Pharmacotherapy Update

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trikafta®
(elexacaftor/tezacaftor/ivacaftor
and ivacaftor)

Trikafta

Trikafta (tezacaftor, elexacaftor, ivacaftor)

- Indication:
  - Treatment of cystic fibrosis (CF) in patients ≥2 years who have *F508del* or other responsive mutation in the *CFTR* gene
- Dosage form:
  - Fixed-dose combination tablets
  - Fixed dose combination granules
- Administration:
  - Give with fat-containing food

Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; June 2021.

Trikafta

Recommended Dosage for Adult and Pediatric Patients Aged 2 Years and Older			
Age	**Weight**	**Morning Dose**	**Evening Dose**
2 to less than 6 years	Less than 14 kg	One packet containing elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg oral granules	One packet containing ivacaftor 59.5 mg oral granules
	14 kg or more	One packet containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg oral granules	One packet containing ivacaftor 75 mg oral granules
6 to less than 12 years	Less than 30 kg	Two tablets, each containing elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg	One tablet of ivacaftor 75 mg
	30 kg or more	Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg	One tablet of ivacaftor 150 mg
12 years and older	-	Two tablets, each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg	One tablet of ivacaftor 150 mg

Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; June 2021.

Trikafta

Warnings/Precautions

- Hepatic injury
- Cataracts (pediatric patients)
- Hypersensitivity reactions

Adverse Effects

- Headache
- URI
- Abdominal pain
- Diarrhea
- Elevated LFTs

Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; June 2021.

Trikafta

Monitoring

- LFTs (AST, ALT, bilirubin)
- Therapeutic drug monitoring of interacting medications

Drug Interactions

- CYP3A4 inducers – avoid co-administration
- CYP3A4 inhibitors – Trikafta dose adjustment required
- Calcineurin inhibitors*

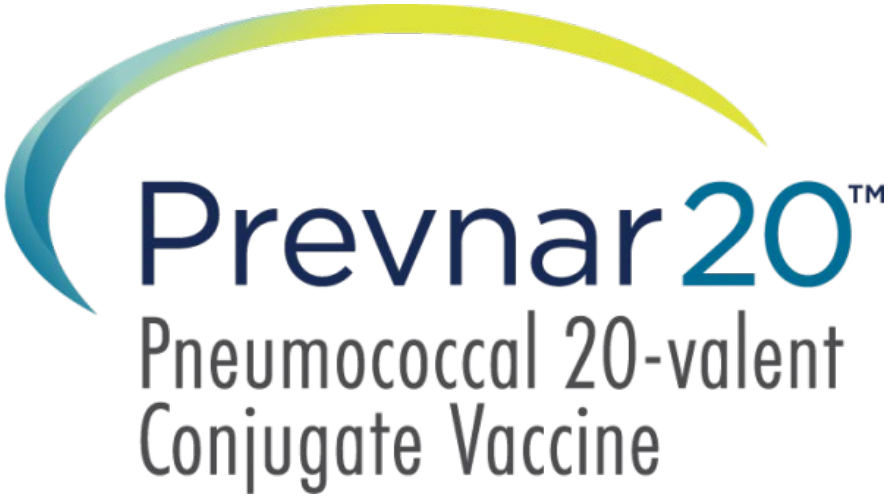
Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; June 2021.

Trikafta

- Place in therapy:
  - Lung transplant
    - May improve extrapulmonary manifestations of CF
  - Liver transplant recipients with CF
    - May be safe with appropriate graft monitoring
    - Provides clinical benefit/improvement in CF symptoms
- Considerations post-transplant
  - Monitor immunosuppression and LFTs closely with initiation of Trikafta
  - Azole antifungals will require Trikafta dose adjustment

Hayes, Don et al. The Journal of Heart and Lung Transplantation, Volume 41, Issue 2, 127 – 128
Benninger, Lauryn A. et al. The Journal of Heart and Lung Transplantation, Volume 40, Issue 12, 1498 – 1501
Ragan, Hunter et al. Pediatr. Pulmonol. 2022, 57, 411–417

New(er) Adult Vaccines



Prevnar 20®

Prevnar 20® (PCV20)

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- PCV20 = pneumococcal 20-valent conjugate vaccine
  - Replaces previous PCV13 vaccine
  - Targets 7 additional *S pneumoniae* serotypes that commonly cause disease in the United States
- Indication: prevention of invasive pneumococcal disease and pneumococcal pneumonia
- Dosage form: 0.5 mL prefilled syringe for IM injection
  - Store refrigerated (2-8°C; 36-46°F). Do not freeze.

