EVIDENCE-BASED DRUG THERAPY UPDATE 2025

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Objectives

Recognize the indications and adverse effects for new medications

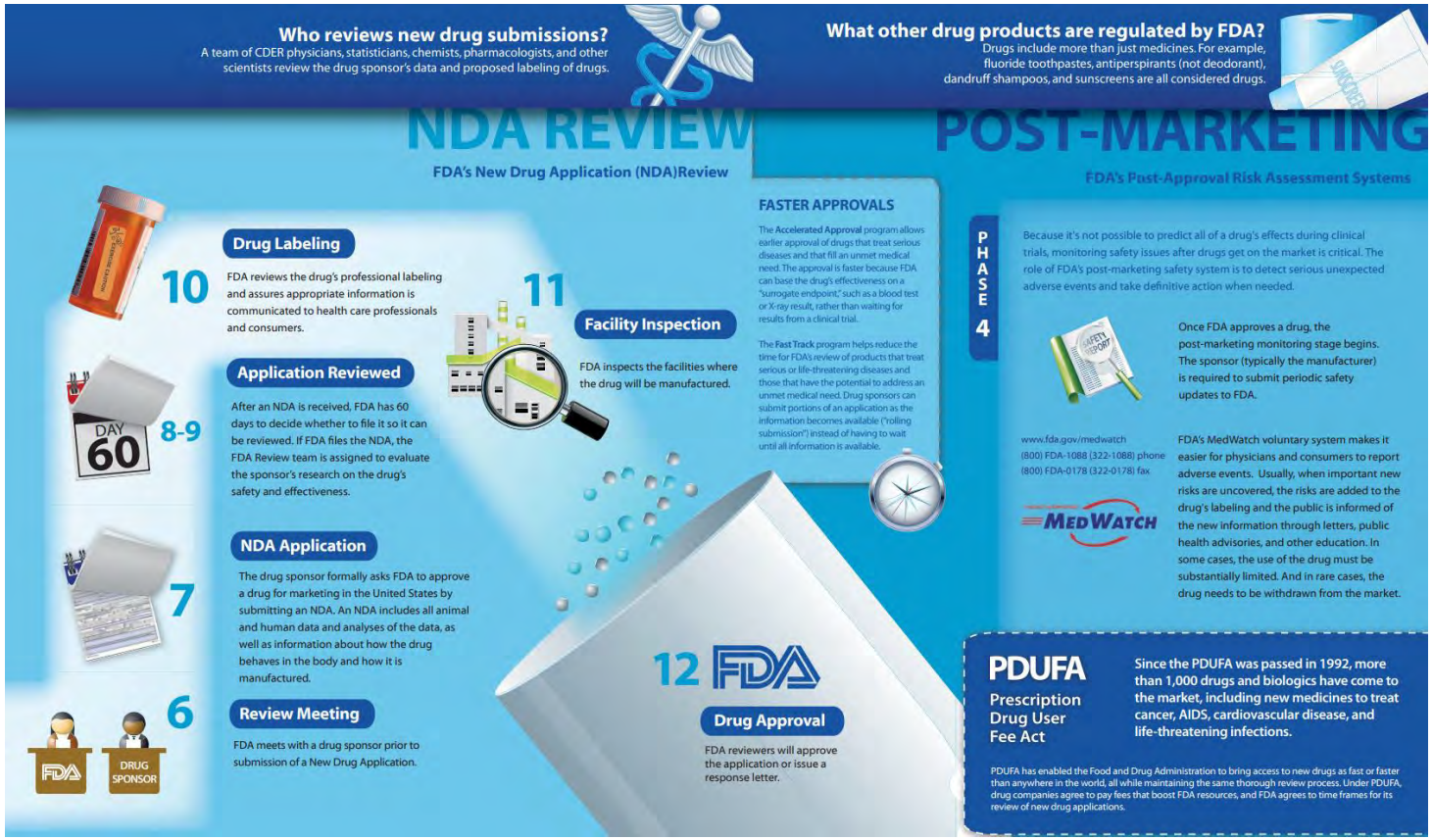
Describe the mechanism of action for new medications

Determine the place in therapy for new drugs based on current evidence

FDA Approval Process

https://www.fda.gov/downloads/drugs/resourcesforyou/consumers/ucm284393.pdf

FDA Approval Process



https://www.fda.gov/downloads/drugs/resourcesforyou/consumers/ucm284393.pdf

Special Circumstances

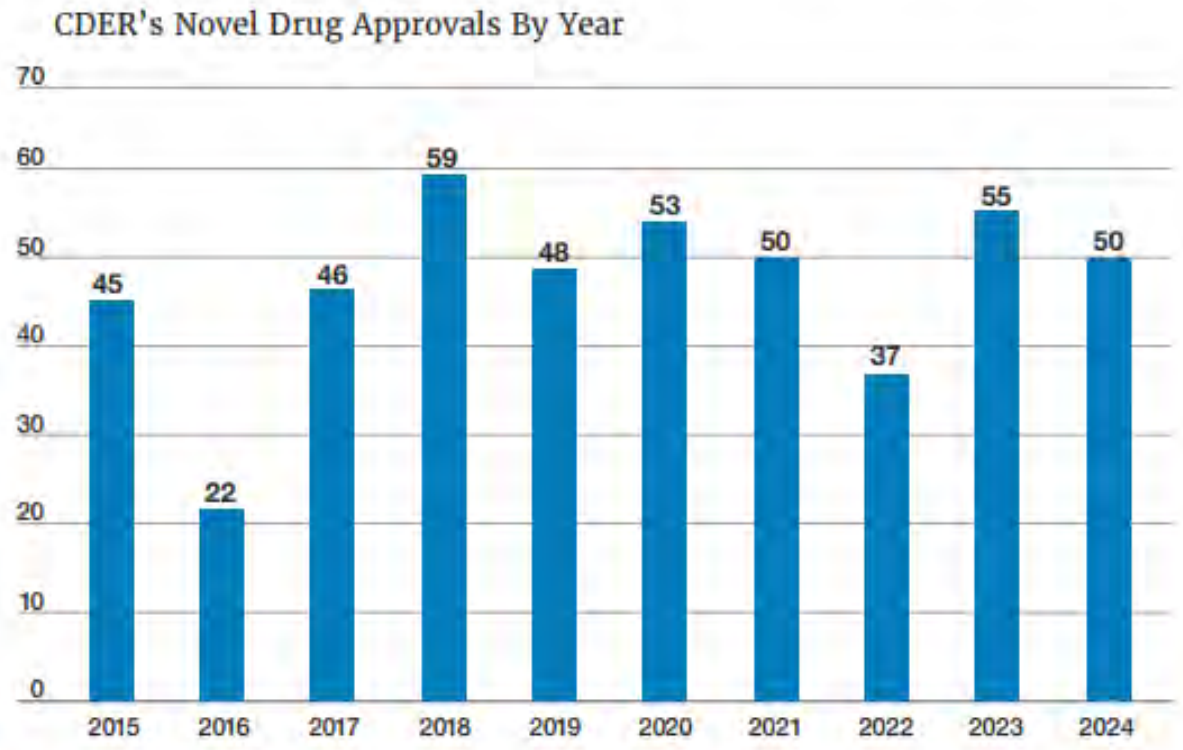
Fast Track	Breakthrough Therapy	Priority Review	Accelerated Approval

• Fulfills an unmet medical need for serious conditions
• Can be based on "promising" animal or human data
• Example: Beyfortus (nirsevimab), Orlynvah (sulopenem/probenecid)
	• Treats a serious condition and preliminary evidence suggests a substantial benefit over currently available therapies
	• Example: Leqembi (lecanemab)
		• Action taken within 6 months for drugs that would significantly improve treatment of serious conditions
		  • Standard review is 10 months
		  • Example: Zurzuvae (zuranolone)
			• Fulfills an unmet medical need for a serious condition
			• May use surrogates or intermediate clinical endpoints

https://www.fda.gov/drugs/developmentapprovalprocess/default.htm

CDER's Annual Novel Drug Approvals: 2015 – 2024

The 10-year graph below shows that from 2015 through 2024, CDER has averaged about 47 novel drug approvals per year.



NEW DRUG APPROVALS

NEW DRUG APPROVALS

First-in-Class Drugs

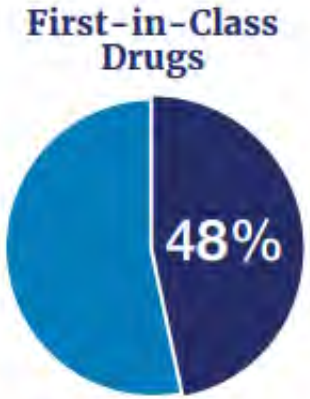
CDER identified 24 of the 50 novel drugs approved (48%) in 2024 as first-in-class. These drugs produce a novel pharmacologic effect, the impact or influence that a drug has on the body or a specific biological target, in a disease.

Novel drugs approved in 2024 that CDER identified as first-in-class were:

Anktiva, Aqneursa, Bizengri, Cobenfy, Crenessity, Duvyzat, Hympavzi, Imdelltra, Iqirvo, Lumisight, Miplyffa, Nemluvio, Niktimvo, Revuforj, Rezdiffra, Rytelo, Tryngolza, Tryvio, Voydeya, Vyloy, Winrevair, Xolremdi, Zelsuvmi, Ziihera

Notable examples of novel first-in-class approvals include:

- **Anktiva (nogapendekin alfa inbakicept-pmln)** intravesical solution (medications placed directly in the bladder through a catheter) to treat nonmuscle invasive bladder cancer with carcinoma in situ with or without papillary tumors that is unresponsive to prior therapy with Bacillus Calmette-Guérin.



CDER identified 24 out of the 50 novel drugs (48%) approved in 2024 as first-in-class.

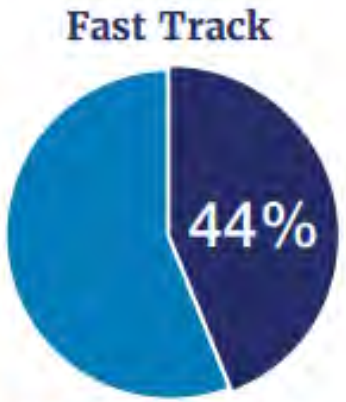
New Drug Approvals

Fast Track

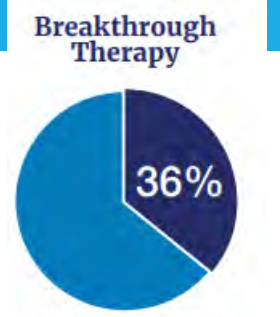
CDER granted fast track status to 22 of the 50 novel drugs (44%) in 2024. Fast track speeds development and review of new drugs and biologics by increasing the level of communication between FDA and drug developers and by enabling CDER to review portions of a drug application on a rolling basis.

Drugs granted Fast Track status were:

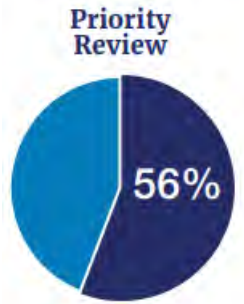
Anktiva, Aqneursa, Bizengri, Crenessity, Duvyzat, Ebglyss, Exblifep, Kisunla, Leqselvi, Lumisight, Miplyffa, Niktimvo, Orlynvah, Revuforj, Rezdiffra, Rytelo, Tryngolza, Voranigo, Vyloy, Xolremdi, Zevtera, Ziihera



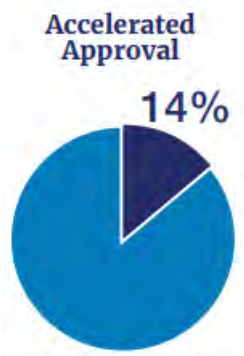
CDER designated 22 of the 50 novel drugs (44%) as fast track.



