CME Disclosure Acknowledgement Notification

All relevant financial relationships have been mitigated.
All other planners/speakers have no financial relationships.

This form must be provided to learners prior to engaging in the educational program.

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2.00 of the 7.00 hours on pharmacotherapeutic education is pharmacotherapeutic/controlled substance prescriptive authority content. These 2.00 hours fulfill the South Carolina Board of Medical Examiners Opioid education mandate related to approved procedures of prescribing and monitoring controlled substances.

Financial Relationships:

Name	Name of Ineligible companies with which relevant financial relationships	Nature of Relationship
Dr. Robert Oliverio	Pfizer	Leadership Advisory Panel
Dr. Toby Fugate	Gilead Sciences	Speaker
Dr. Richard Pierce	Sensus Healthcare	Employee, Medical Director, Stockholder

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No Learner contact information will be shared without learner approval.
Additional Resources have been provided in the enduring presentations.

ROPER ST. FRANCIS HEALTHCARE

Drug Update 2025

Scott Bragg, PharmD
Professor MUSC College of Pharmacy
MUSC Department of Family Medicine

February 8, 2025

ROPER ST. FRANCIS HEALTHCARE

CME Disclosure Statement: F. Strait Fairey, MD – Primary Care Symposium 2025

Dr. Scott Bragg, speaker has no financial relationships with ineligible companies whose primary business is producing, marketing, selling re-selling, or distributing healthcare products used by or on patients.

Objectives

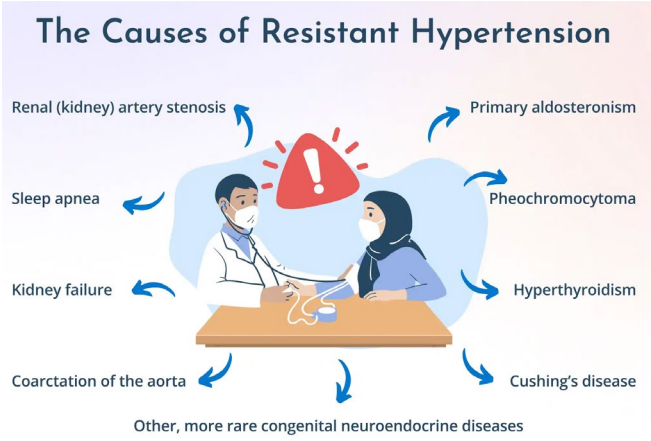
1) Identify new evidence on drug treatments which changes the standard of care

2) Evaluate the drawbacks of new medications compared to existing treatments

3) Develop patient-specific medication plans using new evidence

Resistant Hypertension Patient Case

A 62-year-old male with a history of resistant hypertension presents for evaluation. His current medication regimen includes: lisinopril 40 mg daily, amlodipine 10 mg daily, chlorthalidone 25 mg daily, and spironolactone 25 mg daily. Despite adherence to this regimen, his BP remains elevated (~155/95 mm Hg) and HR is 84. He has a BMI of 32 kg/m², a history of type 2 diabetes mellitus, and chronic kidney disease stage 3 (eGFR 45 mL/min/1.73 m²). His urine ACR is 250 mg/g and other labs are WNL.



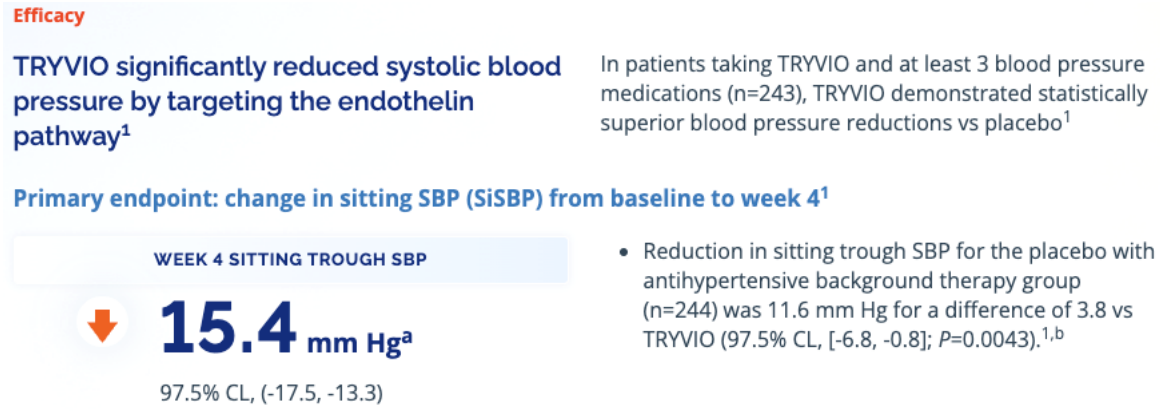
Aprocitentan (Tryvio)

First in class option for resistant hypertension

MOA: blocks endothelin (ET)-1 from binding endothelin receptors ET_A and ET_B to cause vasodilation

Roles

- Resistant HTN not controlled on other options
- Different side effect potential and serious ADEs



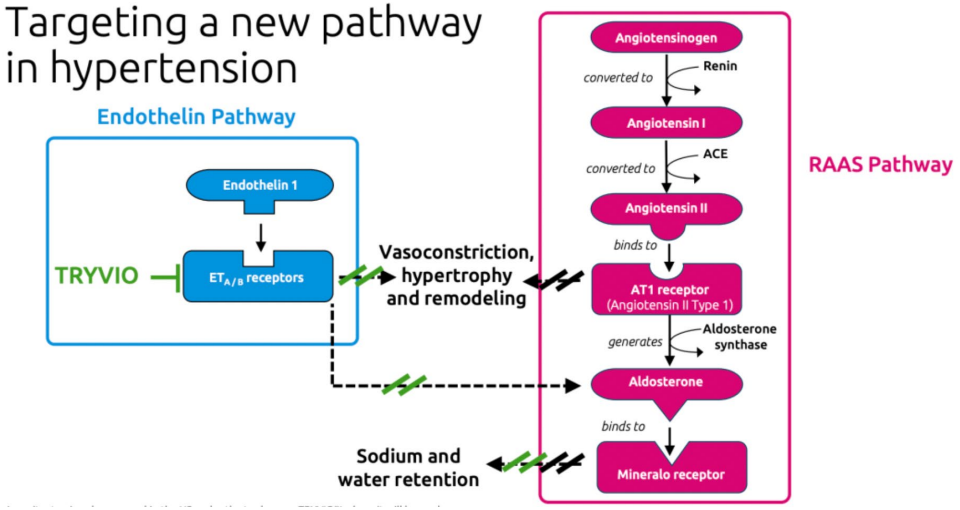
Schlaich MP, et al. Lancet. 2022; 400(10367):1927–1937.

Aprocitentan (Tryvio): Endothelin Receptor Antagonist

Aprocitentan works similarly to ambrisentan (Letairis) used for PAH

Aprocitentan blocks ET_A (lung) and ET_B (systemic) receptors vs. ambrisentan which selectively blocks ET_A receptors

Dosing: 12.5 mg daily



Schlaich MP, et al. Lancet. 2022; 400(10367):1927–1937.

