full-term neonate (7 to 28 days old) with serum creatinine greater than or equal to 1 mg/dL?
   - **NO**

2. **YES**
   - Treatment of symptoms, management per NIH & CDC Guidelines

3. **NO**
   - Consider Veklury (remdesivir)* begin ASAP within 7 days of symptom onset

   - Pediatric patients younger than 12 years and weighing 40 kg or greater: 200 mg IV x 1 dose on Day 1, 100 mg IV x 1 on Days 2–3
   - Pediatric patients 3.5 kg to less than 40 kg or pediatric patients younger than 12 years weighing at least 3.5 kg: 5 mg/kg IV on Day 1, 2.5 mg/kg on Days 2–3

*Use 100 mg lyophilized vial for EUA pediatric use

Reference:
* Veklury (remdesivir) EUA: https://www.fda.gov/media/137389/download

April 18, 2022
COVID-19 OUTPATIENT TREATMENT GUIDELINES ROADMAP

Last Updated: April 5, 2022

This resource is intended to serve as a guide on available outpatient COVID-19 treatment options, with links to FDA Emergency Use Authorization information and guideline recommendations from national guideline-developing organizations, where available. It is not intended to endorse or otherwise promote a specific clinical recommendation or course of action. Additionally, it does not include other forms of guidance that may be available for specific subsets of populations. Finally, the guidelines referenced here may not consider local allocation and availability of scarce resources. Additional information on where to access these therapeutics can be found at the National Infusion Center Association™ and HHS.²

Risk factors for severe COVID-19¹

Included here are some medical conditions that may place patients at a higher risk for progression to severe COVID-19:

- Age 65 years and older
- BMI of more than 25 kg/m²
- Pregnancy
- Chronic kidney disease
- Diabetes mellitus
- Immunosuppressing medications
- Cardiovascular disease or hypertension
- Neurodevelopmental disorders or conditions that confer medical complexity
- Chronic lung disease
- Sickle cell disease
- Medical technological dependence, e.g., tracheostomy

When giving products under Emergency Use Authorization, providers must:

2. Inform patient of alternatives to treatment.
3. Inform patient that this is an unapproved drug.

Options depicted in gray should be considered AFTER other options, if other options are unavailable, or only in certain clinical situations.

Does your patient have COVID?
Positive results of direct SARS-CoV-2 testing

YES

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

YES

See CDC² / IDSA⁴ / NIH³ guidance.

NO

Is your patient hospitalized for COVID-19 or requiring increased O₂ for COVID-19?

NO

Does your patient have any symptoms?

NO

OUTPATIENT treatment options not authorized or recommended. Supportive care

YES

Is Emergency Use Authorization met? Including:

- ONLY FOR USE IN moderate to severe immunocompromise and inadequate vaccine response or inability to be vaccinated or mount adequate vaccine response
- Ages 12 and older
- Weight of 40 kg (88 lbs) and higher
- No known current or recent COVID exposure

(Tixagevimab plus cilgavimab is not a substitute for vaccination)

YES

Has vaccine been given?

YES

Evusheld™ can be given 2 weeks following vaccination. See also IDSA and NIH guidelines.

Dosing: Tixagevimab 300 mg IV plus cilgavimab 300 mg IV

NO

NO
**Paxlovid™ Dosing**

<table>
<thead>
<tr>
<th>GFR</th>
<th>Nirmatrelvir</th>
<th>Ritonavir</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60 mL/min</td>
<td>300 mg 2x daily for 5 days</td>
<td>100 mg 2x daily for 5 days</td>
</tr>
<tr>
<td>30 to &lt;60 mL/min</td>
<td>150 mg 2x daily for 5 days</td>
<td>100 mg 2x daily for 5 days</td>
</tr>
</tbody>
</table>

*Hold prohibited medicines starting 12 hours before Paxlovid™ and reinitiate 3-5 days after final Paxlovid dose.*

**Due to embryofetal toxicity in animals, molnupiravir is not recommended for use in pregnancy.**

If the decision is made to use molnupiravir in pregnancy, the prescriber must document that potential benefits and risks of molnupiravir use in pregnancy from the EUA factsheet were discussed with the patient, and the patient was made aware of Merck’s pregnancy surveillance program at 1-877-888-4231 or molnupiravir.com/pregnancy.
RISK: Criteria for use of treatments for SARS-CoV-2