CDER identified 18 of the 50 novel drugs (36%) approved in 2024 as breakthrough therapies.

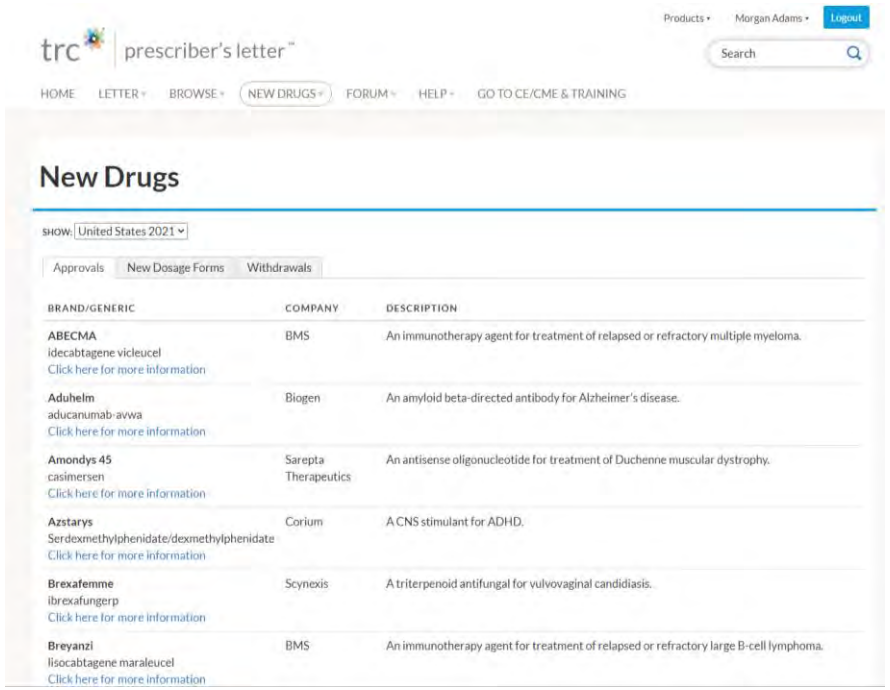


28 of the 50 drugs (56%) approved in 2024 were designated as priority review.

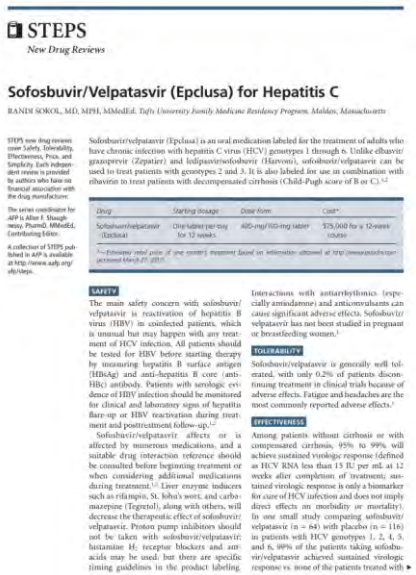


CDER identified 7 of the 50 novel drugs (14%) as accelerated approvals.

Keeping Up with New Drugs



- FDA website
  - https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm592464.htm
- Prescriber's Letter/Medical Letter
- MyDailyMed
- AAFP STEPS review



STEPS
New Drug Reviews

Sofosbuvir/Velpatasvir (Epclusa) for Hepatitis C

RANDI SOKOL, MD, MPH, MMedEd. *Tufts University Family Medicine Residency Program, Malden, Massachusetts*

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

The series coordinator for *AFP* is Allen F. Shaughnessy, PharmD, MMedEd, Contributing Editor.

A collection of STEPS published in *AFP* is available at http://www.aafp.org/afp/steps.

Sofosbuvir/velpatasvir (Epclusa) is an oral medication labeled for the treatment of adults who have chronic infection with hepatitis C virus (HCV) genotypes 1 through 6. Unlike elbasvir/grazoprevir (Zepatier) and ledipasvir/sofosbuvir (Harvoni), sofosbuvir/velpatasvir can be used to treat patients with genotypes 2 and 3. It is also labeled for use in combination with ribavirin to treat patients with decompensated cirrhosis (Child-Pugh score of B or C).[1,2]

Drug	Starting Dosage	Dose Form	Cost*
Sofosbuvir/velpatasvir (Epclusa)	One tablet per day for 12 weeks	400-mg/100-mg tablet	$75,000 for a 12-week course

*—Estimated retail price of one month's treatment based on information obtained at http://www.goodrx.com; accessed March 27, 2017.

SAFETY

The main safety concern with sofosbuvir/velpatasvir is reactivation of hepatitis B virus (HBV) in coinfected patients, which is unusual but may happen with any treatment of HCV infection. All patients should be tested for HBV before starting therapy by measuring hepatitis B surface antigen (HBsAg) and anti-hepatitis B core (anti-HBc) antibody. Patients with serologic evidence of HBV infection should be monitored for clinical and laboratory signs of hepatitis flare-up or HBV reactivation during treatment and posttreatment follow-up.[1,2]

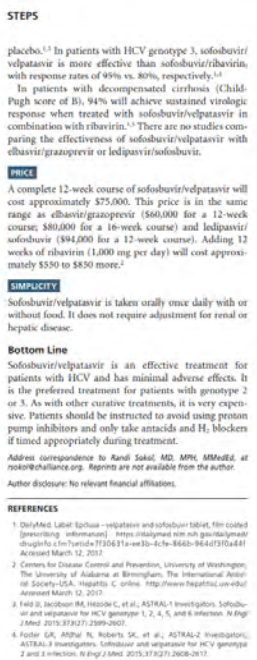
Sofosbuvir/velpatasvir affects or is affected by numerous medications, and a suitable drug interaction reference should be consulted before beginning treatment or when considering additional medications during treatment.[1,2] Liver enzyme inducers such as rifampin, St. John's wort, and carbamazepine (Tegretol), along with others, will decrease the therapeutic effect of sofosbuvir/velpatasvir. Proton pump inhibitors should not be taken with sofosbuvir/velpatasvir; histamine H_2 receptor blockers and antacids may be used, but there are specific timing guidelines in the product labeling. Interactions with antiarrhythmics (especially amiodarone) and anticonvulsants can cause significant adverse effects. Sofosbuvir/velpatasvir has not been studied in pregnant or breastfeeding women.[1]

TOLERABILITY

Sofosbuvir/velpatasvir is generally well tolerated, with only 0.2% of patients discontinuing treatment in clinical trials because of adverse effects. Fatigue and headaches are the most commonly reported adverse effects.[1]

EFFECTIVENESS

Among patients without cirrhosis or with compensated cirrhosis, 95% to 99% will achieve sustained virologic response (defined as HCV RNA less than 15 IU per mL at 12 weeks after completion of treatment); sustained virologic response is only a biomarker for cure of HCV infection and does not imply direct effects on morbidity or mortality. In one small study comparing sofosbuvir/velpatasvir (n = 84) with placebo (n = 116) in patients with HCV genotypes 1, 2, 4, 5, and 6, 99% of the patients taking sofosbuvir/velpatasvir achieved sustained virologic response vs. none of the patients treated with ▸



STEPS

placebo.[1,3] In patients with HCV genotype 3, sofosbuvir/velpatasvir is more effective than sofosbuvir/ribavirin, with response rates of 95% vs. 80%, respectively.[3,4]

In patients with decompensated cirrhosis (Child-Pugh score of B), 94% will achieve sustained virologic response when treated with sofosbuvir/velpatasvir in combination with ribavirin.[1,2] There are no studies comparing the effectiveness of sofosbuvir/velpatasvir with elbasvir/grazoprevir or ledipasvir/sofosbuvir.

PRICE

A complete 12-week course of sofosbuvir/velpatasvir will cost approximately $75,000. This price is in the same range as elbasvir/grazoprevir ($60,000 for a 12-week course; $80,000 for a 16-week course) and ledipasvir/sofosbuvir ($94,000 for a 12-week course). Adding 12 weeks of ribavirin (1,000 mg per day) will cost approximately $550 to $850 more.[2]

SIMPLICITY

Sofosbuvir/velpatasvir is taken orally once daily with or without food. It does not require adjustment for renal or hepatic disease.

Bottom Line

Sofosbuvir/velpatasvir is an effective treatment for patients with HCV and has minimal adverse effects. It is the preferred treatment for patients with genotype 2 or 3. As with other curative treatments, it is very expensive. Patients should be instructed to avoid using proton pump inhibitors and only take antacids and H_2 blockers if timed appropriately during treatment.

Address correspondence to Randi Sokol, MD, MPH, MMedEd, at rsokol@chalfiance.org. Reprints are not available from the author.

Author disclosure: No relevant financial affiliations.

REFERENCES

1. DailyMed. Label: Epclusa - velpatasvir and sofosbuvir tablet, film coated [prescribing information]. https://dailymed.nlm.nih.gov/dailymed/druginfo.cfm?setid=7f730631a-ee3b-4cfe-866b-9f44df3f0a48! Accessed March 12, 2017.
2. Centers for Disease Control and Prevention, University of Washington, The University of Alabama at Birmingham, The International Antiviral Society–USA. Hepatitis C online. http://www.hepatitisc.uw.edu/ Accessed March 12, 2017.
3. Feld JJ, Jacobson IM, Hézode C, et al.; ASTRAL-1 Investigators. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med.* 2015;373(27):2599-2607.
4. Foster GR, Afdhal N, Roberts SK, et al.; ASTRAL-2 Investigators; ASTRAL-3 Investigators. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *N Engl J Med.* 2015;373(27):2608-2617.

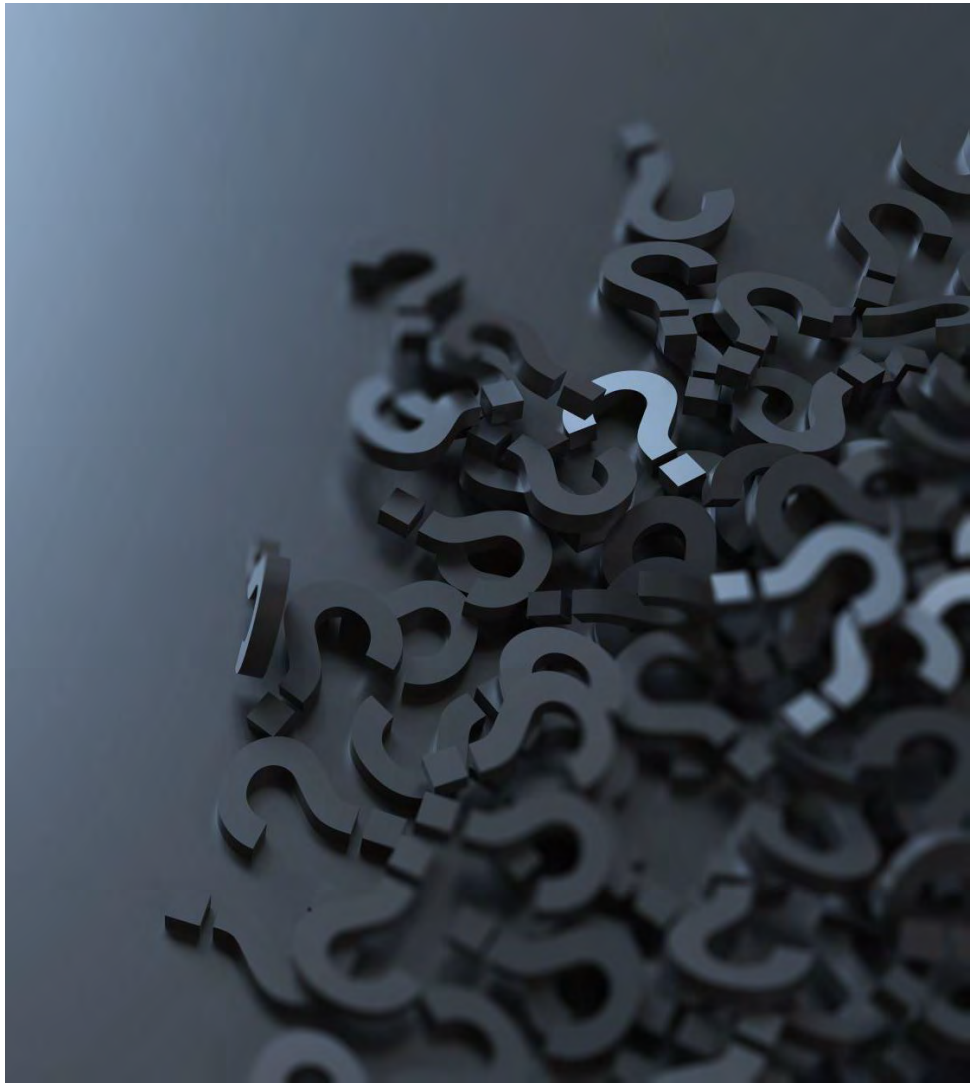
Safety

Tolerability

Efficacy

Price

Simplicity



Reflections on New Meds

- Which of these will you consider integrating into your practice?
- Which of these is the most "game-changing" and why?