Aprocitentan (Tryvio): STEPS

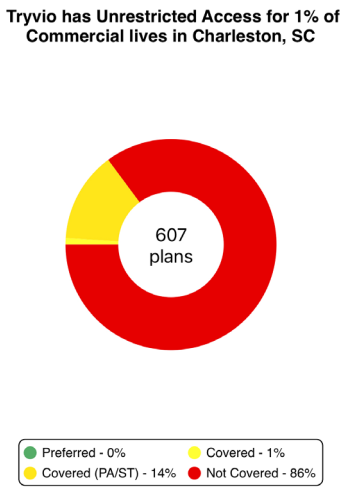
Safety: common ADEs (e.g., fluid retention, peripheral edema); serious ADEs (e.g., hepatotoxicity, decreased Hgb, embryo-fetal toxicity)

Tolerability: generally tolerable more ADEs at higher doses so only recommended to use 12.5 mg daily

Effectiveness: mean systolic BP lowering of 15.4

Price: expensive (> $150); poor insurance coverage

Simplicity: simple with daily use with or w/o food



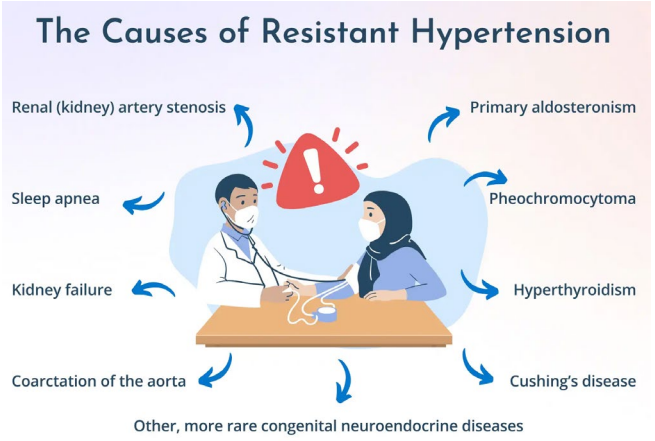
Schlaich MP, et al. Lancet. 2022; 400(10367):1927–1937.

Resistant HTN Patient Case Considerations

A 62-year-old male with a history of resistant hypertension presents for evaluation. His current medication regimen includes: lisinopril 40 mg daily, amlodipine 10 mg daily, chlorthalidone 25 mg daily, and spironolactone 25 mg daily. Despite adherence to this regimen, his BP remains elevated (~155/95 mm Hg) and HR is 84. He has a BMI of 32 kg/m², a history of type 2 diabetes mellitus, and chronic kidney disease stage 3 (eGFR 45 mL/min/1.73 m²). His urine ACR is 250 mg/g and other labs are WNL.

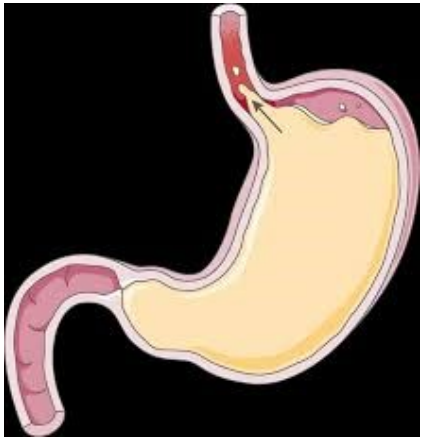
Consider Tryvio, but probably pick other meds

- Carvedilol 6.25 mg twice daily
- Guanfacine 1 mg daily
- Hydralazine 25 mg 3 x day



GERD Patient Case

A 55-year-old male presents with severe erosive esophagitis (Los Angeles Classification Grade C) and a history of inadequate response to proton pump inhibitors (PPIs). He has been on lansoprazole 30 mg daily for 8 weeks with minimal improvement in symptoms and endoscopic findings. Additionally, he has a confirmed Helicobacter pylori (H. pylori) infection, and local antibiotic resistance patterns indicate a high prevalence of clarithromycin-resistant strains.



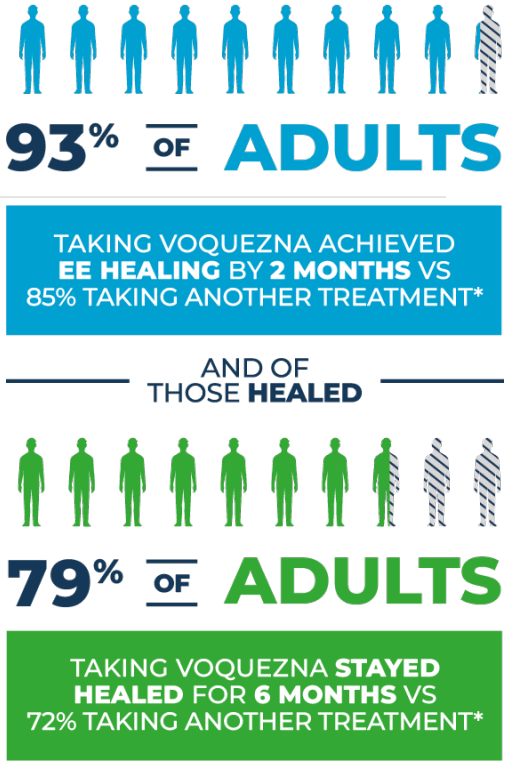
Vonoprazan (Voquezna)

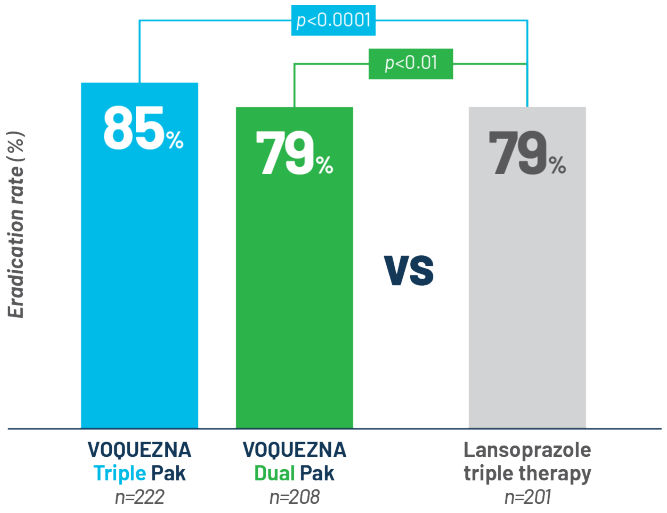
First in class PPI alternative for GERD and H. pylori eradication

MOA: suppresses basal and stimulated gastric acid secretion through inhibition of the H+, K+-ATPase enzyme system

Roles

- GERD uncontrolled by a PPI
- More potent option with erosive GERD
- Preferred option for H. pylori regimens





Laine L, et al. Gastroenterology. 2023;164(1):61-71.
Chey WD, et al. Gastroenterology. 2022;163(3):608-619.

Vonoprazan (Voquezna): Potassium-Competitive Acid Blocker

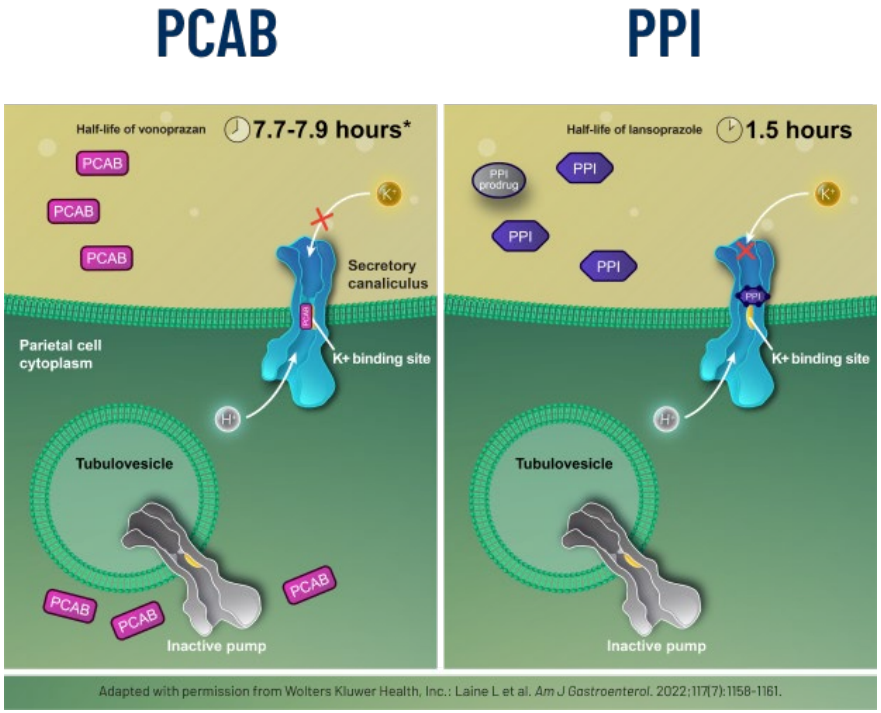
Vonoprazan is a reversible H^+/K^+ ATPase inhibitor

Not dependent on acid

Longer half-life & more potent

GERD Dosing

- Non-erosive: 10 mg daily
- Erosive: 20 mg daily x 8 weeks, then 10 mg for up to 6 months



Laine L, et al. Gastroenterology. 2023;164(1):61-71.

