

Quick Takes

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Suzetrigine

Suzetrigine (Journavx®) (2025)

- New non-opioid pain medication, currently only for acute pain
- First in class selective inhibitor of Na-v1.8 (voltage gated sodium channel)-dependent pain-signaling pathway in the peripheral nervous system
 - ▣ Expressed on dorsal root ganglion on sensory neurons for nociception
- Not known to be and unlikely to be addictive
- AEs: itching, muscle spasms, increased creatine kinase, rash
- 2 RDBPCTs: 2000 adults with moderate-to-severe pain, 48 hrs
 - ▣ Abdominoplasty: Placebo 31% drop, hydro/ACET 43%, suzetrigine 47%
 - ▣ Bunionectomy: Placebo 38%, Hydro/ACET 53%, suzetrigine 51%
 - ▣ Being studied currently for diabetic peripheral neuropathy
- Metabolized by 3A4; also weak inducer of 3A4, adjust dose with 3A4 inhibitor
- May make birth control less effective
 - ▣ Only tested levonorgestrel and norethindrone which didn't affect
 - ▣ Can't guarantee it won't affect others, so recommends not to combine
- May make it more difficult to become pregnant (animal models)
- Dosing: 100mg on empty stomach, then 50mg q12H; use beyond 14 days not studied
- Price: \$18.60/pill; Percocet \$35/pill vs \$0.09-1.90 generic, Zoloft \$18 vs 0.06-2.87
 - ▣ 3 days of opioid will not cause dependence; up to 5 days is safe in vast majority
- Patent expires in 2029
- Someone for which NSAID, Tylenol, and opioid are contraindicated, could consider



July Updates

July Updates

- FDA panel met in July to discuss potential warning or even BBW on SSRIs in pregnancy
 - Brought up the same points I have covered in the podcast
 - A few rare or minimally harmful risks
 - Poor efficacy of SSRIs
 - APA and ACOG are very upset with this panel
 - These warning would be similar to those for suicide; they would lead to less prescribing in those that need them
- Clozapine REMS officially ended in June
- Clozapine + semaglutide Phase II trial with positive results on weight without worsening of psychosis
- Online prescribing of ADHD medications did not increase substance use disorder
- Phase II trial of psychedelic **mebufotenin** improved symptoms of TRD
 - 5-HT_{1A} agonist. 1000x more so than action at 2A
 - Derivative of DMT but 4-10x more potent
 - Found in plants and the Colorado River toad

July Updates

- **U.S. Dietary Guidelines to change recommendation on daily alcohol limits**
- **Extended release stimulants will have warning update regarding weight loss in children under 6 despite not being approved in this age group**
- **Donanemab approved for label change indicating less risk for cerebral edema than similar meds**
- **New study showed smoking quick rates tripled for vaping over nicotine replacement; but did not stop vaping**
 - ▣ Risk is lower except if patient continue low level smoking
- **Push at FDA to remove BBW on HRT for menopause**
- **Sertraline/brexpiprazole combo for PTSD denied approval by FDA**
 - ▣ 80 point CAPS-5 scale -19.2 vs -13.6 for placebo thought to not outweigh risks
- **Gabapentin for chronic back pain linked to higher dementia RR 1.29 and cognitive impairment risk RR 1.85**
 - ▣ Also higher for those with 12 or more prescriptions
 - ▣ Over double the risk in those 18 to 64



September Updates

September Updates

- FDA approved Ketarx (IM ketamine for surgical pain)
 - Seeking approval in depression, ALS, various pain syndromes, and dyskinesia in Parkinson's disease
- Nrx100 (IV ketamine **for** suicidality in depression) fast tracked by FDA
 - Note esketamine is approved for MDD **with** NOT **for** suicidality
- New medications for OSA
 - Atomoxetine + Oxybutynin or Aroxybutynin
 - Dilate pharyngeal muscles during sleep
 - Aroxybutynin being used for patenting purposes
 - MARIPOSA Phase II: 50% reduction in AHI after 1 month
 - SynAIRgy Phase III: top line results, 46.8% vs 6.8% AHI reduction at 26 weeks vs placebo; AHI numbers not released yet
 - LunAIRo Phase III: 1 year trial that is underway
 - Atomoxetine/Trazodone for OSA
 - Trazodone is for sedation
 - 2023 Phase II: AHI 28.3 vs 42.7 for placebo but only 9/18 completed