VACCINES

RSV (mResvia)

FDA approval: Prevention of lower respiratory tract disease caused by respiratory syncytial virus in individuals 60 years of age and older

Single dose 0.5 mL

Frozen, prefilled syringe

Adverse reactions: injection site pain (55.9%), fatigue (30.8%), headache (26.7%), myalgia (25.6%), arthralgia (21.7%), axillary swelling/tenderness (15.2%), chills (11.1%)

RSV (mResvia)

Table 4: Efficacy of MRESVIA to Prevent First Episode of Protocol-Defined RSV-LRTD (Per-Protocol Efficacy Set)

Primary Analyses 3.7 months median follow-up	**MRESVIA (N=17,561) n (%)**	**Placebo (N=17,503) n (%)**	**Vaccine Efficacy* Based on Hazard Ratio (%) (% CI†)**
RSV-LRTD With 2 or More Signs/Symptoms	15 (0.09)	70 (0.40)	78.7 (62.8, 87.9)
RSV-LRTD With 3 or More Signs/Symptoms	5 (0.03)	26 (0.15)	80.9 (50.1, 92.7)
Additional Analyses 8.6 months median follow-up	**MRESVIA (N=18,074) n (%)**	**Placebo (N=18,010) n (%)**	**Vaccine Efficacy* Based on Hazard Ratio (%) (% CI†)**
RSV-LRTD With 2 or More Signs/Symptoms	48 (0.27)	127 (0.71)	62.5 (47.7, 73.1)
RSV-LRTD With 3 or More Signs/Symptoms	20 (0.11)	51 (0.28)	61.1 (34.7, 76.8)

RSV Vaccine: CDC Schedule

Included on SC Board of Pharmacy Protocol to administer to patients WITHOUT a prescription

Pregnancy:

- 1 dose 32 weeks 0 days through 36 weeks and 6 days gestation from September through January
  - No data on additional doses for subsequent pregnancies
- Abryso®

Patients 60-74

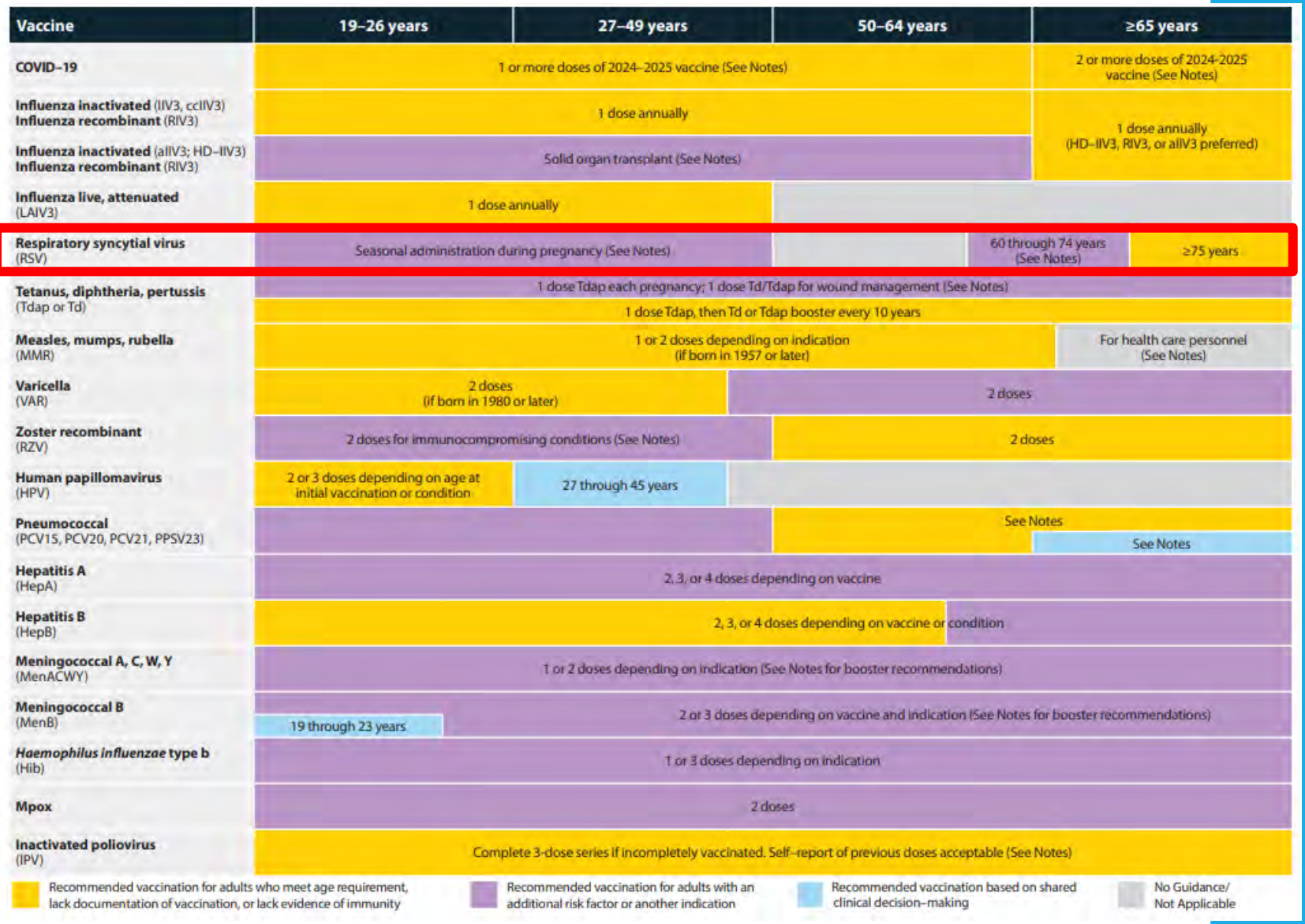
- Shared decision making
- Consider for patients at high risk of severe RSV disease (i.e. lung disease, cardiovascular disease, kidney disease, etc.)
- Can get at any time, but best in August-October before RSV spreads
- Arexvy®, Abryso®, or mResvia®

Patients 75 and older

- Vaccinate (1 dose)
- Arexvy®, Abryso®, or mResvia®

https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf

2025 IMMUNIZATION SCHEDULE



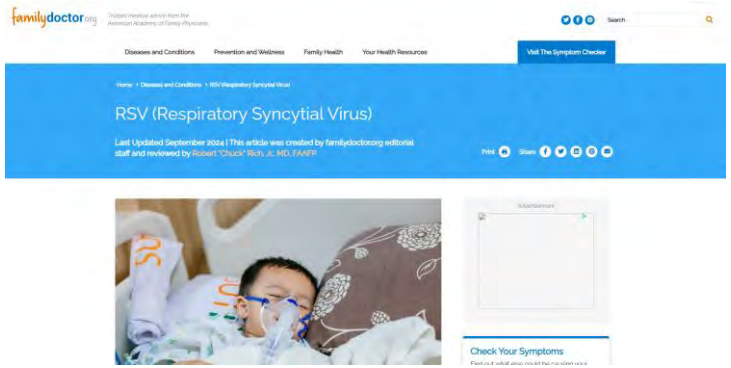
Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID-19	1 or more doses of 2024–2025 vaccine (See Notes)			2 or more doses of 2024-2025 vaccine (See Notes)
Influenza inactivated (IIV3, ccIIV3) **Influenza recombinant** (RIV3)	1 dose annually			1 dose annually (HD–IIV3, RIV3, or aIIV3 preferred)
Influenza inactivated (aIIV3; HD–IIV3) **Influenza recombinant** (RIV3)	Solid organ transplant (See Notes)			
Influenza live, attenuated (LAIV3)	1 dose annually			
Respiratory syncytial virus (RSV)	Seasonal administration during pregnancy (See Notes)		60 through 74 years (See Notes)	≥75 years
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (See Notes)			
	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			For health care personnel (See Notes)
Varicella (VAR)	2 doses (if born in 1980 or later)		2 doses	
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (See Notes)		2 doses	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal (PCV15, PCV20, PCV21, PPSV23)			See Notes	
				See Notes
Hepatitis A (HepA)	2, 3, or 4 doses depending on vaccine			
Hepatitis B (HepB)	2, 3, or 4 doses depending on vaccine or condition			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication (See Notes for booster recommendations)			
Meningococcal B (MenB)	19 through 23 years	2 or 3 doses depending on vaccine and indication (See Notes for booster recommendations)		
***Haemophilus influenzae* type b** (Hib)	1 or 3 doses depending on indication			
Mpox	2 doses			
Inactivated poliovirus (IPV)	Complete 3-dose series if incompletely vaccinated. Self-report of previous doses acceptable (See Notes)			

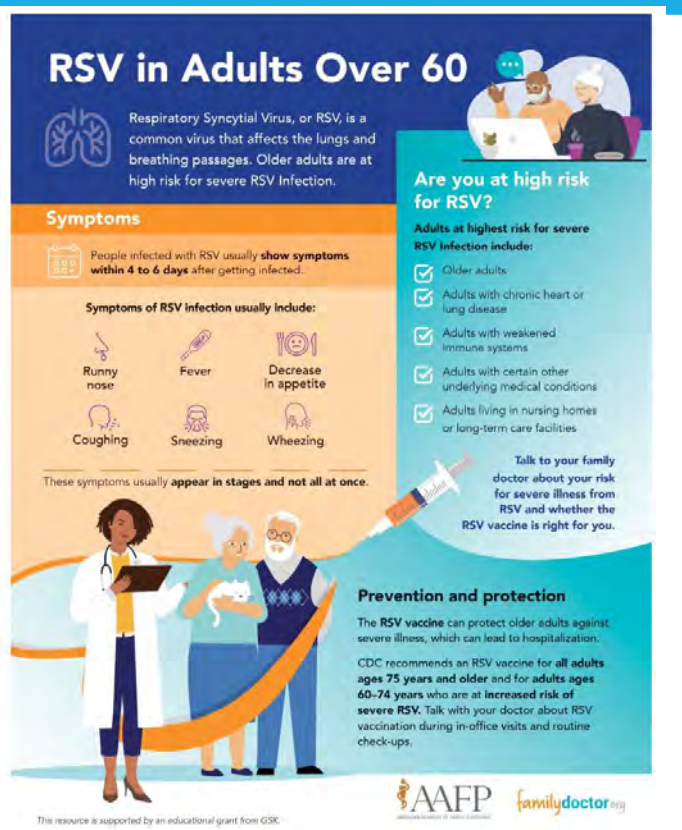
Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of immunity