Vonoprazan (Voquezna): STEPS

Safety: similar to PPIs (e.g., nasopharyngitis, constipation, diarrhea); unclear long-term safety

Tolerability: well-tolerated; potentially fewer ADEs vs. PPIs

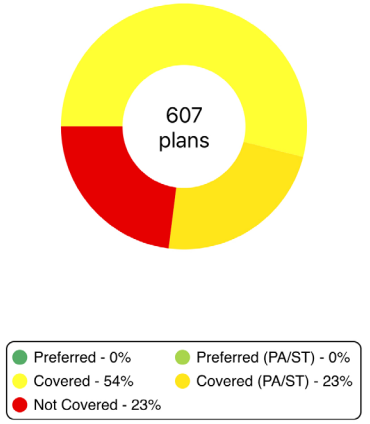
Effectiveness: more effective with GERD and H. pylori vs. PPIs

Price: expensive (> $650 cash); often requires insurance PA

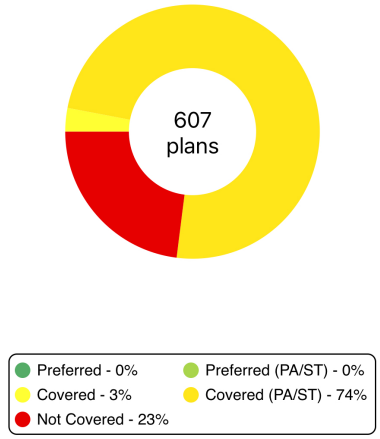
Simplicity: easier than PPIs; taken w/ or w/o food

Laine L, et al. Gastroenterology. 2023;164(1):61-71.

Voquezna Triple Pak has Unrestricted Access for 54% of Commercial lives in Charleston, SC



Voquezna has Unrestricted Access for 3% of Commercial lives in Charleston, SC



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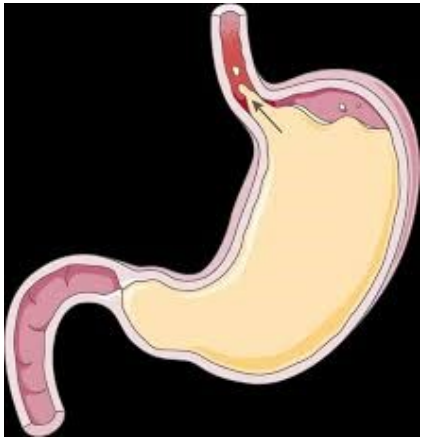
A 55-year-old male presents with severe erosive esophagitis (Los Angeles Classification Grade C) and a history of inadequate response to proton pump inhibitors (PPIs). He has been on lansoprazole 30 mg daily for 8 weeks with minimal improvement in symptoms and endoscopic findings. Additionally, he has a confirmed Helicobacter pylori (H. pylori) infection, and local antibiotic resistance patterns indicate a high prevalence of clarithromycin-resistant strains.

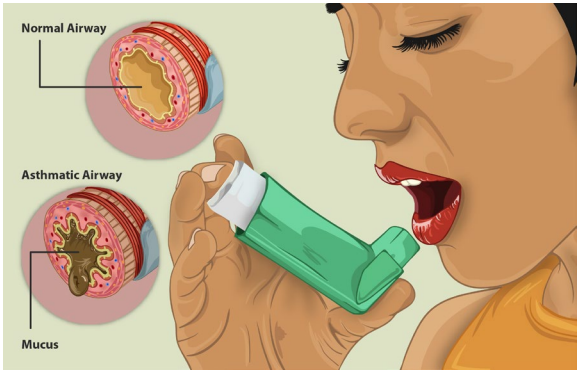
Voquezna (vonoprazan) may be better vs. PPIs

- Superior in healing severe erosive esophagitis
- Higher eradication rates for H. pylori, particularly in clarithromycin-resistant strains



Asthma/Flu Patient Case

A 45-year-old female presents with a 1-day history of SOB and chest tightness. PMH: DM2 (A1c 8.6%), obesity, moderate depression, mild asthma (ICU stay in childhood). Meds: tirzepatide 7.5 mg weekly, metformin 500 mg BID, sertraline 100 mg daily, and albuterol 90 mcg 2 puffs prn every 4-6 hours. Rapid flu positive for influenza A. Labs and vitals were all normal.



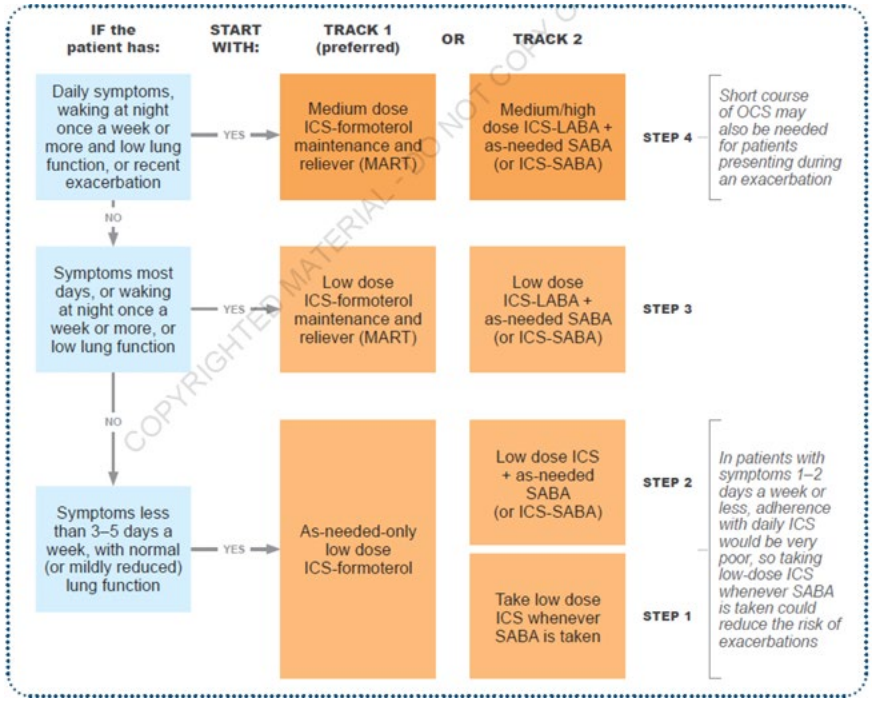
Albuterol and Budesonide (Airsupra)

New combination SABA and ICS

MOA: beta-2 agonist causing bronchial smooth muscle relaxation and a corticosteroid to control the inflammatory cascade

Roles

- Preferred rescue option vs. albuterol monotherapy
- Less preferred compared to formoterol-ICS combinations (Dulera and Symbicort) combos



Box 4-5: 2024 GINA Guidelines

Albuterol and Budesonide (Airsupra): STEPS

Safety: similar to SABA and ICS monotherapy (e.g., headache, oral candidiasis, cough)

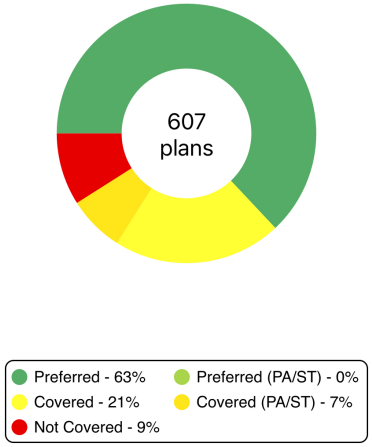
Tolerability: well-tolerated; mostly mild to moderate