Prevnar 20 [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals LLC; April 2023.
Kobayashi M, et al. MMWR Morb Mortal Wkly Rep. 2022;71(4):109-117.

Pneumococcal Vaccine Recommendations

Adults ≥65 years old
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥1 year† → PPSV23
PPSV23 only at any age	≥1 year → PCV20	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20	≥1 year† → PPSV23
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → PCV20	≥5 years§ → PPSV23

- †§Minimum interval between pneumococcal conjugate vaccines (PCV) and polysaccharide vaccines (PPSV23) is ≥8 weeks in immunocompromised patients

http://www.cdc.gov/pneumococcal/vaccination.html

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Pneumococcal Vaccine Recommendations

Adults 19–64 years old with specified immunocompromising conditions
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20	PCV15 → ≥8 weeks → PPSV23
PPSV23 only	≥1 year → PCV20	≥1 year → PCV15
PCV13 only	≥1 year → PCV20	≥8 weeks → PPSV23 → ≥5 years → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 1 dose of PPSV23	≥5 years → PCV20	≥5 years† → PPSV23 Review pneumococcal vaccine recommendations again when your patient turns 65 years old.
PCV13 and 2 doses of PPSV23	≥5 years → PCV20	**No vaccines** recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 65 years old.

http://www.cdc.gov/pneumococcal/vaccination.html

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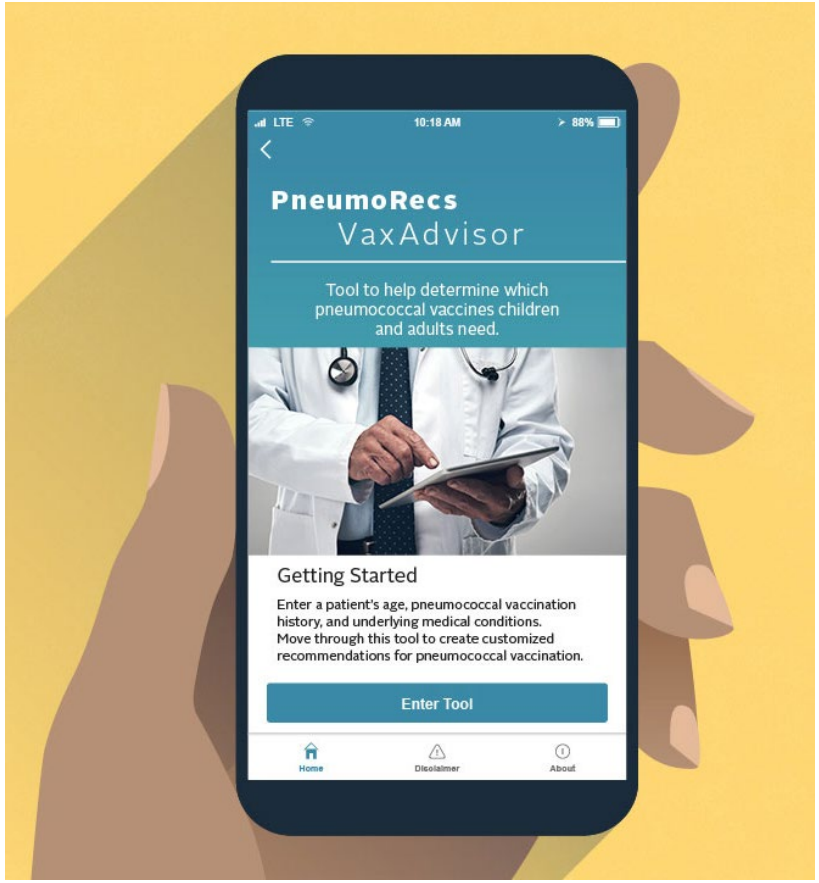
Pneumococcal Vaccine Recommendations