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No Guidance/ Not Applicable





PATIENT INFORMATION

PCV21 (Capvaxive)

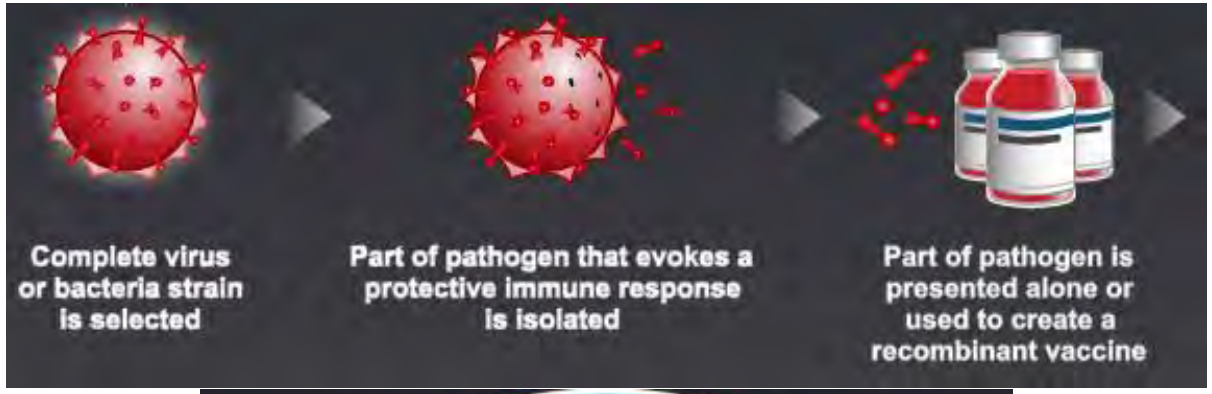
- FDA approval: prevent invasive pneumococcal disease in patients 18 and older
  - Conjugated vaccine

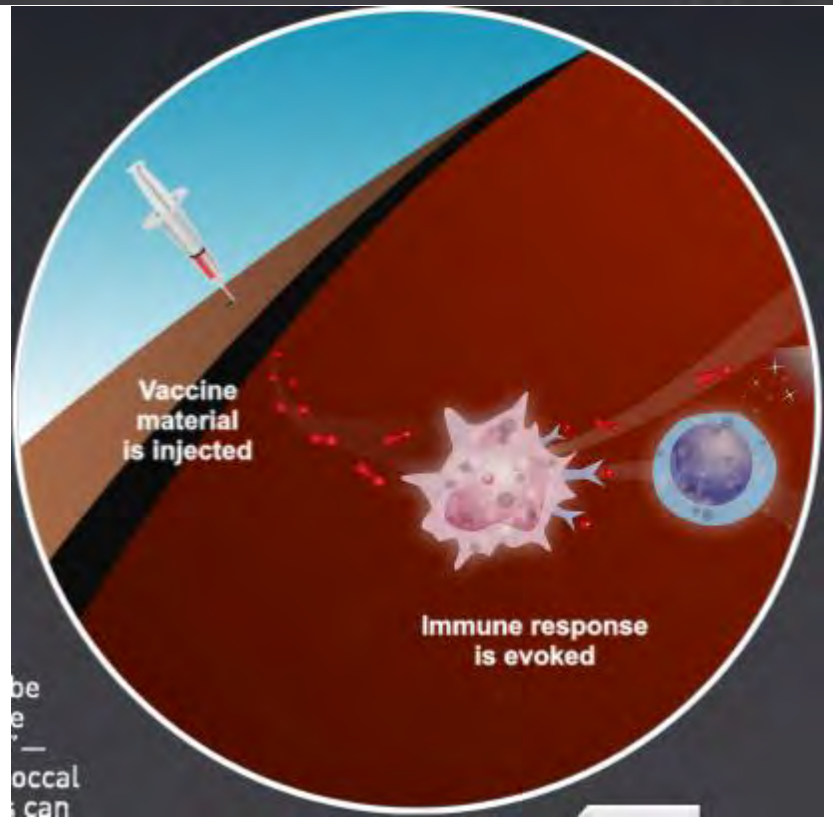
- Covers 21 serotypes
  - Note does NOT cover serotype 4, which there have recently been high rates of in Alaska, Colorado, Navajo Nation, New Mexico, and Oregon

- Dose: 0.5 mL IM

TYPES OF VACCINES

Type of Vaccine		Examples
Live	Attenuated	• MMR • Varicella • Influenza nasal • Rotavirus • Zoster (Zostavax) • Yellow Fever • Typhoid
Inactivated	Killed	• Polio • Hepatitis A • Rabies
	Subunit/conjugate	• Pertussis • Hepatitis B • Influenza • Pneumococcal • Meningococcal • Human papillomavirus
	Toxoid	• Diptheria/tetanus
	Adjuvanted	• Fluad • Zoster (Shingrix) • RSV (Arexvy)
	mRNA	• Pfizer & Moderna Covid vaccines • RSV (mResvia)





Subunit or Conjugate

https://www.historyofvaccines.org/content/types-vaccines

Subunit or Conjugate

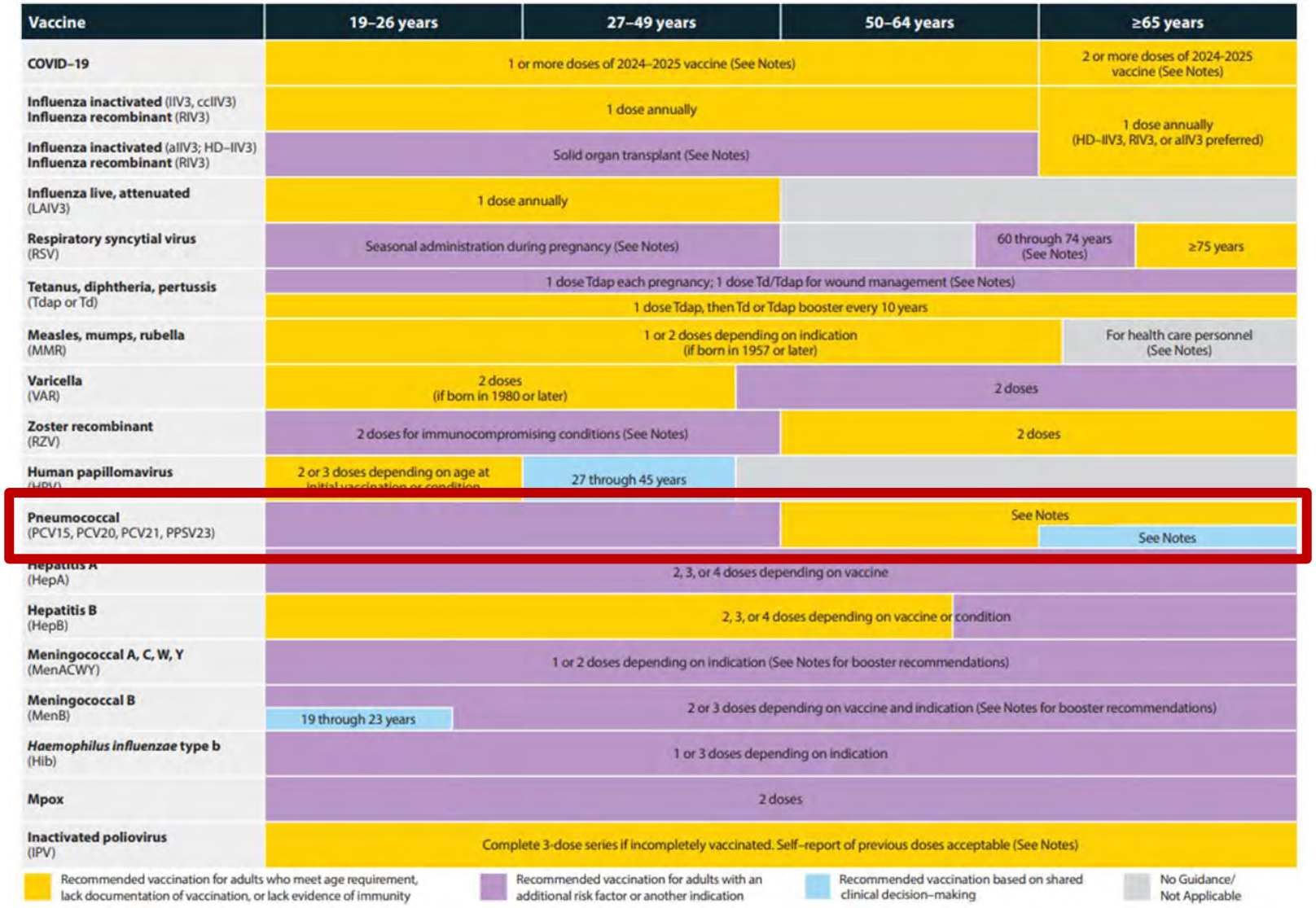
Polysaccharide

- Stimulate T-cell INDEPENDENT immunity
- Short-lived immunity
- No booster
- Not as effective in pediatric patients

Conjugate Polysaccharide

- Stimulate T-cell DEPENDENT immunity
- Immunological memory
- Booster effect
- Better immunogenicity in pediatric patients

2025 CDC Vaccine Schedule



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Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of immunity

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No Guidance/ Not Applicable

2025 CDC Vaccine Schedule

Routine vaccination

- **Age 50 years or older who have:**
  - **Not previously received a dose of PCV13, PCV15, PCV20, or PCV21 or whose previous vaccination history is unknown:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21
    - If PCV15 is used, administer 1 dose PPSV23 at least 1 year after the PCV15 dose (may use minimum interval of 8 weeks for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak).
  - **Previously received only PCV7:** follow the recommendation above.
  - **Previously received only PCV13:** 1 dose PCV20 or 1 dose PCV21 at least 1 year after the last PCV13 dose
  - **Previously received only PPSV23:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21, at least 1 year after the last PPSV23 dose.
    - If PCV15 is used, no additional PPSV23 doses are recommended.
  - **Previously received both PCV13 and PPSV23 but NO PPSV23 was received at age 65 years or older:** 1 dose PCV20 or 1 dose PCV21 at least 5 years after the last pneumococcal vaccine dose.
  - **Previously received both PCV13 and PPSV23, AND PPSV23 was received at age 65 years or older:** Based on shared clinical decision–making, 1 dose of PCV20 or 1 dose of PCV21 at least 5 years after the last pneumococcal vaccine dose.