Effectiveness: reduces annual rate of severe exacerbations vs. albuterol alone

Price: expensive (> $500); variable insurance coverage

Simplicity: requires appropriate inhaler technique; 2 puffs every 20 minutes prn (no more than 6 doses/day)

Airsupra has Unrestricted Access for 84% of Commercial lives in Charleston, SC



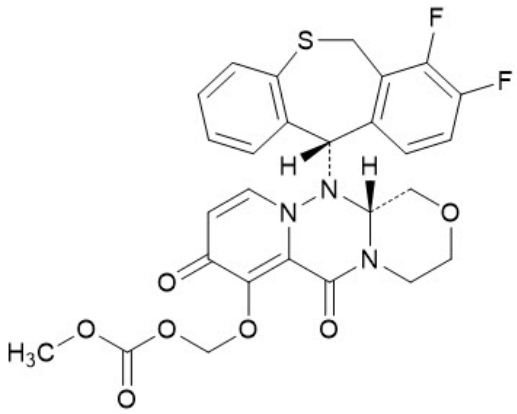
Chipps BE, et al. CHEST. 2023;164(3):585-595.
Papi A, et al. NEJM. 2022;386(22):2071-2083.

Baloxavir (Xofluza)

Newer flu antiviral treatment

MOA: prodrug that inhibits endonuclease activity of selective polymerase acid protein reducing viral gene transcription

Roles
- Active against influenza A and B, including resistant strains
- More effective treatment at preventing severe cases
- Quicker resolution of flu symptoms



Original Investigation

January 13, 2025

Antiviral Medications for Treatment of Nonsevere Influenza

A Systematic Review and Network Meta-Analysis

Ya Gao, PhD[1,2,3,4]; Yunli Zhao, MD[5,6]; Ming Liu, PhD[3,4]; et al

» Author Affiliations

JAMA Intern Med. Published online January 13, 2025. doi:10.1001/jamainternmed.2024.7193

Baloxavir (Xofluza): Cap-Dependent Endonuclease Inhibitor

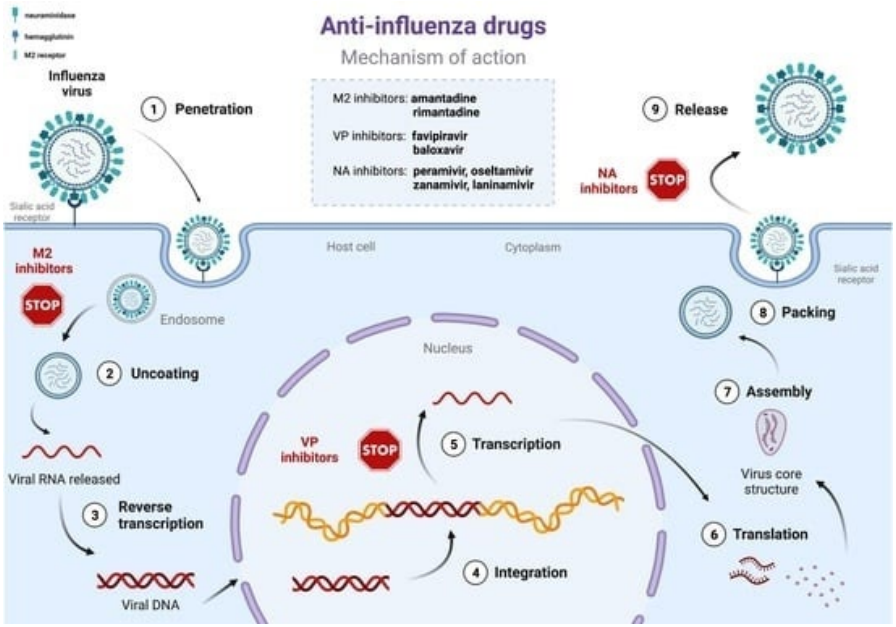
Primary chemoprophylaxis: baloxavir has similar effectiveness vs. neuraminidase inhibitors (e.g., osteltamivir, zanamivir)

Dosing (approved ≥ 5 y/o)

- < 20 kg: 2 mg/kg once
- 20 to < 80 kg: 40 mg once
- ≥ 80 kg: 80 mg once

Note: all options less effective than flu shot at preventing flu, ED visits/hospitalization, mortality

Smyk JM, et al. Int J Mol Sci. 2022;23(20):12244.



Baloxavir (Xofluza): STEPS

Safety: similar to Tamiflu (e.g., diarrhea, vomiting); less psychiatric concerns

Tolerability: well-tolerated; fewer ADEs vs. Tamiflu

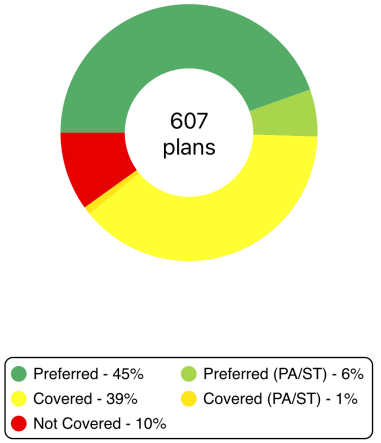
Effectiveness: better at reducing flu duration and serious cases (e.g., ED visits, hospitalizations)

Price: expensive (> $170 cash); well covered by commercial insurance but not Medicare

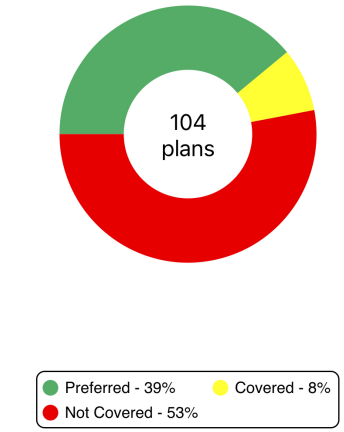
Simplicity: simple single dose regimen

Gao Y, et al. JAMA Intern Med. 2025; Published online January 13, 2025.

Xofluza has Unrestricted Access for 83% of Commercial lives in Charleston, SC



Xofluza has Unrestricted Access for 47% of Medicare lives in Charleston, SC



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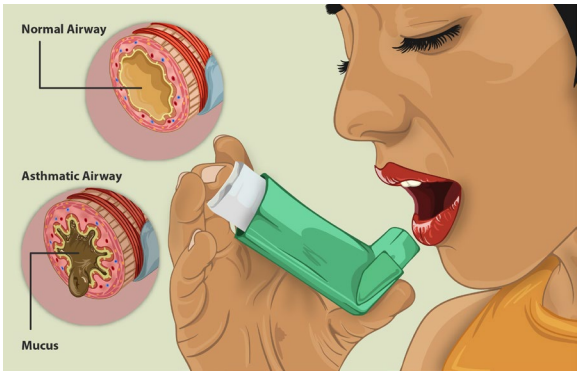


Baloxavir (Xofluza) is a better option vs. Tamiflu

- Superior: reducing ED visits and hospitalization
- Fewer GI and psych ADEs

ICS-formoterol (Symbicort or Dulera) preferred vs. Airsupra

- MART treatment with ICS-formoterol: track 1
- Airsupra better than albuterol alone: track 2

2025 CDC Adult Vaccine Schedule

Vaccine Update: RSV

Single dose of RSV vaccine recommended with:

- Everyone ≥ 75 years young
- Adults 60–74 at increased risk
  - Most chronic diseases and people in nursing homes
- Pregnant patients 32–36 weeks gestation

Approved vaccines:

- Abrysvo (Pfizer): only one approved in pregnancy
- Arexvy (GSK)
- mResvia (Moderna): no cases of Guillain-Barré seen yet

