

New Drug Update 2020

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Conflict of Interest

- I have no conflict of interest to declare

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Objectives

- Discuss new pharmacotherapy choices
- Describe indications, mechanism of action, common adverse effects and significant drug interactions for these products
- Highlight safety concerns with selected new choices
- Compare selected new choices with established therapies

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Assessment Question

1. Which of the following medications is a novel drug for postpartum depression?
 - a) Zulresso
 - b) Xolair
 - c) Zirabev

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Assessment Question

2. What is the indication for Wakix?
- a) Skin and skin structure infections
 - b) Hypoactive sexual desire disorder
 - c) Excessive daytime sleepiness

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Assessment Question

3. Which of the following medications has a black box warning for serious infections, malignancies and thrombosis?
- a) Yupelri
 - b) Rinvoq
 - c) Motegrity

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Assessment Question

4. Which of the following is/are purported benefit(s) of Jatenzo?
- a) Oral dosing
 - b) No inadvertent testosterone exposure
 - c) All of the above

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Our Agenda

- Novel agents
- New formulations
- Biosimilars
- New combinations

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NOVEL AGENTS

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Yupelri (revefenacin)

- Indications: COPD
- Mechanism of action: long-acting muscarinic antagonist
- Adverse effects: nasopharyngitis, upper respiratory tract infection, headache, back pain

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Yupelri (revefenacin)

- Warnings/precautions
 - Not for acute episodes
 - Paradoxical bronchospasm
 - Worsening of narrow-angle glaucoma
 - Worsening of urinary retention
 - Immediate hypersensitivity
- Drug interactions
 - Anticholinergics
 - Organic-anion-transporting polypeptide (OATP)1B1 and OATP1B3 inhibitors

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Motegrity (prucalopride)

- Indications: chronic idiopathic constipation in adults
- Mechanism of action: Serotonin-4 (5-HT₄) receptor agonist
- Contraindications
 - Hypersensitivity
 - Intestinal perforation or obstruction

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Motegrity (prucalopride)

- Warnings: suicidal ideation
- Adverse effects: headache, abdominal pain, nausea, diarrhea, distension, dizziness, vomiting, flatulence, fatigue
- Drug interactions: CYP3A4 inhibitors

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Sunosi (solriamfetol)

- Indications: excessive daytime sleepiness due to narcolepsy or obstructive sleep apnea
- Mechanism of action: unclear, but it is a dopamine and norepinephrine reuptake inhibitor
- Adverse effects: decreased appetite, insomnia, anxiety, headache, palpitations, nausea, dry mouth, constipation

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Sunosi (solriamfetol)

- Warnings/precautions
 - Increased blood pressure and heart rate
 - Psychiatric symptoms
- Drug interactions
 - Monoamine oxidase inhibitors (MAOIs)
 - Dopaminergic drugs
 - Drugs that increase HR or BP

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Wakix (pitolisant)

- Indications: excessive daytime sleepiness due to narcolepsy
- Mechanism of action: Unclear but it is a histamine-3 receptor antagonist
- Adverse effects: headache, insomnia, nausea, upper respiratory infections, musculoskeletal pain, anxiety, increased heart rate, hallucinations, irritability, abdominal pain, sleep disturbance, decreased appetite, cataplexy, dry mouth, rash

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Wakix (pitolisant)

- Warnings/precautions
 - QT prolongation
- Drug interactions
 - Strong CYP2D6 inhibitors
 - Strong CYP3A4 inducers
 - H1 blockers
 - Other medications that can increase QT intervals

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Dayvigo (lemborexant)

- Indications: insomnia in adults with issues of sleep onset and/or maintenance
- Mechanism of action: unclear, but it is thought to be orexin receptor antagonism
- Adverse effects: somnolence/fatigue, headache, abnormal dreams

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Dayvigo (lemborexant)

- Warnings/precautions
 - CNS depressant effects and daytime impairment
 - Sleep paralysis, hallucinations, cataplexy-like symptoms
 - Complex sleep behaviors
 - Those with decreased respiratory function
 - Depression/suicidal ideation
 - Appropriate evaluation of other conditions

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Dayvigo (lemborexant)

- Drug interactions
 - CYP3A inhibitors
 - CYP3A inducers
 - Alcohol
 - CYP2B6 substrates

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Caplyta (lumateprenone)

- Indications: treatment of schizophrenia
- Mechanism of action: unclear, but it is an antagonist at 5-HT_{2a} receptors and postsynaptic antagonist at D₂ receptors
- Adverse effects: somnolence, sedation, dry mouth, increased creatinine phosphokinase, fatigue, vomiting, increased hepatic transaminases, decreased appetite, extrapyramidal symptoms

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Caplyta (lumateprenone)