- Obesity or being overweight (e.g., adults with BMI > 25 kg/m², or, if age 12 to 17, have BMI ≥ 85th percentile for age and sex)
- Pregnancy
- Chronic kidney or liver disease
- Diabetes mellitus
- Immunosuppression, HIV
- Cancer
- Cardiovascular disease (including congenital heart disease) or hypertension
- Sickle cell disease
- Chronic lung diseases
- Disabilities (even intellectual)
- Dependence on a medical-related technology (e.g., gastrostomy)
- Mental health conditions (depressions, schizophrenia)
- Physical inactivity
- Smoking (current or former)
- Substance use disorder
- TB

Not an exhaustive list - clinician judgement is paramount

CDC People with Underlying Medical Conditions
O!Micron

- Bam/ete does not work against Omicron variant $^1$
- Regencov does not work against Omicron $^2$
- Sotrovimab retained activity in pre-clinical studies $^3$

\[ - \text{EUA was updated for use within 7 days of symptom onset (previously 10 days) and shorter infusion time} \]

1. Gruel et al preprint, open access
2. Wilhelm et al, preprint MedRxIV
3. Cathart et al, preprint, biorxIV
BA.2

- First detected in IL mid Jan 2022
- Sotrovimab with 27 fold reduction in activity
- **Bebtelovimab and Remdesivir** retain activity
- Mixed data about Evusheld
- Oral antivirals expected to retain activity
- **VACCINES RETAIN** activity

Zhou et al, BioRxIV Pre-print Jan 2022
Iketani et al BioRxIV Pre-print Jan 2022
U.K. Health Security Agency Report Jan 2022
PreP: Getting ahead of the curve

- Pre-exposure prophylaxis mAB Evusheld approved by the FDA
- Restricted to those who are
  - Immunocompromised and will not mount a good response to the vaccine
  - Have a vaccine contraindication
- Use in those above the age of 12 years/40 kg
  - Intramuscular injections q6M
- Delay Evusheld 2 weeks after Covid vaccine if vaccine received first
Attachment inhibitors:

Bebtelovimab (anti-Spike mAb)

- EUA just issued 2/11/22
- Now available for ordering through IDPH
- mAb indicated for treatment of outpatients with COVID-19 in patients at risk for development of moderate to severe disease
- For adults and children > 12 who weigh > 40kg
- Given as single IV push injection of 175mg over 30 seconds with 1 hour of post-dose observation
- Given within 7 days of symptom onset
- Only use if no adequate/available/approved alternative given limited data
- In vitro, no reduction in activity against Omicron (BA1.1 or BA.2 variants)
  - Slight reduction against Mu variant

- **Efficacy:** BLAZE-4 study
  - Looked at lower risk patients
  - A higher proportion in the placebo arm vs. Tx arm had persistently high viral load at 7 days 21% vs. 14%, RRR of 34%
  - Symptoms resolved more quickly: 6 days vs. 8 days for Tx vs. placebo
- Studied in higher risk patients but no placebo group makes comparison difficult

- **Safety:** BLAZE-4 study, N = 602 patients
  - Nausea 0.8%
  - Infusion-related reactions 0.3% (N=2)
  - Pruritus 0.3%
  - Rash 0.8%

https://www.fda.gov/media/156152/download

Slide courtesy: Dr. Lubelchek
mAB and COVID-19 vaccine/booster

• Limited data on how they may interact with each other
• If vaccine is administered first, no delay in mAB
• If mAB is administered first, CDC suggests a 90 day delay till vaccine administered considering that re-infection in 30 days from receipt of such therapies is rare.
• NO DELAY if mAB given before vaccine

HHS clinical implementation guide for Monoclonal Antibodies, Dec 2021
Remdesivir (Veklury)

• RNA polymerase inhibitor
• CARAVAN Phase 2/3 study for children under the age of 12 years
  – hospitalized
• Active against Omicron, BA.1 and BA.2
• Side effects: hypersensitivity reaction, increased AST, ALT
• Consider checking AST/ALT during treatment
REMDESIVIR (ANTIVIRAL)