NEW as of October 2024- ACIP reduced age for routine vaccination to 50 years (was 65+)

Recommendation for patients <50 with risk still need vaccine as well

Special situations

- **Age 19–49 years with certain underlying medical conditions or other risk factors** who have:**
  - **Not previously received a PCV13, PCV15, PCV20, or PCV21 or whose previous vaccination history is unknown:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21
    - If PCV15 is used, administer 1 dose PPSV23 at least 1 year after the PCV15 dose (may use minimum interval of 8 weeks for adults with an immunocompromising condition,* cochlear implant, or cerebrospinal fluid leak).
  - **Previously received only PCV7:** follow the recommendation above.
  - **Previously received only PCV13:** 1 dose PCV20 or 1 dose PCV21 at least 1 year after the last PCV13 dose
  - **Previously received only PPSV23:** 1 dose PCV15 or 1 dose PCV20 or 1 dose PCV21, at least 1 year after the last PPSV23 dose.
    - If PCV15 is used, no additional PPSV23 doses are recommended.
  - **Previously received PCV13 and 1 dose of PPSV23:**
    - Cochlear implant, cerebrospinal fluid leak, or an immunocompromising condition*: 1 dose PCV20 or 1 dose PCV21 at least 5 years after the last pneumococcal vaccine dose.
    - Alcoholism, chronic heart/liver/lung disease, cigarette smoking, or diabetes mellitus: no additional PCV or PPSV23 doses recommended at this time. Review pneumococcal recommendations when age 50 years or older.

Adults aged 19 years and older who have received PCV20 or PCV21: no additional pneumococcal vaccine dose recommended.

Initial options

- PCV15, then PPSV23
- PCV20
- PCV21

Serotype	PCV21 (Capvaxive)	PPSV23 (Pneumovax 23)	PCV20 (Prevnar 20)	PCV15 (Vaxneu-vance)
1		■	■	■
3	■	■	■	■
4		■	■	■
5		■	■	■
6A	■		■	■
6B		■	■	■
7F	■	■	■	■
9V		■	■	■
14		■	■	■
18C		■	■	■
19A	■	■	■	■
19F		■	■	■
23F		■	■	■
22F	■	■	■	■
33F	■	■	■	■
8	■	■	■	
10A	■	■	■	
11A	■	■	■	
12F	■	■	■	
15B		■	■	
2		■		
9N	■	■		
17F	■	■		
20	■	■		
15A	■			
15C	■			
16F	■			
23A	■			
23B	■			
24F	■			
31	■			
35B	■			

PCV = pneumococcal conjugate vaccine; PPSV = pneumococcal polysaccharide vaccine.

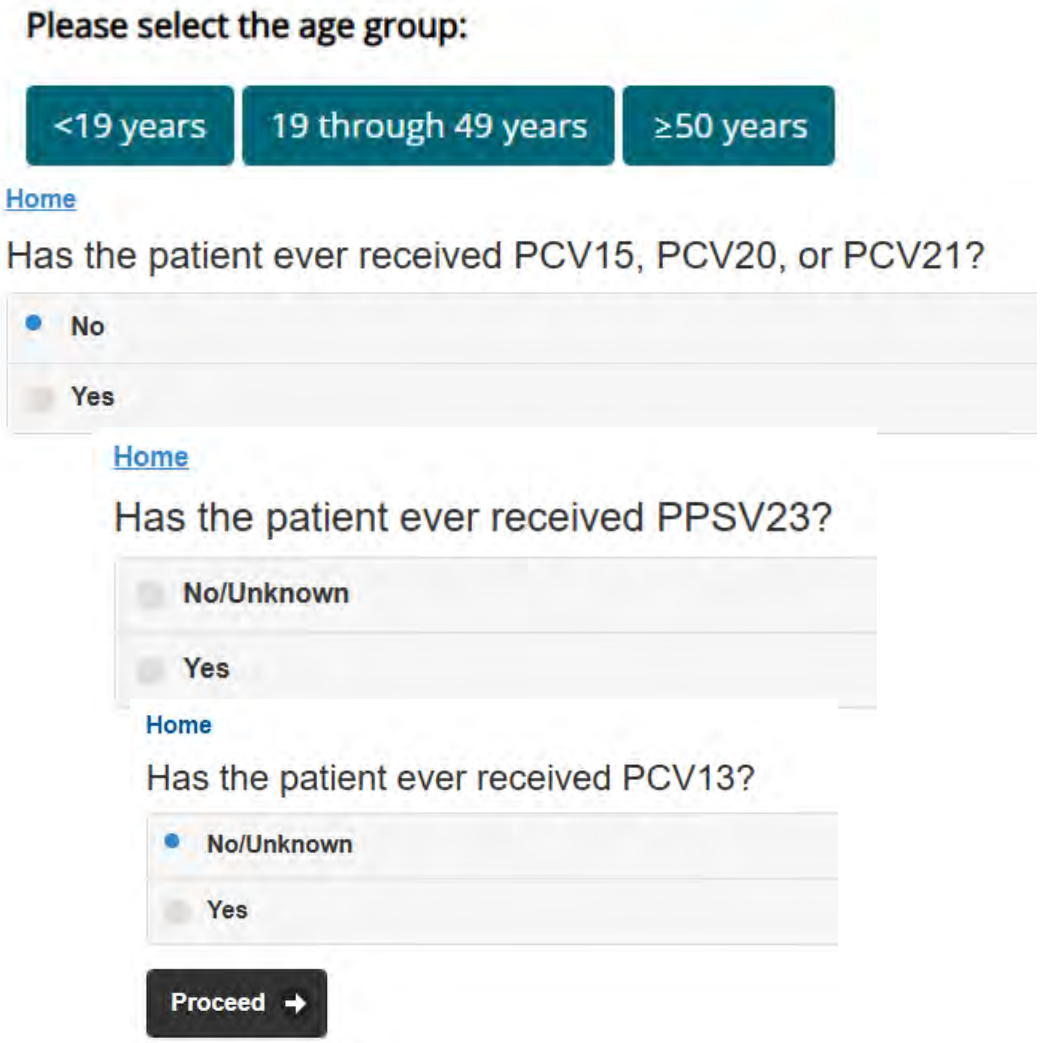
TABLE 2

Selected Recommendations for Catch-Up Pneumococcal Vaccination in Adults

Previously received vaccines	Recommendations
Adults ≥ 65 years of age	
None or PCV7 only, at any age	Single dose of PCV21, PCV20, or PCV15; if PCV15 is administered, a single dose of PPSV23* should be administered ≥ 1 year after the PCV15 dose
PPSV23 only	Single dose of PCV21, PCV20, or PCV15 ≥ 1 year after the last PPSV23 dose
PCV13 only	Single dose of PCV21, PCV20, or PPSV23 ≥ 1 year after the PCV13 dose
Adults 19 to 64 years of age with chronic medical conditions†	
None or PCV7 only at any age	Single dose of PCV21, PCV20, or PCV15; if PCV15 is administered, a single dose of PPSV23* should be administered ≥ 1 year after the PCV15 dose
PPSV23 only	Single dose of PCV21, PCV20, or PCV15 ≥ 1 year after the last PPSV23 dose
PCV13 only	Single dose of PCV21, PCV20, or PPSV23 ≥ 1 year after the PCV13 dose
PCV13 and 1 dose of PPSV23	The pneumococcal vaccination recommendations should be reviewed again when the person reaches 65 years of age

AAFP RECOMMENDATIONS FOR CATCH-UP

Clear as mud?



PneumoRecs
VaxAdvisor

Available for iOS and Android

Recommendation

Give one dose of PCV15, PCV20, or PCV21. If PCV20 or PCV21 is used, their pneumococcal vaccinations are complete. If PCV15 is used, follow with one dose of PPSV23[1] to complete their pneumococcal vaccinations. The recommended interval between PCV15 and PPSV23 is at least 1 year. The minimum interval is 8 weeks and can be considered in adults with immunocompromising conditions[2], cochlear implants, or cerebrospinal fluid leaks.

PSYCH & MIGRAINE

Xanomeline/trospium chloride (Cobenfy)

FDA approval: treatment of schizophrenia

Dosing: 50/20 mg twice a day for ≥ 2 days, then 100/20 mg twice a day for ≥ 5 days, then 125/30 mg twice a day if needed

- Give 1 hour before or 2 hours after a meal

Mechanism of action: xanomeline (muscarinic agonist) and trospium (muscarinic antagonist)

1st medication for schizophrenia that targets cholinergic receptors and not dopamine receptors

No superiority data over other agents

Xanomeline/trospium chloride (Cobenfy)

Adverse effects: urinary retention, tachycardia, decreased gastric movement, or angioedema

Cost: $1900 for 1 month

Place in therapy:

- Defer to specialists, but just to know this drug is out there in case you see the patient for its side effects (urinary retention, tachycardia)

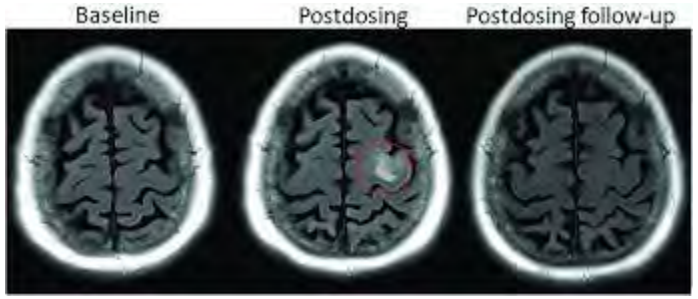
Donanemab-azbt (Kisunla)

FDA approval: treatment patients with Alzheimers with mild cognitive impairment or mild dementia

Dosing: 700 mg IV every 4 weeks x 3, then 1400 mg every 4 weeks

MOA: beta-amyloid monoclonal antibodies

Donanemab-azbt (Kisunla)



Monitoring:

- MRI at baseline, then prior to 2nd, 3rd, 4th, 7th infusions due to risk of amyloid related imaging abnormalities (ARIA)

Side effects:

- BBW ARIA (usually asx, but can cause serious/life threatening events such as intracerebral hemorrhages and ischemic stroke)
- Infusion-related reaction (slow infusion rate, pretx with antihistamines, APAP, and CSs)

Efficacy:

- Cognitive decline slowed by about 4.5-7.5 months
- Almost 50% of those taking the drug remained at the same cognitive level after 1 year in the study, versus 29% of placebo

Cost: $32,000/year

- Compare to Leqembi ($26,500/year),which Medicare estimates it will spend $3.5 billion on in 2025

Place in therapy: Limited, defer to specialists

A Note on Naming Convention

2017 FDA Guidance

- Biologic products must "bear a nonproprietary name that includes an FDA-designated suffix"
  - Suffix must be "devoid of meaning and composed of 4 lowercase letters…attached with a hyphen to the core name"
- Applies to new biologic products as well as biosimilars and follow-on biologics
- Aim is to help minimize inadvertent substitutions for products that aren't interchangeable

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM459987.pdf

Zuranolone (Zurzuvae)

FDA approval: treatment of postpartum depression (monotherapy or adjunct to other antidepressants)

- Schedule IV controlled substance

Dosing: 50 mg daily in the evening for 14 days with fat-containing food

Mechanism of action: neuroactive steroid GABA A receptor positive modulator

Zuranolone (Zurzuvae)

WARNING: IMPAIRED ABILITY TO DRIVE OR ENGAGE IN OTHER POTENTIALLY HAZARDOUS ACTIVITIES

See full prescribing information for complete boxed warning.

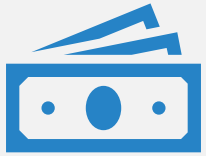
ZURZUVAE causes driving impairment due to central nervous system (CNS) depressant effects. Advise patients not to drive or engage in other potentially hazardous activities until at least 12 hours after administration. Patients may not be able to assess their own driving competence or the degree of impairment caused by ZURZUVAE *(5.1, 5.2)*.