Infants and kids w/o passive immunity: recommend nirsevimab (Beyfortus)

https://www.cdc.gov/mmwr/volumes/73/wr/mm7332e1.htm

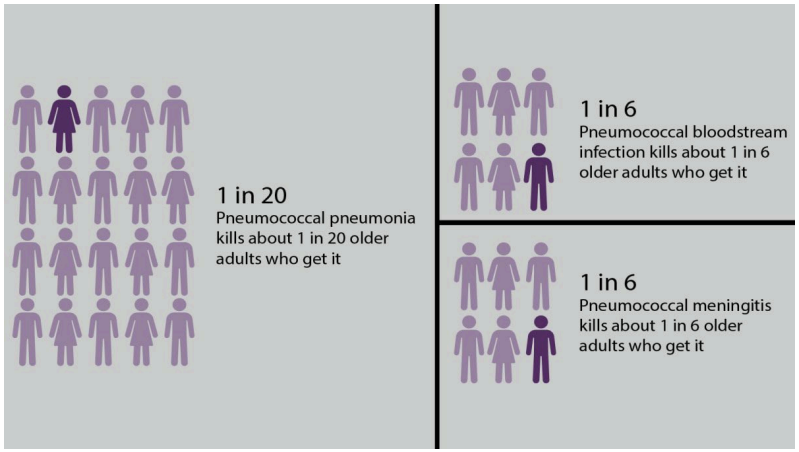
Vaccine Update: Pneumonia

Pneumonia vaccines recommended with:

- Everyone ≥ 50 years young
- Adults 19–49 with risk factors
- Kids 2 months to 15 months of age (4-dose series)

Approved vaccines:

- PCV21 (Capvaxive)
- PCV20 (Prevnar 20)
- PCV15 (Vaxneuvance)
- PPSV23 (Pneumovax 23)



Generally, prefer PCV20 or PCV21

https://www.cdc.gov/mmwr/volumes/73/wr/mm7332e1.htm

Allergy Patient Case

A 10-year-old male with a history of severe tree nut allergies (cashew and walnut) presents with a history of anaphylaxis following accidental exposures. Family treated past cases of anaphylaxis with an EpiPen 0.3 mg IM but noted confusion with administration and if this can be prevented. The patient and his family are considering options for managing his condition.

Epinephrine Nasal Spray (Neffy)

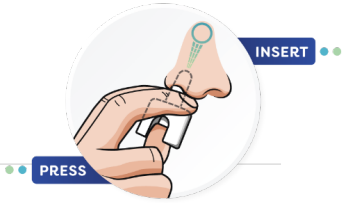
New anaphylaxis alternative 2 mg intranasal vs. IM epinephrine

MOA: stimulates alpha, beta 1&2 receptors causing bronchial smooth muscle and skeletal muscle dilation, cardiac stimulation

Roles

- Alternative to IM epinephrine anaphylaxis reversal
- Easier to use reversal agent and quicker onset
- Note: not yet 1st line in guidelines, but may change

Epinephrine Nasal Spray (Neffy): STEPS



Safety: approved on drug levels and hemodynamic changes in patients w/o anaphylaxis; cautions: CAD, HTN, DM, Parkinson's Disease, hyperthyroidism, renal impairment

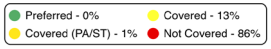
Tolerability: unique ADEs vs. IM (e.g., throat irritation, headache, nasal discomfort), but some are similar (e.g., jittery, tremor)

Effectiveness: Levels similar to IM options; Physiologic effects are similar or better

Price: expensive (~$200); poor insurance coverage

Simplicity: easier than IM and possibly quicker

Neffy has Unrestricted Access for 13% of Commercial lives in Charleston, SC



Tanimoto S, et al. Ann Allergy Asthma Immunol. 2023;130(4):508-514.e1.

Omalizumab (Xolair)

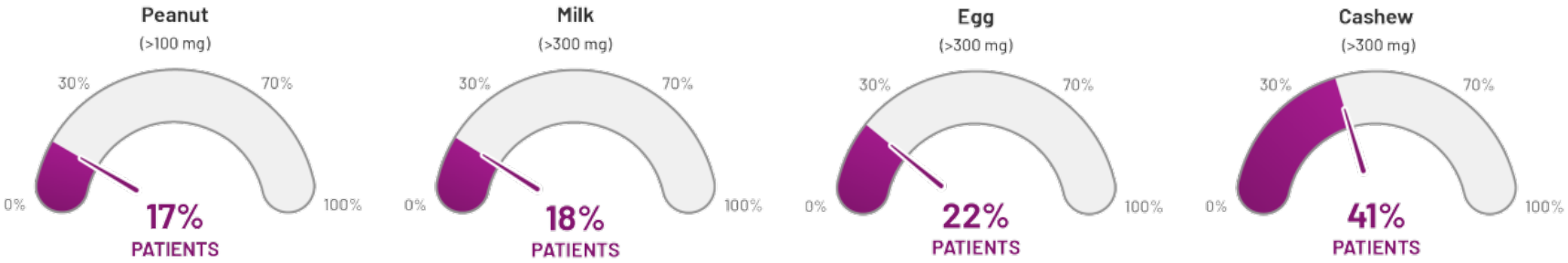
New approval for IgE food allergies

MOA: IgG monoclonal antibody that binds to IgE on mast cells and basophils reducing early and late phase allergic reactions

Roles

- May improve the severity of anaphylaxis if it occurs
- Note: will not eliminate food allergies or allow patients to eat food causing an allergy

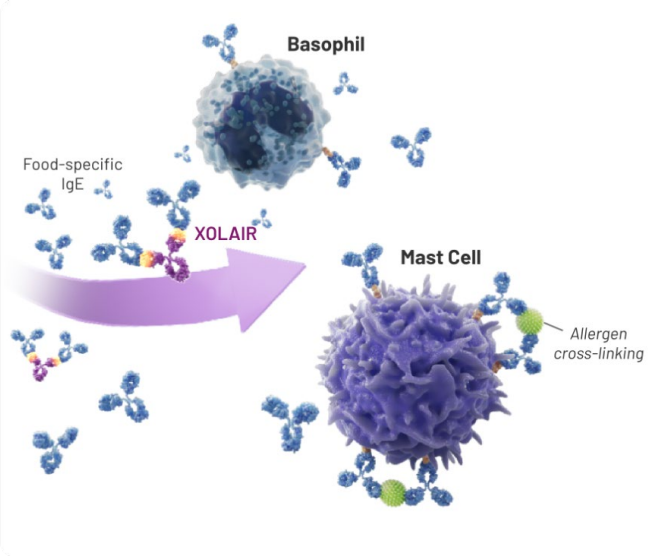
Daily Med: Xolair



Omalizumab (Xolair): IgG Monoclonal Antibody Binding IgE Receptors

Omalizumab Adult Dosing

Pretreatment serum IgE	Actual body weight (kg)	Dose (mg) SUBQ	Frequency (weeks)
≥30 to 100 units/mL	30 to 40 kg	75 mg	Every 4 weeks
	>40 to 90 kg	150 mg	
	>90 to 150 kg	300 mg	
>100 to 200 units/mL	30 to 40 kg	150 mg	Every 4 weeks
	>40 to 90 kg	300 mg	
	>90 to 125 kg	450 mg	
	>125 to 150 kg	600 mg	
>200 to 300 units/mL	>30 to 40 kg	225 mg	Every 4 weeks
	>40 to 60 kg	300 mg	
	>60 to 90 kg	450 mg	
	>90 to 125 kg	600 mg	
	>125 to 150 kg	375 mg	Every 2 weeks
>300 to 400 units/mL	>30 to 40 kg	300 mg	Every 4 weeks
	>40 to 70 kg	450 mg	
	>70 to 90 kg	600 mg	
	>90 to 125 kg	450 mg	Every 2 weeks
	>125 to 150 kg	525 mg	



Dosing Considerations:

- Pre-treatment IgE level
- Body weight

Lexi-Comp: Xolair

Omalizumab (Xolair): STEPS

Safety: common ADEs (e.g., injection site reactions, fever); serious list of precautions (e.g., CV events, eosinophilia/vasculitis, cancer)