- Mobile app and online tool to help healthcare providers determine which pneumococcal vaccines are needed
- Maintained by the CDC
- Does not provide recommendations for other (non-pneumococcal) vaccines

https://www.cdc.gov/vaccines/vpd/pneumo/hcp/pneumoapp.html

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Respiratory Syncytial Virus (RSV) Vaccines

RSV Vaccines

- Two RSV vaccines approved in 2023
- Indication: prevention of symptomatic lower respiratory tract disease (LRTD) caused by RSV in individuals ≥ 60 years of age
- Timing:
  - Typical RSV seasonality was disrupted by the COVID-19 pandemic
  - For 2023-2024, vaccination is recommended as early as supply becomes available
  - Currently, RSV vaccination consists of a single dose
    - Long-term studies are ongoing

https://www.cdc.gov/vaccines/vpd/rsv/hcp/older-adults.html
Melgar M, et al. MMWR Morb Mortal Wkly Rep. 2023;72:793-801.

Arexvy

- Efficacy (vs placebo): Reduced symptomatic LRTD by 82.6% during the first RSV season after vaccination
- Includes an adjuvant intended to enhance the immune response to vaccination
- Dosage form:
  - 0.5 mL reconstituted suspension for IM injection
  - Before reconstitution, store vials refrigerated (2-8°C; 36-46°F). Do not freeze.

Arexvy [package insert]. Durham, NC: GlaxoSmithKline Biologicals; May 2023.
https://www.cdc.gov/vaccines/acip/recs/grade/GSK-Adjuvanted-RSVPreF3-adults-etr.html

Abrysvo

- Efficacy (vs placebo): reduced symptomatic LRTD by 88.9% during the first RSV season after vaccination
- Does not contain an adjuvant
- Dosage form:
  - 0.5 mL reconstituted suspension for IM injection
  - Supplied in a kit that includes a needle-free vial adapter for reconstitution
  - Before reconstitution, store kit refrigerated (2-8°C; 36-46°F). Do not freeze.

Abrysvo [package insert]. New York, NY: Pfizer Labs; Oct 2023.

Fidaxomicin

Fidaxomicin

- Indication:
  - Macrolide antibiotic for treatment of Clostridioides difficile-associated diarrhea (CDAD)
  - Approved for adults and pediatric patients ≥ 6 months of age

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Dificid™ package insert. Optimer Pharmaceuticals, Inc. San Diego CA 2011.

Fidaxomicin

Clinical Infectious Diseases

IDSA GUIDELINES

Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults

CDAD Treatment Recommendations

- Initial infection:
  - Fidaxomicin recommended rather than standard course of oral vancomycin
  - Oral vancomycin remains an acceptable alternative
- Recurrent infection:
  - Fidaxomicin (standard or extended-pulsed regimen) recommended rather than standard course of oral vancomycin
    - Fidaxomicin pulse regimen: 200mg twice daily for 5 days followed by 200mg every other day for 20 days
  - Oral vancomycin tapered and pulsed regimen remains an acceptable alternative

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Johnson S, et al. *Clinical Infectious Diseases*. Published online June 14, 2021.

Fidaxomicin vs Oral Vancomycin

	Fidaxomicin	Vancomycin
Dosing frequency	BID dosing	QID dosing
Relative cost	$$$	$
Renal dose adjustment	Not required	Not Required
Drug interactions	None	None
Adverse effects	Nausea, vomiting, abdominal pain	Nausea, vomiting, abdominal pain

Dificid™ package insert. Optimer Pharmaceuticals, Inc. San Diego CA 2011.
VANCOCIN® (Vancomycin Hydrochloride Capsules), Package insert, Merus Labs Inc., Control No.203124, October 27, 2017

Questions?