Adverse reactions: somnolence, dizziness, diarrhea, fatigue, nasopharnygitis, UTI

Lactation:

- Present in human milk at low levels
- Limited data on effects on infant and milk production
- "The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZURZUVAE and any potential adverse effects on the breastfed child from ZURZUVAE or from the underlying maternal condition"

Zuranolone (Zurzuvae)



Cost: $15,900 for 14 days

Place in therapy: LIMITED due to cost; side effect profile (and it being PO) is much improved compared to other drug for postpartum depression on the market (brexanolone or Zulresso), but not sure it will be worth it

PAIN

Zavegepant (Zavzpret)

FDA approval: acute treatment of migraine with or without aura

Dosing: 10 mg (1 spray) PRN

- Max dose per day 10 mg

Mechanism of action: calcitonin gene-related peptide receptor (CGRP) antagonist (CGRP is a vasodilator/pain sensitizer present during a migraine)

- Only nasal spray in the class available

Zavegepant (Zavzpret)

Side effects: taste disturbance, nausea, nasal discomfort, vomiting

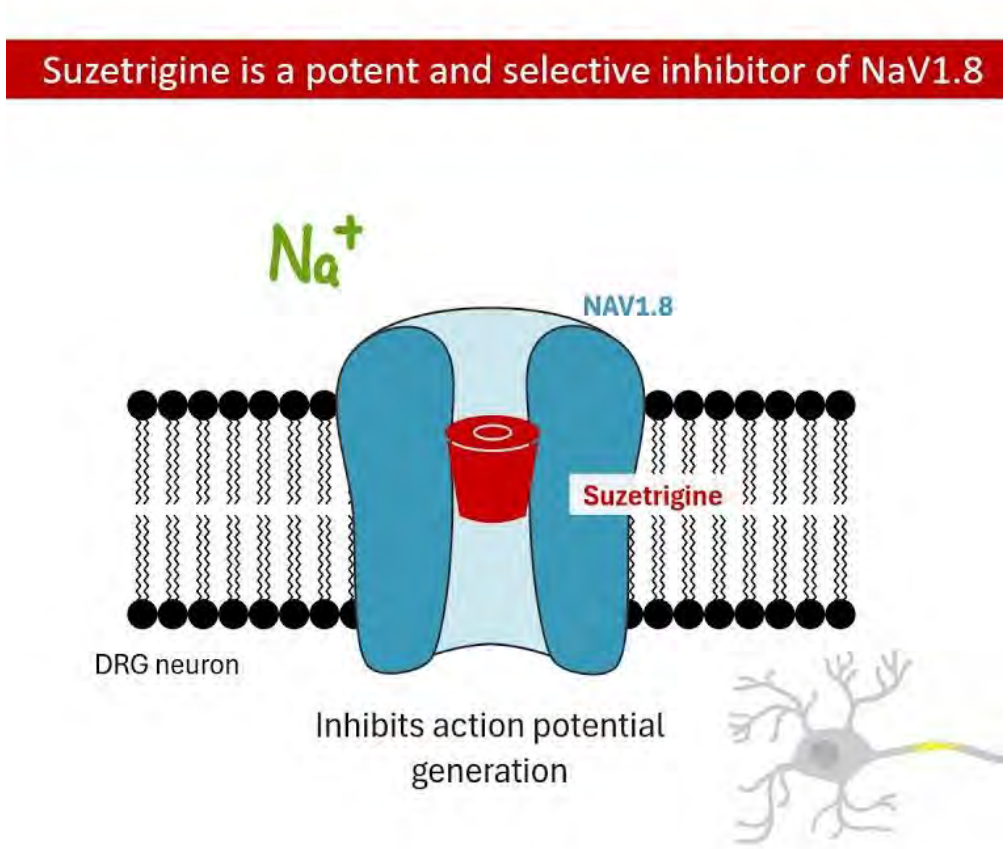
Cost: $1000/6 sprays

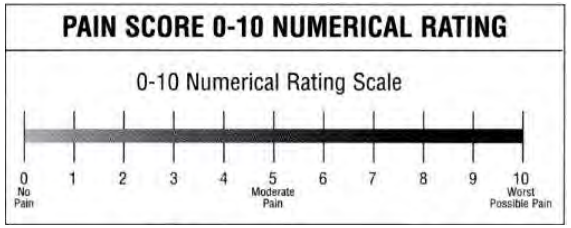
Place in therapy: Maybe an option if it becomes cheaper, or for patients with severe nausea/vomiting with their migraines

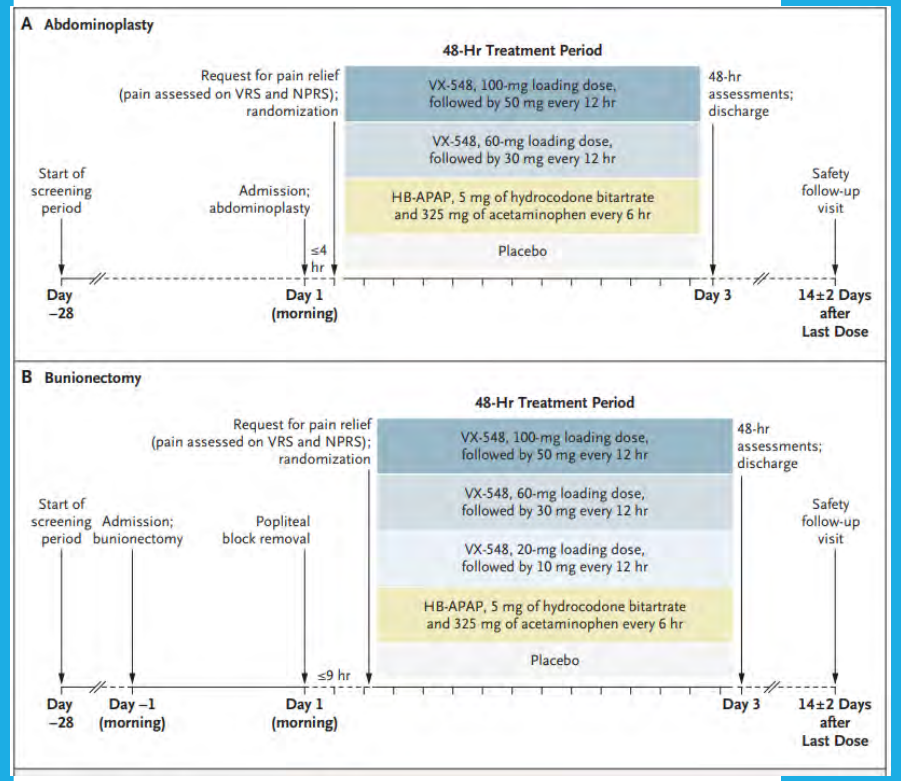
- Other abortive CGRP options: Nurtec (Rimegepant), Qulipta (atogepant), Ubrelvy (Ubrogepant)
- Less effective than triptans, can be used if triptans don't work or patient can't take triptans (prior MI/stroke, etc)
  - However, less likely to cause overuse headache than triptans, butalbital, etc
- Limited data if can be taken with triptans, but probably not harmful
- Also limited data if can be used with preventive CGRP antagonists, but also probably not harmful

Suzetrigine (Journavx)

- FDA approval: treatment of moderate to severe acute pain
  - "With the approval of JOURNAVX, a non-opioid, pain signal inhibitor and the first new class of pain medicine approved in more than 20 years, we have the opportunity to change the paradigm of acute pain management and establish a new standard of care."
- Dosing (oral): 100 mg, then 50 mg q12 hours
  - 1st dose must be taken on an empty stomach, subsequent doses can be with or without food
  - Take for shortest duration possible (not studied >14 days)
- Mechanism of action
  - Potent and selective inhibitor of voltage-gated sodium channel 1.8 ($Na_V1.8$)
    - Pain target that is selectively expressed in peripheral pain-sensing neurons and not in the CNS







Suzetrigine (Journavx)

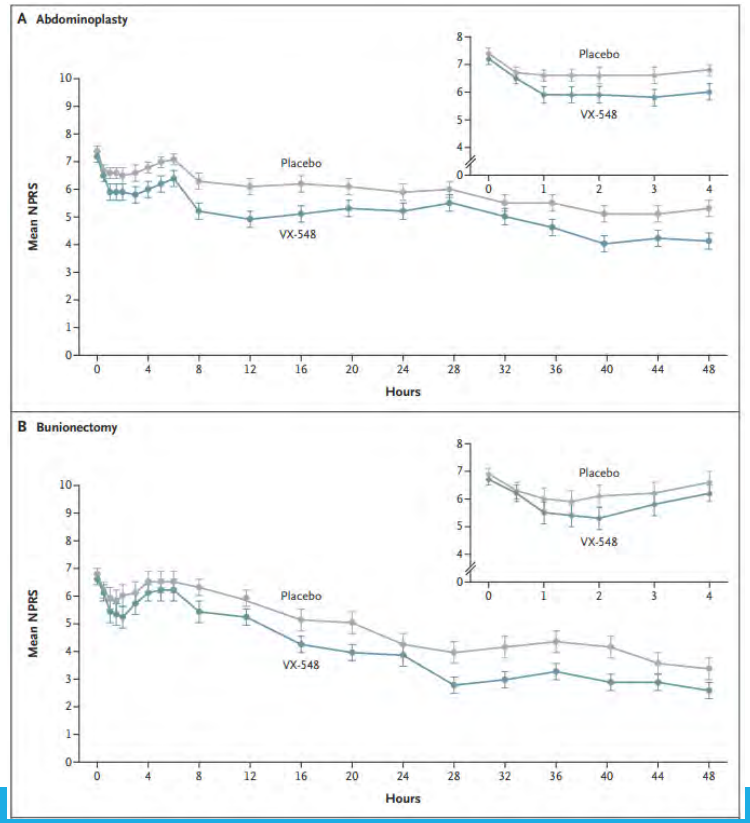
- Efficacy data
  - Studied in patients with acute pain after abdominoplasty or bunionectomy
  - 2 randomized, double blind, placebo controlled trials
    - High dose: 100 mg x 1, then 50 mg BID
    - Middle dose: 60 mg x 1, then 30 mg BID
    - Hydrocodone/APAP 5mg/325 mg q6 hours
    - Placebo q6 hours
  - Reduction in pain measured by NPRS Score (Numeric Pain Rating Scale)

	Suzetrigine		Hydrocodone/APAP		Placebo	
	Abdominoplasty (n=76)	Bunionectomy (n=60)	Abdominoplasty (n=76)	Bunionectomy (n=60)	Abdominoplasty (n=77)	Bunionectomy (n=59)
LSM differences vs placebo	37.8+/-14.5	36.8 +/-16.3	12.5+/-14.5	14.7 +/-16.3	N/A	N/A
≥30% pain reduction @ 48 hours-n(%)	46 (61)	50 (83)	41 (54)	41 (68)	37 (48)	40 (68)
≥50% pain reduction @ 48 hours-n(%)	34 (45)	40 (67)	32 (42)	37 (62)	26 (34)	36 (61)
≥70% pain reduction @ 48 hours-n(%)	19 (25)	31 (52)	18 (24)	30 (50)	11 (14)	24 (41)

SUZETRIGINE (JOURNAVX)

Suzetrigine (Journavx)

	Suzetrigine		Hydrocodone/APAP		Placebo	
	Abdominoplasty (n=76)	Bunionectomy (n=60)	Abdominoplasty (n=76)	Bunionectomy (n=60)	Abdominoplasty (n=77)	Bunionectomy (n=59)
Any adverse event- n (%)	42 (55)	18 (30)	46 (61)	25 (42)	54 (70)	23 (39)



VX-548=suzetrigine at dose of 100 mg load, then 50 mg BID

Suzetrigine (Journavx)