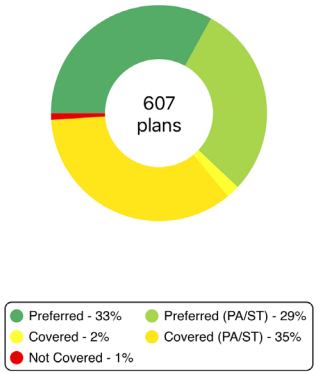
Tolerability: well-tolerated; may have mild to moderate injection site reactions

Effectiveness: increases the threshold for tolerating food allergens with or without immunotherapy; unclear effects on POEMs

Price: expensive biologic, but fairly covered on insurance

Simplicity: requires frequent office visits/lab testing, but can be given every 2–4 weeks via SubQ pen

Xolair has Unrestricted Access for 35% of Commercial lives in Charleston, SC



Daily Med: Xolair

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A 10-year-old male with a history of severe tree nut allergies (cashew and walnut) presents with a history of anaphylaxis following accidental exposures. Family treated past cases of anaphylaxis with an EpiPen 0.3 mg IM but noted confusion with administration and if this can be prevented. The patient and his family are considering options for managing his condition.

Consider Neffy vs. EpiPen prn

- Likely easier administration and quicker if covered

Xolair requires shared decision making

- Could be a candidate for prophylaxis
- Many serious ADEs and high costs warrant further discussion

New FDA Warning: Denosumab (Prolia)

Prolia (denosumab): Drug Safety Communication – FDA Adds Boxed Warning for Increased Risk of Severe Hypocalcemia in Patients with Advanced Chronic Kidney Disease

Patients on Dialysis or with Mineral and Bone Disorder at Highest Risk

- Ensure calcium/vitamin D use occurs with Prolia
- Treat CKD-MBD appropriately: phosphate binders, vitamin D analogs, calcimimetics (caution with Prolia)
- Monitor labs closely with advanced CKD

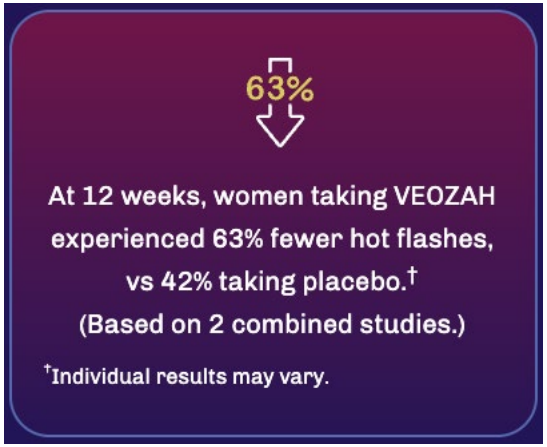
https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-increased-risk-severe-hypocalcemia-patients-advanced-chronic-kidney-disease

Fezolinetant (Veozah)

Non-hormonal option for vasomotor symptoms of menopause

MOA: neurokinin 3 receptor antagonist which modulates neuronal activity in the thermoregulatory center

Dosing: 45 mg daily w/ or w/o food



Roles

- Level-1 option for women who cannot or prefer not to use hormone therapy
- More effective for vasomotor symptoms than other non-hormonal options

Morga A, et al. Menopause. 2024;31(1):68–76.

New FDA Warning: Fezolinetant (Veozah)

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

- Rare but serious liver injury in a post-marketing report
- LFTs: baseline, monthly x 3 months, then at 6 and 9 months, or if having signs/symptoms of liver injury
- Discontinue if AST/ALT > 5 x ULN or if AST/ALT > 3 x ULN and T. bili > 2 x ULN

https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-warning-about-rare-occurrence-serious-liver-injury-use-veozah-fezolinetant-hot-flashes-due

Resmetirom (Rezdiffra)

First FDA approved treatment for noncirrhotic metabolic dysfunction-associated steatotic liver disease (MASLD)

MASLD also known as non-alcoholic fatty liver disease (NAFLD) is an earlier stage of non-alcoholic steatohepatitis (NASH)

MOA: partial agonist of thyroid hormone receptor-beta which reduces intrahepatic triglycerides

Steatohepatitis resolution with no worsening of fibrosis

Individual Pathologists[2] | Combined Analysis | Paired Biopsy/Imputed

	Placebo (n=294)	Rezdiffra 80 mg (n=298)	Rezdiffra 100 mg (n=296)
Response rate, Pathologist A (%)	**13**	**27**	**36**
Difference in response rate vs placebo (95% CI)		14 (8, 20)	23 (16, 30)
Response rate, Pathologist B (%)	**9**	**26**	**24**
Difference in response rate vs placebo (95% CI)		17 (11, 23)	15 (9, 21)

Rezdiffra achieved statistically significant results for steatohepatitis resolution for both doses in a statistical analysis incorporating both pathologists' independent readings.[1,‡]

Role: unclear

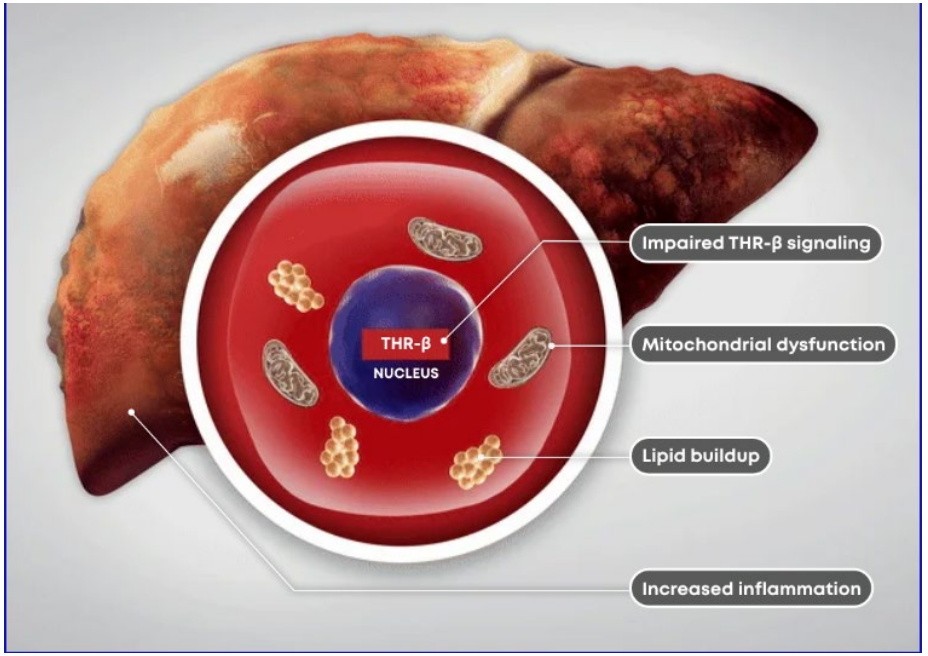
- Improves fibrosis with F2 or F3 (moderate to severe fibrosis)
- Ongoing research with other options (e.g., pioglitazone, vitamin E, GLP-1)

Harrison SA, et al. NEJM. 2024;390(6):497–509.

Resmetirom (Rezdiffra): Thyroid Hormone Receptor-Beta Agonist

Dosing

- < 100 kg: 80 mg daily
- ≥ 100 kg: 100 mg daily



Monitoring

- LFTs: baseline, then 1–2 months, then 3–6 months
- Signs/symptoms: gallbladder disease or hepatotoxicity
- Drug interactions: rhabdomyolysis with statins

DailyMed: Rezdiffra

Harrison SA, et al. NEJM. 2024;390(6):497–509.