September Updates

- Tonmya® (2025) aka cyclobenzaprine approved for fibromyalgia
 - ▣ Other approved agents: pregabalin (2007), duloxetine (2008), milnacipran (2009)
 - ▣ Alternatives: amitriptyline or other TCA, gabapentin, previously cyclobenzaprine
 - ▣ Risks: CNS depressant, serotonin syndrome, anticholinergic
 - ▣ DDI: D ratings for many CNS depressants
 - Notable X ratings: azelastine (nasal), glycopyrrolate, hydroxyzine, MAOis, olopatadine (nasal), potassium chloride/citrate (ulceration)
 - ▣ Available late 2025 in 2.8mg SL tablets (much lower dose than Flexeril®)
- Nelivaptan had significant results in Phase IIb trial for MDD
 - ▣ Selective vasopressin V1b receptor antagonist (CNS selective)
 - ▣ Effect size of 0.44, however a genetically defined subgroup had 0.55
- Kanna update from South Africa
- First 2-SORA, seltorexant, Phase II trial for insomnia showed benefit
 - ▣ Phase III trials for MDD adjunctive treatment are ongoing

September Updates

- ADHD drug treatment and risk
 - ▣ Swedish study of 148,581 adults and children with ADHD
 - ▣ Suicidal behaviors: adjusted incidence rate ratio (aIRR) 0.83
 - ▣ Substance misuse: 0.85
 - ▣ Transport accidents: 0.88
 - ▣ Criminality: 0.87
- Case of new onset psychosis caused by ingestion of sodium bromide
 - ▣ ChatGPT recommended replacing chloride in table salt with the bromide
 - ▣ He had hyperchloremia, negative anion gap, low phosphate, elevated bicarb
 - ▣ This was pseudohyperchloremia as bromide interferes with the results
 - ▣ Can also be caused by salicylate poisoning but this was ruled out
 - ▣ FDA eliminated bromide by 1989, however it is showing up in supplements, sedatives, and excess dextromethorphan

September Updates

- Are Gabapentinoids Effective at Reducing Pain and Improving Sleep After Nerve Injury > A Systematic Review and Meta-analysis
 - Bottom line: not really
- Weekly subcutaneous formulation of monoclonal antibody, lecanemab, for Alzheimer's Disease approved by the FDA
 - Study showed equal efficacy with biweekly IV infusions
- Orforglipron Phase III results in and suggest FDA approval in sight
- Case of fecal microbiota transplant in 2017 in Australian woman with BP1 is still without symptoms and no longer on medications
 - Funding has been difficult to obtain to do research
- Wearable lithium in sweat sensor may become available
- New synthetic opioid 7-hydroxymitragynine (7-OH)
 - Found naturally in kratom but up to 50 times as potent
 - Also now appearing in vape and similar shops

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November Updates

November Updates

- Anti-inflammatory effects of vortioxetine
 - ▣ Modulates PPAR γ : anti-inflammatory, immunomodulatory
 - ▣ Promotes anti-inflammatory shift in microglia from M1 to M2 phenotype
 - Via 5-HT_{2B} and 5-HT₇ receptors?
 - Many antidepressants, lithium, and ketamine also have this effect
 - ▣ Modulates NF- κ B pathway reducing expression of TNF- α , IL-1 β , and IL-6
 - Many antidepressants have this effect (fluoxetine, sertraline, venlafaxine)
 - ▣ COX1/2 inhibition: stronger than most NSAIDs with fewer adverse effects
 - ▣ Has shown promise in treatment of “Long COVID”
 - ▣ Reconsidering placement in D tier
- Pramipexole augmentation for the acute phase of treatment-resistant, unipolar depression: a placebo-controlled, double-blind, randomised trial in the UK. Lancet Psychiatry 2025.
 - ▣ 151 participants, had failed at least 2 med trials, 3-4 on average
 - ▣ QIDS dropped from 16.4 to 10 in pramipexole group and 16.2 to 13.8 in the placebo after 12 weeks; Effect size of 0.9

November Updates

- FDA grants fast track designation for ALTO-101
 - ▣ Small molecule phosphodiesterase-4 inhibitor
 - ▣ Cognitive impairment associated with schizophrenia (CIAS)
- Tramadol
 - ▣ Barakji JA et al. Tramadol versus placebo for chronic pain: a systematic review with meta-analysis and trial sequential analysis. *MBJ Evid Based Med.* 2025.
 - 19 studies
 - Reduced pain but by a clinically insignificant margin
 - Raised risks, OR 2.13, cardiac events and neoplasms
 - Nausea, dizziness, constipation, somnolence
 - Patients more likely to continue opioids long-term than oxycodone and hydrocodone
 - ▣ Wei Y-J J et al. Risk of seizure associated with concomitant use of tramadol and antidepressants (2D6 inhibitors) in older nursing home residents. *Neurology.* 2025.