- Side effects: pruritic, muscle spasms, increased creatine phosphokinase, rash
  - Avoid with strong CYP3A inhibitors (and grapefruit juice)
- Cost: ~$500 for 28 tablets (50 mg) for a 14 day course
- Place in therapy:
  - Appreciate a non-opioid option for acute pain
  - NOT a controlled substance (no risk of addiction)
  - Cost is a huge limitation

WOMEN'S HEALTH

Sulopenem etzadroxil/ probenecid (Orlynvah)

FDA approval: treatment of uncomplicated urinary tract infection(s) (uUTI) caused by certain bacteria (*Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis*) in adult women who have limited or no alternative oral antibacterial treatment options

Last drug approved for uncomplicated UTI last in 1996 (fosfomycin)

Dosing: 500 mg/500 mg twice a day for 5 days

MOA:

Sulopenem: penem antibiotic

Probenecid: reducing the kidney clearance of sulopenem, this increases the concentration

Sulopenem etzadroxil/probenecid (Orlynvah)

Efficacy: compared to ciprofloxacin and amoxicillin/clavulanic acid

- Sulopenem etzadroxil/probenecid was superior at 62.6% compared with ciprofloxacin at 36%
- Clinical success and microbiological success were 77.3% with 75.2% sulopenem etzadroxil/probenecid, respectively, and 76.7% and 66.7% with amoxicillin/clavulanic acid, respectively

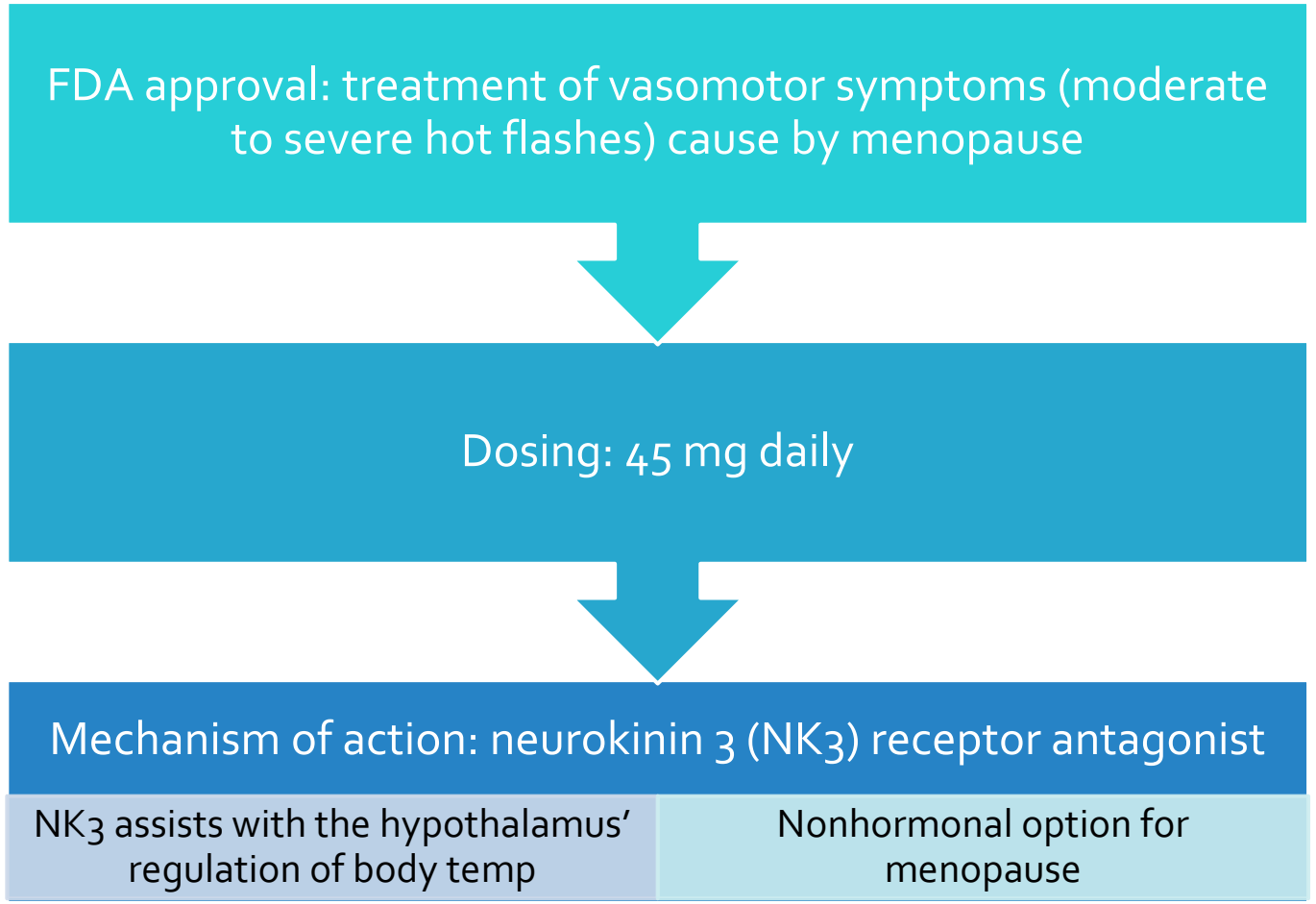
Adverse effects: diarrhea (worse than comparators), nausea, vulvovaginal mycotic infection, headache, and vomiting

Cost: TBD (FDA approved 10/24/24)

Place in therapy: could be an option for patients resistant to other first line agents

- Fosfomycin is probably still cheaper

Fezolinetant (Veozah)



Fezolinetant (Veozah)

- Monitoring: hepatic function at baseline, monthly x 3 months, then at 3 & 9 months of treatment
  - Discontinue if LFTs >5 x ULN or LFTs >3 x ULN and total bili >2 x ULN

Adverse reactions: abdominal pain, diarrhea, insomnia, back pain, hot flush

Cost: $550/month

Place in therapy: okay for the right patient who wants a nonhormonal option for hot flashes (and has tried other options first)

FDA adds warning about rare occurrence of serious liver injury with use of Veozah (fezolinetant) for hot flashes due to menopause

Stop medicine if signs and symptoms of liver injury occur

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Español | 药物安全通讯 | Drug Safety Podcast

09-12-2024 FDA Drug Safety Communication

Drug Safety Communication (PDF - 189 KB)

- What safety concern is FDA announcing?
- What is FDA doing?
- What is Veozah (fezolinetant) and how can it help me?
- What should patients and parents/caregivers do?
- What should health care professionals do?
- What did FDA find?

PULM

Ensifentrine (Ohtuvayre)

FDA approval: COPD maintenance

Dosing: 3 mg via nebuilizer twice a day

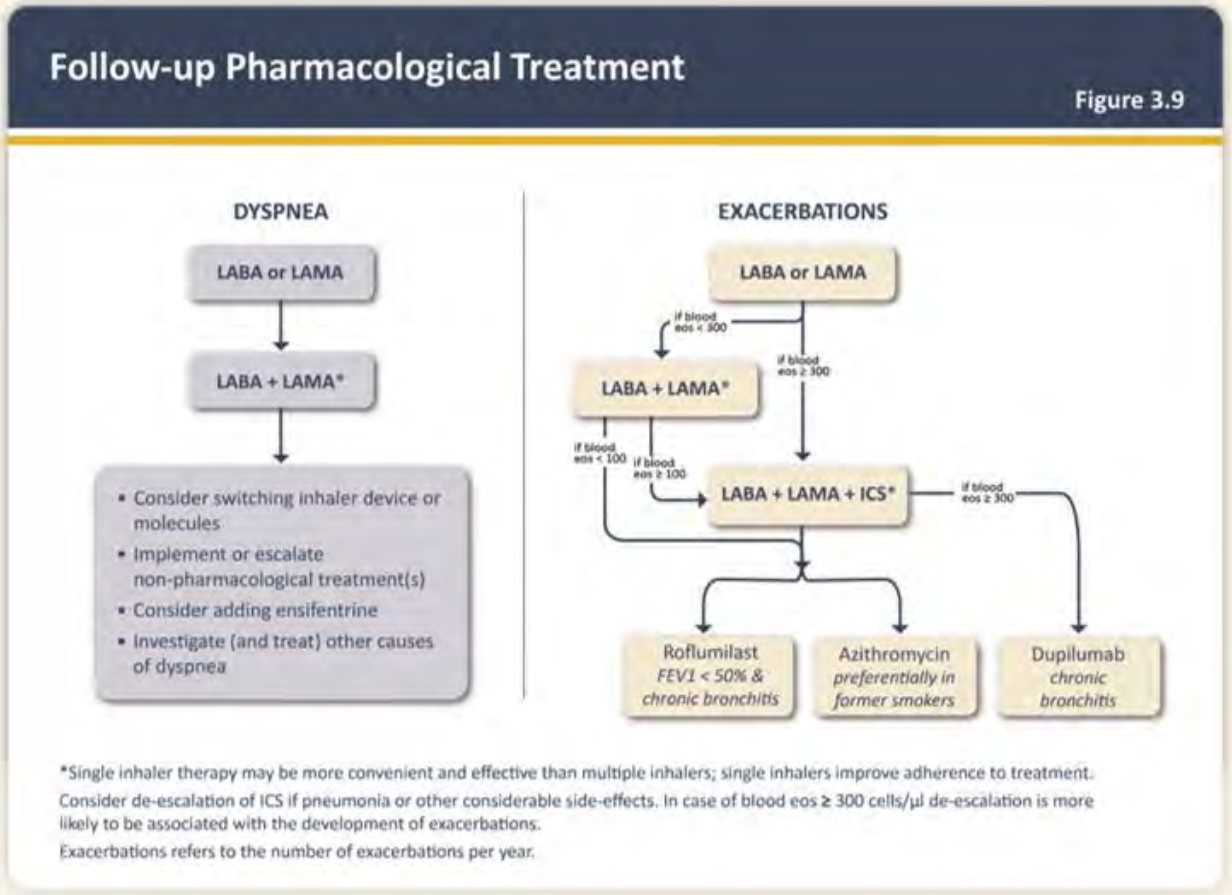
Mechanism of action: PDE3/4 inhibitor → bronchodilation

- "Help your patients reclaim their breath with Ohtuvayre, a novel approach to bronchodilation and non-steroidal anti-inflammation"

Ensifentrine (Ohtuvayre)

- Efficacy:
  - Clinical trials included patients on a LABA or LAMA +/- ICS, but NOT on triple therapy or LABA/LAMA
  - Improvement in FEV1, QOL (based on St. George's Respiratory Questionnaire)
  - Reduction in exacerbation risk by 36-43% (although patients selected were at lower exacerbation risk at baseline)
- Cost: $3000/month
- Place in therapy: probably specialists for now due to cost, but is a promising option in the future for patients on dual therapy with dyspnea

2025 GOLD GUIDELINES: COPD



- Ensifentrine significantly improves lung function **(Evidence A)**, dyspnea **(Evidence A)** and health status **(Evidence B)**

OVER-THE-COUNTER

OTC CGMs

- Stelo by Dexcom
- Approved for patients 18+ with T2DM not on insulin
- Cost: $99/2 sensors
  - Also a subscription model for $89/month