- **Remdesivir 200 mg** IV on Day 1, followed by **100 mg** IV daily on Days 2 and 3
  - initiated as soon as possible
  - within 7 days of symptom onset
  - aged (12 years or 40 kg)
  - **Pediatric use >=3.5 kg**
  - Approved for non hospitalized patients at risk of progression to severe disease

RRR = 87%, ARR = 4.6%, NNT = 22 (PINETREE trial)
Oral pills for outpatient treatments:

- **Paxlovid** authorized by the FDA (~89% effective in reducing hospital admissions)
  - Twice a day for 5 days
  - Combined with a boosting agent ritonavir (significant drug interactions)
  - NNT=18 to prevent 1 hospitalization or death

- **Molnupiravir** authorized by the FDA (~30% effective in reducing hospital admissions)
  - 800 mg twice a day for 5 days
  - Given within 5 days of symptom onset
  - Safety concerns- mutagenesis
  - NNT =35 to prevent 1 hospitalization
Prescribe an alternative COVID-19 therapy for patients who are receiving any of the medications listed.

Before prescribing ritonavir-boosted nirmatrelvir (Paxlovid), determine whether the patient is receiving any of the medications listed.

- If the patient is receiving any of these medications, withhold the medication if clinically appropriate.
- If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.

<table>
<thead>
<tr>
<th>Medications</th>
<th>Medications</th>
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<tbody>
<tr>
<td>Amiodarone</td>
<td>Alfuzosin</td>
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<tr>
<td>Apalutamide</td>
<td>Alprazolam</td>
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<tr>
<td>Bosentan</td>
<td>Atorvastatin</td>
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<tr>
<td>Carbamazepine</td>
<td>Avanafil</td>
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<tr>
<td>Cisapride</td>
<td>Ciazepam</td>
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<tr>
<td>Clopidogrel</td>
<td>Codeine</td>
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<tr>
<td>Clozapine</td>
<td>Cyclosporine&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Colchicine in patients with renal and/or hepatic impairment</td>
<td>Diazepam</td>
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<tr>
<td>Disopyramide</td>
<td>Everolimus&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>Dofetilide</td>
<td>Fentanyl</td>
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<tr>
<td>Dronedarone</td>
<td>Hydrocodone</td>
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<tr>
<td>Eplerenone</td>
<td>Lomitapide</td>
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<tr>
<td>Ergot derivatives</td>
<td>Lovastatin</td>
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<tr>
<td>Flocaainide</td>
<td>Meperidine (pethidine)</td>
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<tr>
<td>Flibanserin</td>
<td>Midazolam (oral)</td>
</tr>
<tr>
<td>Glicaprevir/pibrentasvir</td>
<td>Oxycodone</td>
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<tr>
<td>Ivabradine</td>
<td>Piroxicam</td>
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<tr>
<td>Lumatapiron</td>
<td>Propoxyphene</td>
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<tr>
<td>Lurasidone</td>
<td>Rosuvastatin</td>
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<tr>
<td>Mexiletine</td>
<td>Salmeterol</td>
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<tr>
<td>Phenobarbital</td>
<td>Sildenafil for erectile dysfunction</td>
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<tr>
<td>Phenytoin</td>
<td>Silodosin</td>
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<tr>
<td>Pimozide</td>
<td>Sinvastatin</td>
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<tr>
<td>Propafenone</td>
<td>Sirolimus&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>Quinidine</td>
<td>Suvorexant</td>
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<tr>
<td>Ranolazine</td>
<td>Tacrolimus&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Tadalafil for erectile dysfunction</td>
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<tr>
<td>Rifaxentine</td>
<td>Tamsulosin</td>
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<tr>
<td>Rivaroxaban</td>
<td>Tramadol</td>
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<tr>
<td>Sildenafil for pulmonary hypertension</td>
<td>Triazolam</td>
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<tr>
<td>St. John's wort</td>
<td>Vardenafil</td>
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<tr>
<td>Tadalafil for pulmonary hypertension</td>
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<tr>
<td>Ticagrelor</td>
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<tr>
<td>Vorapaxar</td>
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<sup>a</sup> Expert consultation may be considered. In some cases, dose reduction of the concomitant medication may be an appropriate management strategy.
Paxlovid (Drug Interactions)

