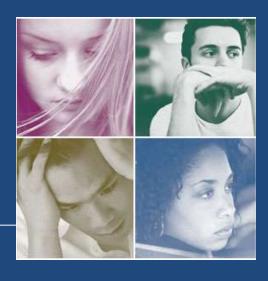
#### **Quick Takes**



Cody Armstrong, MD

Diplomate of the American Board of Psychiatry and Neurology

## 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
  - Abdomninoplasty: 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-HT1A 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

- □ FDA approved KETARx (IM ketamine) for post-surgical pain
  - Seeking approval in depression, ALS, various pain syndromes, and dyskinesia in Parkinson's disease possibly with a microneedle patch
- 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 that are still in trials but showing promises
  - 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, not much different from atomoxdetine alone
    - SynAlRgy Phase III: top line results, 46.8% vs 6.8% AHI reduction at 26 weeks vs placebo;
      AHI numbers not released yet
    - LunAlRo 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
    - 2023 study: Placebo 18.2, Traz 7.4, no effect for lemborexant
      - No effect on TST, worsened self-reported sleep quality, but unlike with oxybutynin did not lower arousal threshold

- □ 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

- 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

- Are Gabapentinoids Effective at Reducing Pain and Improving Sleep After
  Nerve Injury: A Systematic Review and Meta-analysis
  - Bottom line: not really
- Weekly lecanemab SQ (Lequembi Iqlik®) formulation approved by FDA
  - Monoclonal antibody treamtment for Alzheimer's Disease
  - 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