Resmetirom (Rezdiffra): STEPS

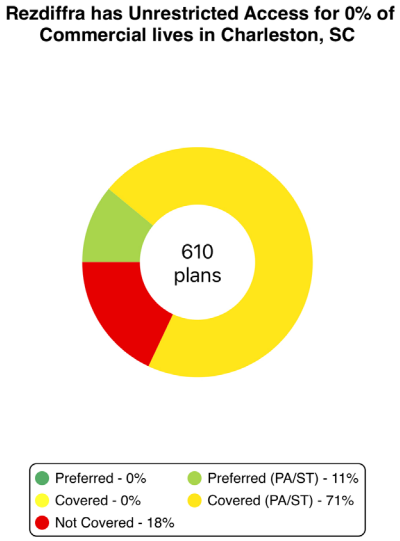
Safety: common ADEs (e.g., pruritus, diarrhea, nausea, increased AST/ALT); precautions: gallbladder/liver injury

Tolerability: well-tolerated; mostly mild to moderate

Effectiveness: improves disease-oriented evidence (DOE) with liver fibrosis

Price: expensive; typically requires PA; only available in specialty pharmacies

Simplicity: simple if available; take daily w/ or w/o food



Daily Med: Rezdiffra

OpenEvidence

- New AI tool developed by the Mayo Clinic
- Queries PubMed for data, but unable to access some articles/resources (e.g., Elsevier, Up-to-Date, Lexi-Comp)
- Useful tool for quickly learn and answer clinical questions
- *Note: double check responses with other resources

OpenEvidence®

OpenEvidence: Example Query

Expanded question: Is a daily **dose** of 100 mg of amiodarone as effective as a daily **dose** of 200 mg for rhythm control over the course of **several** months?

Yes, a daily dose of 100 mg of amiodarone can be as effective as a daily dose of 200 mg for rhythm control over the course of several months.

The 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation, published by the American College of Cardiology, states that low-dose amiodarone (100-200 mg/day) is reasonable for the long-term maintenance of sinus rhythm in patients with atrial fibrillation, particularly when other rhythm control strategies are ineffective, not preferred, or contraindicated.[1]

Additionally, a study by Jong et al. demonstrated that very low-dose amiodarone (100 mg daily) was effective in maintaining sinus rhythm in patients with chronic atrial fibrillation after successful direct-current cardioversion, with similar efficacy to a 200 mg daily dose but with fewer adverse effects.[3]

Therefore, both 100 mg and 200 mg daily doses of amiodarone are effective for rhythm control, with the choice of dose potentially influenced by the patient's tolerance and the risk of adverse effects.

Share Helpful Not Helpful

References

1. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.
   Joglar JA, Chung MK, Armbruster AL, et al.
   Circulation. 2024;149(1):e1-e156. doi:10.1161/CIR.0000000000001193.
   ☆ Leading Journal ⓘ
2. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.
   Joglar JA, Chung MK, Armbruster AL, et al.
   Journal of the American College of Cardiology. 2024;83(1):109-279. doi:10.1016/j.jacc.2023.08.017.
   ☆ Leading Journal ⓘ

Follow-Up Questions

- What are the common side effects of long-term amiodarone use in different dosages? ›
- How does the efficacy of amiodarone compare with other antiarrhythmic drugs for rhythm control? ›
- Are there specific patient populations that benefit more from lower doses of amiodarone? ›

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Questions?

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Psych Patient Case

A 35-year-old male with a 10-year history of schizophrenia presents with persistent positive (delusions, disorganized speech/thinking) and negative symptoms (blunted affect, asociality, anhedonia) despite trials of risperidone and olanzapine. He experienced weight gain and EPS from both leading to poor adherence and frequent relapses. He is seeking alternative options to better manage his condition.

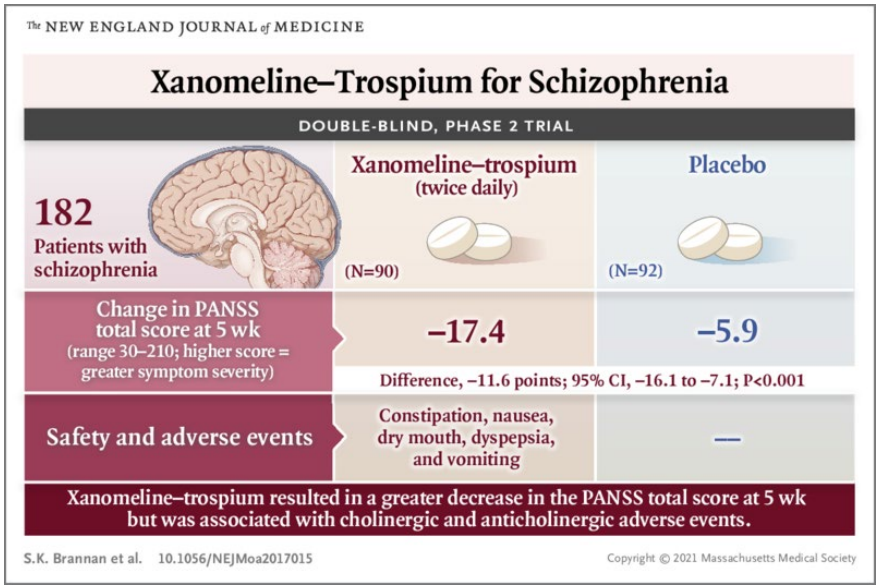
Xanomeline and Trospium Chloride (Cobenfy)

First antipsychotic for schizophrenia targeting cholinergic receptors

MOA: xanomeline is a CNS M1 & M4 muscarinic agonist; trospium is a peripheral tissue muscarinic receptor antagonist

Roles

- Alternative to dopamine receptor blocking drugs with a lower risk of EPS
- Not yet studied: add-on agent if having poorly controlled schizophrenia



Brannan SK, et al. NEJM. 2021;384:717–726.

Xanomeline and Trospium Chloride (Cobenfy): M1/M4 muscarinic agonist & M2/M4 antagonist