- Use another Covid-19 agent if the patient is on
  - Clopidogrel, rivaroxaban
  - Sildenafil or tadalafil (for pulm HTN)
  - Phenytoin
  - Colchicine
  - Amiodarone
  - 12 other agents

- Hold these agents while on Paxlovid
  - Atorvastatin, simvastatin, rosuvastatin
  - Tacrolimus, sirolimus
  - Clonazepam, midazolam
  - Tramadol, hydrocodone, oxycodone

NIH Statement on Paxlovid
Drug-Drug interactions
PAXLOVID AND HIV

• Ritonavir has an antiviral effect
  – Do not use in children with unsuppressed HIV
• Could result in HIV antiviral resistance

Interaction Checker
Access our free, comprehensive and user-friendly drug interaction charts

Discover Our COVID-19 iChart Mobile App
COVID-19 iChart gives easy access to our drug interaction information on mobile devices. Click the links below to get the app for your iPhone or Android device.

University of Liverpool drug interaction checker
Paxlovid and Contraception

- Ritonavir component can decrease efficacy of combined hormonal contraception
  - Use ALTERNATE forms of contraception e.g. barrier methods while on Paxlovid

<table>
<thead>
<tr>
<th>Contraceptives</th>
<th>Weak interaction</th>
<th>No interaction expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethinylestradiol</td>
<td>Proceed with NMV/r</td>
<td>Proceed with NMV/r</td>
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<tr>
<td>Etonogestrel (IMP)</td>
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<tr>
<td>Etonogestrel (VR)</td>
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<tr>
<td>Levonorgestrel (COC)</td>
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<td>Levonorgestrel (EC)</td>
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<td>Levonorgestrel (IDU)</td>
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<tr>
<td>Levonorgestrel (POP)</td>
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<tr>
<td>Medroxyprogesterone (depot injection)</td>
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<tr>
<td>Norethisterone (COC)</td>
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<td>Norethisterone (IM)</td>
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<td>Norethisterone (POP)</td>
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<tr>
<td>Norgestrel (COC)</td>
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</table>

University of Liverpool drug interaction checker
Paxlovid and Cancer

f. The decision to pause or dose adjust dasatinib should be made in conjunction with the patient’s oncologist. *Chronic phase chronic myelogenous leukaemia:* pause dasatinib and restart 3 days after completing NMV/r. Alternatively, consider reducing dasatinib dose to 20 mg (in patients receiving 100 mg daily) or 40 mg (in patients receiving 140 mg daily) and monitor for toxicity. *Accelerated or blast phase chronic myelogenous leukaemia:* do not coadminister, use alternative COVID-19 therapy.

g. The decision to pause or dose adjust erlotinib should be made in conjunction with the patient’s oncologist. If it is decided to pause treatment, restart erlotinib 3 days after completing NMV/r treatment. If pausing erlotinib treatment is not feasible, continue full dose erlotinib with patient self-monitoring for rash and diarrhoea. If these do occur, reduce erlotinib dose in 50 mg decrements or re-assess for a short pause.

h. The decision to pause imatinib should be made in conjunction with the patient’s oncologist. If it is decided to hold treatment, restart imatinib 3 days after completing NMV/r treatment. Alternatively, imatinib may be coadministered with monitoring for adverse effects (fluid retention, nausea and neutropenia). NMV/r is expected to have a modest effect on imatinib exposure. Coadministration with ritonavir (600 mg once daily) for 3 days did not significantly alter imatinib exposure (van Erp NP et al. Clin Cancer Res. 2007;13(24):7394-400).

i. The decision to pause or dose adjust vinblastine should be made in conjunction with the patient’s oncologist. Vinblastine may be paused in the context of acute infection. Restart vinblastine 3 days after completing NMV/r treatment. Alternatively, vinblastine may be coadministered with close monitoring for haematologic toxicity and neurotoxicity. Some providers may wish to empirically reduce vinblastine dose, especially in patients who have previously experienced or are at high risk for toxicity.
Paxlovid other key interactions