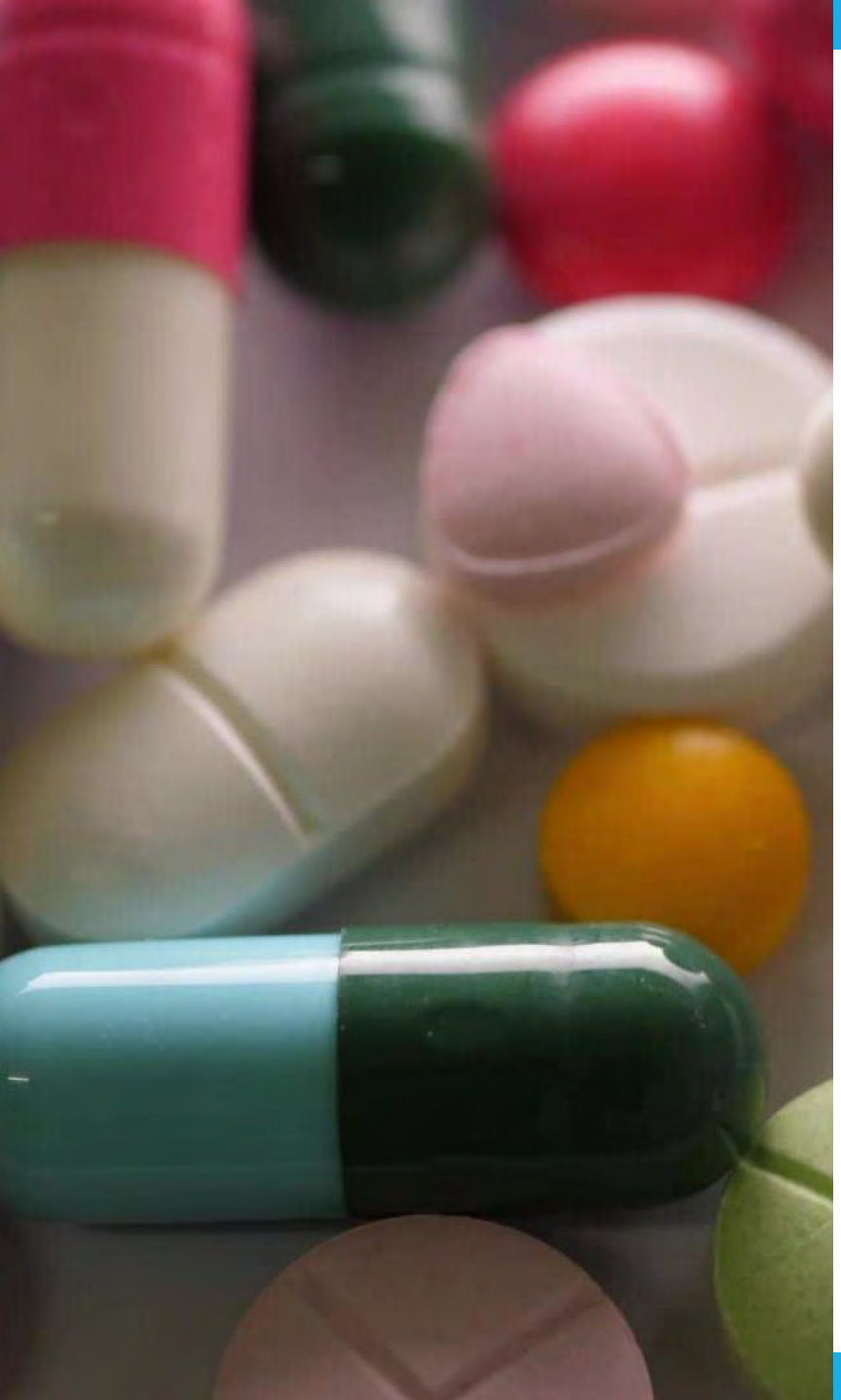
https://www.reuters.com/business/healthcare-pharmaceuticals/dexcom-announces-launch-over-the-counter-continuous-glucose-monitor-2024-08-26/?utm_source=MarketingCloud&utm_medium=email&utm_campaign=PT+Daily+August+28%2c+2024&utm_content=PT+Daily+August+28%2c+2024

OTC CGMs

- Freestyle Libre Rio
  - Patients 18+ not on insulin (T2DM or prediabetes)
  - No cost yet
- Freestyle Lingo
  - Patients 18+ for health and wellness
  - Only compatible with iPhone currently
  - Cost:
    - 2 weeks: $49
    - 4 weeks: $89
    - 12 week subscription: $249

Abbott Enters U.S. Consumer Biowearables Market With Lingo and Libre Rio | Abbott Newsroom
Lingo - Made by Abbott: Your body has the answers (hellolingo.com)

DRUG SHORTAGES



Medication shortages

- FDA works with manufacturers to publicly report drugs in short supply
  - Goal: prevent or reduce impact of shortages
- GLP1 drug shortage started late 2022
- As of 3/21/25…
  - Dulaglutide and liraglutide in shortage
  - Tirzepatide and semaglutide shortages resolved

https://www.statnews.com/2024/08/27/lilly-launches-zepbound-vials-in-move-that-could-ease-supply-constraints/?utm_source=MarketingCloud&utm_medium=email&utm_campaign=PT+Daily+August+28%2c+2024&utm_content=PT+Daily+August+28%2c+2024

FDA alerts health care providers, compounders and patients of dosing errors associated with compounded injectable semaglutide products

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What health care providers, compounders and patients should know

FDA has received reports of adverse events, some requiring hospitalization, that may be related to overdoses due to dosing errors associated with compounded semaglutide injectable products. Dosing errors have resulted from patients measuring and self-administering incorrect doses of the drug and health care providers miscalculating doses of the drug.

FDA encourages patients to talk with their health care provider or compounder about how to measure and administer the intended dose of compounded semaglutide.

Many of the patients who received vials of compounded semaglutide lacked experience with self-injections, according to the adverse event reports. Unfamiliarity with withdrawing medication from a vial into a syringe and coupled with confusion between different units of measurement (e.g., milliliters, milligrams and “units”) may have contributed to dosing errors.

FDA encourages health care providers and compounders to provide patients with the appropriate syringe size for the intended dose and counsel patients on how to measure the intended dose using the syringe.

What about compounded GLP1s?

- Not recommended
- Pharmacies cannot compound commercially available drugs, except in shortage situations

https://www.fda.gov/drugs/human-drug-compounding/fda-alerts-health-care-providers-compounders-and-patients-dosing-errors-associated-compounded
https://www.businessinsider.com/buy-compounded-semaglutide-online-risks-wegovy-ozempic-2023-1

FDA clarifies policies for compounders as national GLP-1 supply begins to stabilize

[3-10-25] FDA is providing the following timeline updates for compounders:

Tirzepatide: On March 5, 2025, the district court denied the plaintiffs' preliminary injunction motion in Outsourcing Facilities Association v. FDA, 4:24-cv-00953 (N.D. Tex.). Therefore, consistent with FDA's February 11, 2025 update:

- For a state-licensed pharmacy or physician compounding under section 503A of the FD&C Act, the period of enforcement discretion described below has ended.
- For outsourcing facilities under section 503B, FDA does not intend to take action against compounders for violations of the FD&C Act arising from conditions that depend on tirzepatide injection products' inclusion on FDA's drug shortage list until March 19, 2025.

Semaglutide: The timeframes during which the agency does not intend to take action against compounders for violations of the FD&C Act arising from conditions that depend on semaglutide injection products' inclusion on FDA's drug shortage list are:

- For a state-licensed pharmacy or physician compounding under section 503A of the FD&C Act, until April 22, 2025, or until the date of the district court's decision on the plaintiffs' forthcoming preliminary injunction motion in Outsourcing Facilities Association (OFA) v. FDA, 4:25-cv-00174 (N.D. Tex.), whichever is later.
- For outsourcing facilities under section 503B of the FD&C Act, until May 22, 2025, or until the date of the district court's decision on the plaintiffs' forthcoming preliminary injunction motion in OFA v. FDA, 4:25-cv-00174, whichever is later.

FDA CEASE AND DESIST ON 3/10/25

Allowed pharmacies 60 days to stop comounding

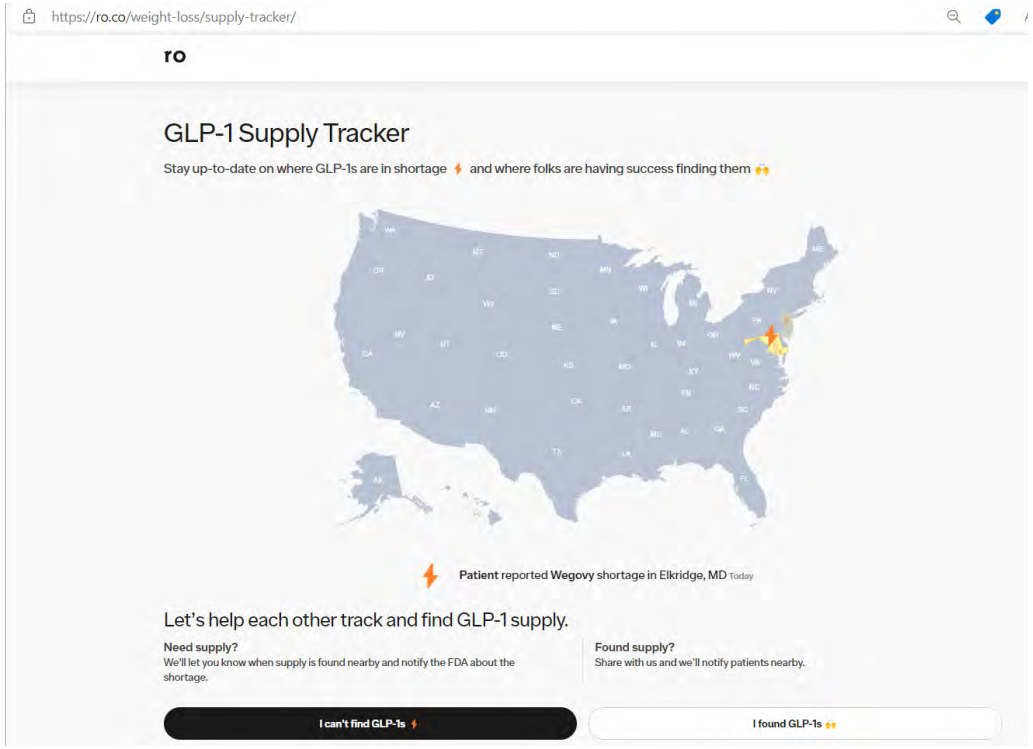
Compounded GLP1s

All GLP1s and GLP1/GIP are still under patent

- Manufacturers NOT selling raw drug

So how are pharmacies getting the drug?

- Using a different salt (semaglutide sodium or acetate, neither approved for human use)
- Using the oral tablet
- Use higher strength pens and dilute with water, vitamin B6, etc



Navigating drug shortages

- Switch to another medication in the same class
- Use alternate agents
- Switch pharmacies
- Crowdsourcing?
  - Ro GLP-1 Supply Tracker
- 2025 ADA guidelines
  - Use of compounded products that are not approved by the FDA is not recommended due to uncertainty about their content and resulting concerns about safety, quality, and effectiveness.
  - If a glucose-lowering medication is unavailable (e.g., in shortage), it is recommended to switch to a different FDA-approved medication with similar efficacy, as clinically appropriate.
  - Upon resolution of the unavailability (e.g., shortage), reassess the appropriateness of resuming the original FDA-approved medication.

Summary

Meds to consider using	Meds to consider using if not cost prohibitive	Meds for specialists
• RSV vaccine (mResvia) • Pneumococcal vaccine (PCV21)	• OTC CGMs (Stelo, Lingo, Rio) • Sulopenem etzadroxil/probenecid (Orlynvah) • Fezolinetant (Veozah) • Zavegepant (Zavzpret)	• Ensiferntrine (Ohtuvayre) • Xanomeline/trospium (Cobenfy) • Zuranolone (Zurzuvae) • Donanemab (Kinsula) • Suzetrigine (Journavx)

THANK YOU!

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