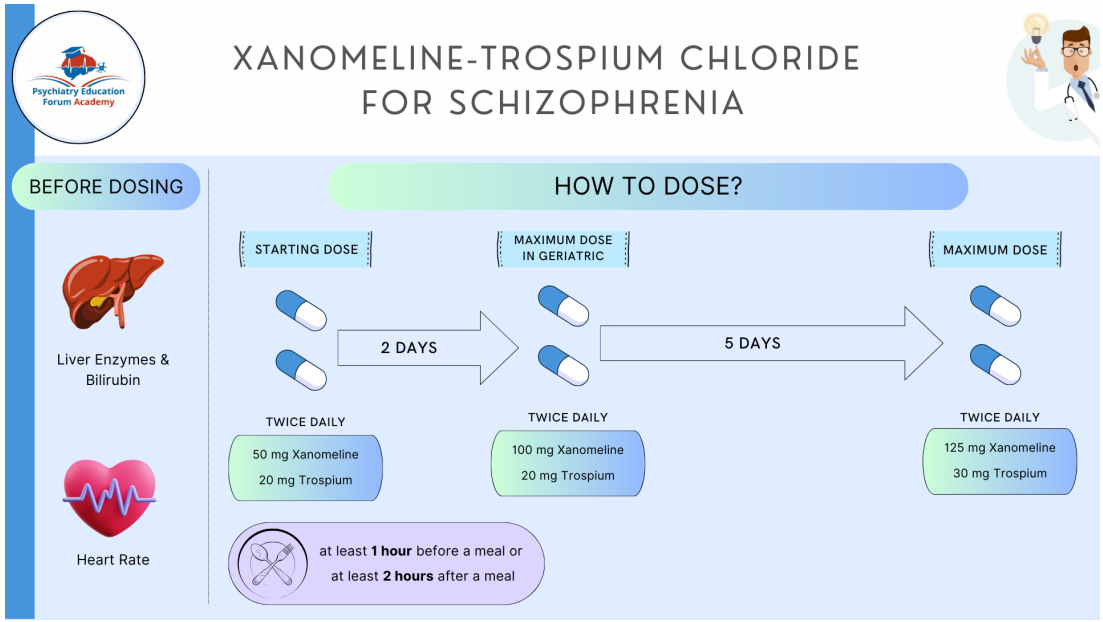


Photo Credit:
Psychiatry Education Forum

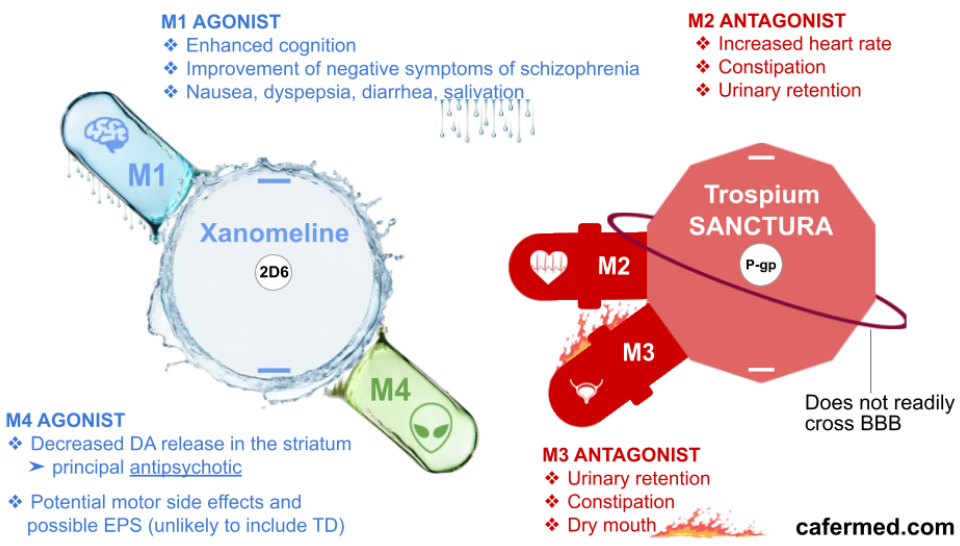


Photo Credit:
Cafer's Psychopharmacology

Xanomeline and Trospium Chloride (Cobenfy): STEPS

Safety: little EPS/metabolic risk; cholinergic and anticholinergic ADEs (e.g., N/V, dyspepsia, urinary retention, dry mouth)

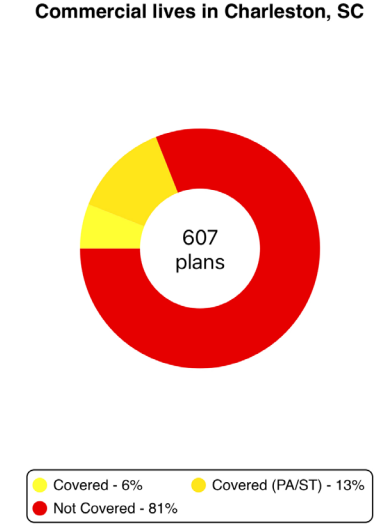
Tolerability: well-tolerated; mild to moderate

Effectiveness: improves positive and negative symptoms and potential cognitive function benefit

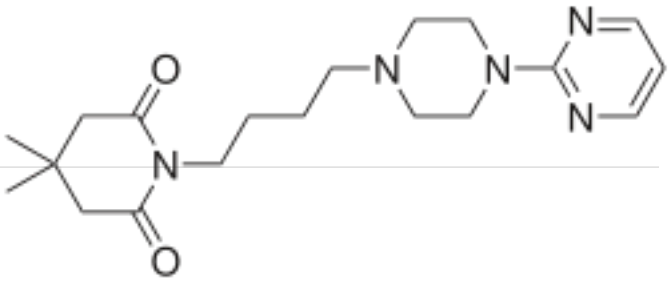
Price: expensive (> $1,900); poor insurance coverage

Simplicity: relatively simple, but is dosed BID; needs close monitoring

Brannan SK, et al. NEJM. 2021;384:717–726.
Kaul I, et al. Lancet. 2024;403(10422):160–170.



Gepirone (Exxua)



First in class antidepressant

MOA: not fully recognized but modulates serotonin as a 5HT1A receptor agonist; metabolite inhibits alpha-2 adrenergic receptors

Roles

- Partial response to SSRIs and SNRIs
- Patients with moderate to severe MDD
- Concern about sexual dysfunction and weight gain
- Patients with anxious depression

Foster SR, et al. *Am Fam Physician*. 2025;111(1):87-88.

Gepirone (Exxua)

Dosing

- Initial: 18.2 mg daily
- Day 4: 36.3 mg daily
- Day 7: 54.5 mg daily
- Day 14: 72.6 mg daily (max dose)

½ max dosing:

- Liver dose adjust: Child-Pugh class B
- Renal dose adjust: CrCl < 50

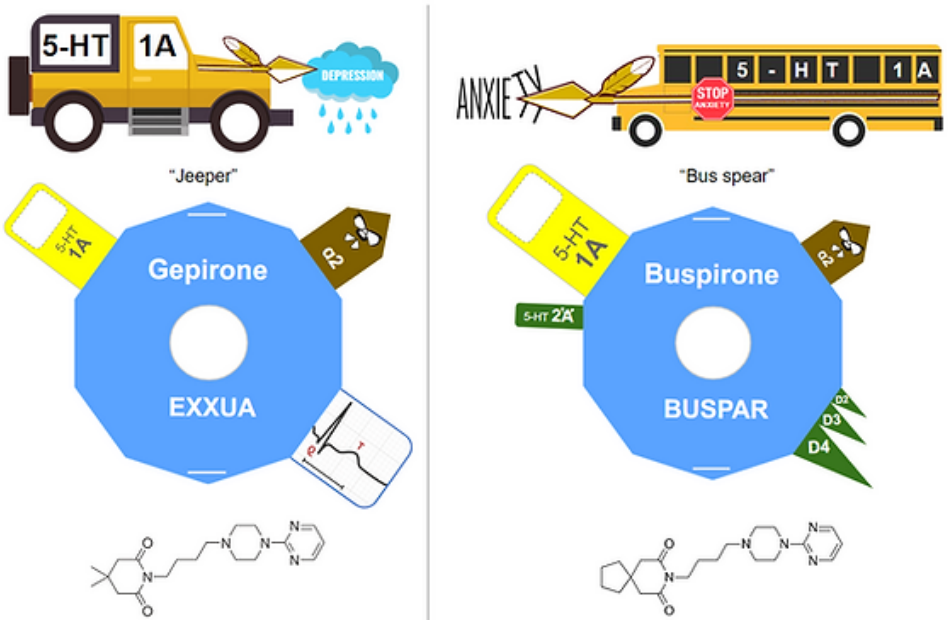


Photo Credit: Cafer's Psychopharmacology

Gepirone (Exxua): STEPS

STEPS

New drug reviews that cover Safety, Tolerability, Effectiveness, Price, and Simplicity.

Safety: similar to SSRIs with common ADEs (e.g., dizziness, nausea, insomnia, abdominal pain, dyspepsia) and serious concerns (e.g., QT prolongation, serotonin syndrome, suicidal ideation)

Tolerability: well-tolerated; low rate of discontinuation

Effectiveness: unclear clinical significance of depression improvements and effect on remission rates

Price: expensive (> $700); unclear insurance coverage

Simplicity: requires baseline testing, close titration, and daily administration with food

Foster SR, et al. *Am Fam Physician*. 2025;111(1):87-88.

Psych Patient Case Considerations

A 35-year-old male with a 10-year history of schizophrenia presents with persistent positive (delusions, disorganized speech/thinking) and negative symptoms (blunted affect, asociality, anhedonia) despite trials of risperidone and olanzapine. He experienced weight gain and EPS from both leading to poor adherence and frequent relapses. He is seeking alternative options to better manage his condition.

Cobenfy preferred, but Exxua is an option

- Cobenfy would help positive and negative symptoms while reducing EPS/metabolic ADEs
- Exxua may help significant negative symptoms and cognitive deficits
- Consider: symptoms, response, side effects, cost