<table>
<thead>
<tr>
<th>Anticonvulsants</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Ergometrine</td>
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<tr>
<td>Ethosuximide</td>
<td>Levodopa</td>
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<tr>
<td>Lamotrigine</td>
<td>Levothyroxine</td>
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<tr>
<td>Phenobarbital</td>
<td>Steroids</td>
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<td>Phenytoin</td>
<td>Beclomethasone</td>
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<td>Valproate</td>
<td>Betamethasone</td>
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<td>Fludrocortisone</td>
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<td>Antidepressants</td>
<td>Prednisolone</td>
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<tr>
<td>Amitriptyline</td>
<td>Testosterone</td>
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<tr>
<td>Clomipramine</td>
<td>Triamcinolone</td>
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<td>Fluoxetine</td>
<td>Immunosuppressants</td>
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<tr>
<td>Lithium</td>
<td>Azathioprine</td>
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<td></td>
<td>Ciclosporin</td>
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<tr>
<td>Antidiabetics</td>
<td>Everolimus</td>
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<tr>
<td>Glibenclamide</td>
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<tr>
<td>Gliclazide</td>
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<td>Insulin</td>
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<tr>
<td>Metformin</td>
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</table>

**Do not co-administer**

- **Do not use NMV/r ⇒ alternative COVID-19 therapy**
  - Strong inducer can jeopardize NMV/r efficacy due to persisting induction after stopping the drug.

- **NMV/r use ONLY possible if drug is paused or replaced by a non-interacting drug**
  - Risk of serious toxicity. Only start NMV/r if the drug can be safely paused or replaced. Drug can be resumed 3 days after completing NMV/r therapy.
Paxlovid

Renal impairment

- Reduce to 150 mg of nirmatrelvir if GFR is 30-60 ml/min
- Avoid if GFR <30 ml/min

Hepatic Impairment

- Avoid if Child Pugh C
Molnupiravir

ONLY use when other agents not available in a timely manner

Can cause DNA mutations in humans (theoretical risk)
- Equivocal data in rodents

Avoid in
- Pregnancy (especially under 10 weeks gestation)
- Age under 18 years (damage to bone and cartilage)
Molnupiravir

• Contraception
  – Natal females should use contraception during and for 4 days after completing last dose
  – Natal males should use contraception for THREE MONTHS after completing last dose

• Breastfeeding
  – Unknown- advised to avoid for up to 4 days after last dose
LONG HAULERS

• Long Covid
  – 25% of children
  – Higher RR in children with dyspnea, aguesia/anosmia and fever
  – > four weeks after being first infected with SARS-CoV-2
• Unknown duration but most recover within 1-5 months

• Most common symptoms in children were
  – Mood disorders
  – Fatigue
  – Sleep disorder

• Covid – heart effects
  – 60% heart inflammation in adults

Lopez-leon et al, Medrxiv 2022
Hopkins Medicine
AMA
Long Covid treatment

• Follow-up visits with a healthcare professional every 2–3 months (frequency depends on clinical condition)
• Comprehensive rehabilitation plan
  – physical and occupational therapy
  – speech and language therapy
  – vocational therapy
  – neurologic rehabilitation
• Gradual return to exercise as tolerated
• Patient support groups

• ANTIVIRALS OR MONOCLONAL ANTIBODIES?

CDC guidance
Paxlovid Rebound!

A puzzling phenomenon: Patients report a rebound of COVID-19 symptoms after taking the antiviral Paxlovid