November Updates

- Lang, U et al. Doxycycline Use in Adolescent Psychiatric Patients and Risk of Schizophrenia: An emulated Target Trial. Am J Psychiatry. 2025.
 - ▣ Finnish registry 1987-1997, 56,395 individuals
 - ▣ 1.4% developed schizophrenia with doxycycline at all dose ranges vs 2.1% for those with no doxycycline exposure
 - ▣ Doxycycline has neuroprotective properties
- Brezis M. Failing Public Health Again? Analytical Review of Depression and Suicidality From Finasteride. J Clin Psychiatry. 2025.
- Saito H et al. Successful treatment of five cases of catatonia treated with guanfacine without ECT: a case series from psychiatric hospital in Japan

November Updates

- First 2-SORA, seltorexant, Phase III data showed equal performance with quetiapine for depression and insomnia with less adverse effects
- Decker D. A pilot study examining a ketogenic diet as an adjunct therapy in college students with MDD. *Translational Psychiatry*. 2025.
 - ▣ Depressive symptoms decreased by 69-71% within 2-6 weeks in 10-12 week intervention
 - ▣ Global well-being increased nearly 3-fold
 - ▣ 6.2% weight loss, 13% fat mass loss, 52% leptin decrease,
 - ▣ BDNF 32% increase, improvement on cognitive tasks
 - ▣ Case series shows improvement in anorexia nervosa
- Robison R et al. Single Treatment with MM120 (Lysergide) in GAD: A Randomized Clinical Trial. *JAMA Network*. 2025.
 - ▣ Significant dose-dependent reduction in anxiety for LSD-containing drug
- FDA requires earlier MRI screening for lecanemab patients

November Updates

- More than 4-fold risk of neuropsychiatric events on Montelukast in children with psychiatric history
- Lumateperone approved as adjunct for MDD
- Terava-Utti E et al. Association between hyperemesis gravidarum and depression: a national register-based controlled study in Finland. *The Lancet Psychiatry*. Nov 2025.
 - 8.8% vs 1% had pre-pregnancy depression
 - 4.9% vs 1% had new onset diagnosed depression
- Morisaki A et al. Menstrual psychosis with a marked response to carbamazepine. *Psychiatry and Clinical Neuroscience Reports*. 2025.
- Potential new ADHD medication, CTx-1301 positive Phase III
 - Uses Precision Timed Release® (PTR®) to release 3 doses to give full day coverage

November Updates

- Pillinger T et al. The effects of antidepressants on cardiometabolic and other physiological parameters: a systematic review and network meta-analysis. The Lancet. 2025.
 - ▣ Weight: Escitalopram is highest SRI>Traz>Mirt>Fluvox>Mil>TCA
 - ▣ Cholesterol: Parox>Dulox>Ven>Desven
 - ▣ Glucose: Duloxetine
 - ▣ HR/BP: SNRI>Levomil>TCA
 - ▣ QTc: TCAs were slightly higher than placebo, but none very sig
 - ▣ AST/ALT: Parox>Vil>Desven>Levomil>Dulox, but none very sig
 - ▣ Sodium: none significant
- Phase III trial to start for roluperidone to treat negative schizophrenia symptoms; FDA rejected last year
 - ▣ 5HT2A and sigma-2 antagonist

November Updates

- Risperidone LAI
 - ▣ Consta is now generic
 - ▣ Uzedy is now approved as adjunct for BP1, joins Maintena®
- Zhang X et al. Clinical efficacy of fecal microbiota transplantation in alleviating depressive symptoms: a meta-analysis of randomized trials. *Front. Psychiatry*. 2025.
 - ▣ ES > 1.0, highest in those with IBS and direct GI delivery

February 26 Updates

February Updates

- SAINT TMS changed name to SNT TMS
- Accelerated Deep TMS like SWIFT (doesn't use fMRI)
- New study results of eTNS for ADHD showed it was no better than sham treatment in treating ADHD symptoms
- Systematic review of high-quality studies showed no link between prenatal acetaminophen use and autism, ADHD, or intellectual disability in children
- FDA requests GLP-1 medications drop suicide risk warning
- First FDA-approved blood test for AD: p-tau217/bA1-42
- Cohort study of ~4.3M pregnancies suggested exposure to Z-drugs in the 1st trimester was not associated with increased risk of congenital malformations
- BZD use in pregnancies link to increased risk of abortion, preterm birth, and small for gestational age compared to nonuse

ProlivRx (2026)

- FDA approved at-home brain neuromodulation device for adults with treatment-resistant MDD
- Electrical stimulation of occipital and trigeminal nerves via wearable headset
- App-guided at-home treatment
- Adjunctive treatment
- Approved for those that have failed at least one medication
- Two 40 min sessions at least 5 hours apart
- Effect size: 0.8



February Updates

- New LAI olanzapine submitted for FDA approval
- Ketogenic Diets and Depression and Anxiety: A Systematic Review and Meta-Analysis.
 - ▣ ES for depression 0.48. Anxiety: 0.03
- A Ketogenic Diet for Treatment-Resistant Depression: A Randomized Clinical Trial
 - ▣ Combination with medication
 - ▣ Few wanted to continue the diet
 - ▣ ES at 6 weeks of 0.68 and 12 weeks of 0.58
- Colorado is one step closer to approving Ibogaine
 - ▣ Will join psilocybin in its Natural Medicine program