By Kay Lazar  Globe Staff. Updated April 21, 2022, 6:59 a.m.
## Summary of available outpatient agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
<th>Risk reduction/NNT</th>
<th>Administration</th>
<th>Pros</th>
<th>Cons</th>
<th>Notes</th>
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<tr>
<td>Evusheld</td>
<td>Pre-exposure prophylaxis</td>
<td>RRR = 77% ARR 0.8% NNT = 125</td>
<td>IM injection x 2</td>
<td>Single IV infusion; effect thought to last 6 months</td>
<td>IV infusion</td>
<td>For immunocompromised; reduced activity, but still active to prevent Omicron</td>
</tr>
<tr>
<td>Bebtelovimab</td>
<td>Treatment w/in 7 days of symptom onset of test+</td>
<td>NA</td>
<td>IV infusion (30 seconds)</td>
<td>single IV infusion;</td>
<td>IV infusion</td>
<td>For increased risk to progress to severe disease</td>
</tr>
<tr>
<td>Paxlovid</td>
<td>Treatment w/in 5 days of symptom onset of test+</td>
<td>RRR = 87% ARR = 6% NNT = 18 NNT (death) = 91</td>
<td>PO BID x 5 days</td>
<td>High efficacy, oral therapy</td>
<td>Drug/drug interactions</td>
<td>For increased risk to progress to severe disease</td>
</tr>
<tr>
<td>Molnupiravir</td>
<td>Treatment w/in 5 days of symptom onset of test+</td>
<td>RRR = 30% ARR = 3% NNT = 35 NNT (death) = 333</td>
<td>PO BID x 5 days</td>
<td>Oral therapy; relatively large supply</td>
<td>For 18 and up; potential for fetal toxicity/mutagenicity</td>
<td>For increased risk to progress to severe disease</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Treatment w/in 7 days of symptom onset or test+</td>
<td>RRR = 87% ARR = 5% NNT = 22</td>
<td>IV infusion daily x 3 days</td>
<td>High efficacy; significant experience; EUA for as small as &gt;3.5kg</td>
<td>3-days of IV infusion</td>
<td>For increased risk to progress to severe disease</td>
</tr>
</tbody>
</table>
Access to medications

• There are
  – >1200 therapeutics locations across the state
  – ALL CVS stores and Drive-through Walgreens
  – 136 Walmarts and 23 Sam’s Clubs
  – Covering 96.7% of the state population within a 10 mile radius, by county
ALLOCATIONS

• Distributed through state agencies
  – Direct ordering by providers

• WEEKLY Allocations based on population distribution and case rates
  – LTCs assigned protected allocation
  – Some FQHCs qualified for separate allocation
  – Test to Treat T2T

• DAILY UTILIZATION REPORTING THROUGH the HPoP platform
Test to Treat (T2T) locator

How to get medication

1. Locations to testing, medical visits, and medication (Test-to-Treat)

Some pharmacy clinics and health centers can prescribe and give you medication at the same location.

Learn more about the Test-to-Treat program.

2. Locations to fill a prescription

Any healthcare provider can evaluate and prescribe you COVID-19 medication just as they normally would. You can fill those prescriptions at any location in this tool.
T2T Participants
• 138 predominantly in Chicagoland area

Walgreens sites have been added back to the T2T locator. Advocate is now operational and has started the program.
Therapeutics Utilization – week ending 5/3/22

• Current Total Utilization For Therapeutics

• Paxlovid & Bebtelovimab
  – Courses On Hand = 34,876
  – Courses Used = 3982
Monoclonal antibody treatment & Pre-exposure – Last week

**Bebtelovimab**
- 6348 Courses Reported On Hand
- 815 Courses Reported Used

**Evusheild (PreP)**
- 17691 Courses Reported On Hand
- 381 Courses Reported Used

Molnupiravir
- 62676 Courses Reported On Hand
- 241 Courses Reported Used
- ~7 hospitalizations averted

Paxlovid
- 28341 Courses Reported On Hand
- 3,150 Courses Reported Used
- ~175 hospitalizations averted
POCKETBOOK MATH!
REIMBURSEMENT AND COVERAGE

• Monoclonal antibodies are expensive but are free through the federal government
  – ~$2000 cost per dose

• Bebtelovimab: Medicare will pay approximately
  – $350.50 in most healthcare settings
  – $550.50 in the beneficiary’s home or residence
BILLING CODES

**Bebtelovimab product codes**

- **M0222:**
  - Intravenous injection, includes infusion or injection, and post administration monitoring

- **M0223:**
  - Intravenous injection, includes post administration monitoring in the home or residence; this includes a beneficiary’s home that has been made provider-based to the hospital during the covid-19 public health emergency

**Remdesivir Codes**

- J0248 to administer in the outpatient setting
- Observation for 1 hr post infusion is required
## CMS: Coverage of Monoclonal Antibody Products to Treat COVID-19

### Medicare

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Payable by Medicare</th>
<th>Expected Patient Cost-Sharing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Hospital</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Hospital or “Hospital without Walls”</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Outpatient Physician Office/Infusion Center</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Nursing Home (See third bullet in Key Facts on CMS enforcement discretion)</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
<tr>
<td>Home</td>
<td>✓</td>
<td>No patient cost-sharing</td>
</tr>
</tbody>
</table>

1. Services must be furnished within the scope of the product’s FDA authorization or approval and within the provider’s scope of practice.
2. Under the Hospital Without Walls Initiative, hospitals can provide hospital services in other healthcare facilities and sites that would not otherwise be considered to be part of a healthcare facility, or can set up temporary expansion sites to help address the urgent need to increase capacity to care for patients.
3. Cost-sharing may apply to Medicare beneficiaries when they receive care from a provider that doesn’t participate in Medicare.
4. Certain monoclonal antibody products to treat COVID-19 have been authorized under Food and Drug Administration Emergency Use Authorizations since November 10, 2020. More information including the level II HCPCS codes for the administration/infusion and post administration monitoring of these products can be found online in the Program Instruction.

### Expected Payment to Providers: Key Facts

- Medicare payment for monoclonal antibody products to treat COVID-19 is similar across sites of care, with some small differences.
- Medicare pays for the administration of monoclonal antibody products to treat COVID-19. For example, Medicare will pay a national average of approximately $450 for the administration of certain monoclonal antibody products. Home infusion is reimbursed at a higher rate.
- CMS will exercise enforcement discretion to allow Medicare-enrolled immunizers working within their scope of practice and subject to applicable state law to bill directly and receive direct reimbursement from the Medicare program for administering monoclonal antibody treatments to Medicare Part A Skilled Nursing Facility residents.
- Medicare will pay the provider for these monoclonal antibody products when they are purchased by the provider. Medicare won’t pay if the product is given to the provider for free by, for example, a government entity.
- When purchased by the provider, Medicare payment is typically at reasonable cost or at 95% of the Average Wholesale Price (an amount determined by the manufacturer). These payment amounts vary depending on which type of provider is supplying the product. Original Medicare will pay for these products for beneficiaries enrolled in Medicare Advantage.
- For more specific information about Medicare payments to providers for these monoclonal antibody products, please see these Frequently Asked Questions.

Additional information can be found at: https://www.cms.gov/files/document/covid-infographic-coverage-monoclonal-antibody-products
Reimbursement

• Home health agencies can use their home health provider ID or hospice provider ID to bill Medicare Part B on a TOB 34x.

• HRSA COVID-19 Uninsured Program will Reimburse Monoclonal Antibody Treatments based on Medicare Rates

New challenges

• HRSA Uninsured Program no longer fulfills claims for outpatient treatment of Covid-19 as of March 25, 2022.

• These therapies are extremely cost effective, especially monoclonal antibodies, in decreasing hospitalization and death (Jovanoski et al 2022).
Equity Concerns

• Disparity in outpatient covid treatment for monoclonal antibodies:
  • Hispanic patients received mAb 58% less often than did non-Hispanic patients
  • Black received mAb 22% less often than did White patients
  • “Other” race patients 47% less often than did White patients (CDC MMWR Jan 2022).

• Not every patient will be eligible to receive the oral pill Paxlovid given the significant drug interactions
Hospitalization Rates per 100,000 population by age and race and ethnicity
— COVID-NET, March 1, 2020–April 02, 2022

COVID-19 can make some children very sick
Among nearly 400 children ages 5–11 years
hospitalized with COVID-19 during the first few months of Omicron:

- 3 in 10 had NO underlying conditions
- 9 in 10 were unvaccinated
- 2 in 10 required ICU care

Protect all eligible children by keeping their vaccinations up to date

* Dec 19, 2021–Feb 28, 2022
bit.ly/MMWR7116
APRIL 19, 2022

0–17, 18–49, 50–64, 65–74, 75–84 and 85+ years.

5 Starting the week ending December 4, Maryland temporarily halted data transmission on COVID-19-associated hospitalizations, impacting COVID-NET age-adjusted rate calculations. Hospitalization rates are likely underestimated.
In Summary

• Therapeutics can prevent hospitalizations in children with Covid
• Oral agents are widely accessible and work against variants
• The Need-to-Use gap should decrease especially in high risk children
• Need visibility into locations providing Veklury
  – https://app.smartsheet.com/b/form/88437eb8fbfc45a6af3fffc17da5f11bb
THANK YOU

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IEM team, OPR team