- Warnings/precautions
 - Increased mortality in elderly patients with dementia related psychosis
 - Neuroleptic malignant syndrome
 - Tardive dyskinesia
 - Metabolic changes
 - Leukopenia, neutropenia, agranulocytosis
 - Orthostatic hypotension and syncope
 - Seizures
 - Cognitive and motor impairment
 - Body temperature dysregulation
 - Dysphagia

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Caplyta (lumateprenone)

- Drug interactions
 - CYP3A4 inhibitors
 - CYP3A4 inducers
 - UGT inhibitors

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Xcopri (cenobamate)

- Indications: partial onset seizures in adults
- Mechanism of action: believed to be due to the inhibition of voltage gated sodium channels and modulation of the GABA_a
- Adverse effects: somnolence, dizziness, fatigue, diplopia, headache

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Xcopri (cenobamate)

- Warnings/precautions
 - Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) and multi-organ hypersensitivity
 - QT shortening
 - Suicidal ideation
 - Neurological adverse reactions
 - Withdrawal antiepileptic drugs

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Xcopri (cenobamate)

- Drug interactions
 - Phenytoin: decrease phenytoin by up to 50%
 - Phenobarbital and clobazam: reduce doses of these as needed
 - Lamotrigine and carbamazepine: reduce doses of these as needed
 - CYP2B6 and CYP3A substrates
 - CYP2C19 substrates
 - Oral contraceptives

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Conjupri (levamlodipine)

- Indications: hypertension in those who are 6 years of age or older
- Mechanism of action: calcium channel blocker that leads to vasodilation
- Adverse effects: edema, fatigue, nausea, abdominal pain, somnolence

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Conjupri (levamlodipine)

- Warnings/precautions
 - Hypotension
 - Worsening of angina and acute myocardial infarction
 - Slow titration in hepatic impairment
- Drug interactions
 - CYP3A inhibitors
 - Sildenafil
 - Simvastatin
 - Cyclosporine
 - Tacrolimus

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Aklief (trifarotene)

- Indications: acne vulgaris in those 9 years of age or older
- Mechanism of action: believed to be a result of its function as a retinoic acid receptor agonist
- Adverse effects: irritation, itching, sunburn

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Aklief (trifarotene)

- Warnings/precautions
 - Redness, scaling, dryness, stinging/burning
 - Increased risk of UV burns
- Drug interactions: None provided

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Reyvow (lasmiditan)

- Indications: acute treatment of migraine with or without aura
- Mechanism of action: unclear but it is a 5-HT_{1F} receptor agonist
- Adverse effects: dizziness, fatigue, paresthesia, sedation

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Reyvow (lasmiditan)

- Warnings/precautions
 - CNS depression
 - Driving impairment
 - Serotonin syndrome
 - Medication overuse headache
- Drug interactions
 - Medications that lower heart rate
 - P-glycoprotein (P-gp) substrates
 - Breast Cancer Resistant Protein (BCRP) substrates

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Ubrelvy (ubrogepant)

- Indications: acute treatment of migraine with or without aura
- Mechanism of action: believed to be through its effects as a calcitonin gene-related peptide receptor antagonist
- Adverse effects: nausea, somnolence

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Ubrelvy (ubrogepant)

- Warnings/precautions: none provided
- Drug interactions
 - CYP3A4 inhibitors
 - CYP3A4 inducers
 - P-gp and BCRP inhibitors

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Skyrizi (risankizumab-rzaa)

- Indications: moderate to severe plaque psoriasis
- Mechanism of action: antibody that binds IL-23
- Adverse effects: Upper respiratory infections, headache, fatigue, injection site reactions, tinea infections

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Skyrizi (risankizumab-rzaa)

- Warnings/precautions: infections
- Drug interactions: none reported

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Nourianz (istradefylline)

- Indications: adjunct to levodopa/carbidopa for “off” episodes
- Mechanism of action: unclear, but it is an adenosine A_{2a} receptor antagonist
- Adverse effects: dyskinesia, dizziness, constipation, nausea, diarrhea, hallucinations, insomnia, decreased appetite, upper respiratory infections, rash

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Nourianz (istradefylline)

- Warnings/precautions
 - Dyskinesia
 - Psychiatric symptoms
- Drug interactions
 - CYP3A4 inducers and inhibitors
 - P-gp substrates

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Rinvoq (upadacitinib)

- Indications: moderate to severe rheumatoid arthritis who have tried methotrexate
- Mechanism of action: it is a Janus kinase inhibitor which affects the activation of Signal Transducers and Activators of Transcription
- Adverse effects: upper respiratory infections, cough, pyrexia

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Rinvoq (upadacitinib)

- Warnings/precautions
 - *Infections*
 - *Malignancy*
 - *Thrombosis*
 - GI perforation
 - Lab monitoring
 - Embryo-fetal toxicity
- Drug interactions: strong CYP 3A4 inducers and inhibitors

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Vyleesi (bremelanotide)

- Indications: treatment of hypoactive sexual desire disorder in premenopausal women
- Mechanism of action: it is a melanocortin receptor agonist and there is expression of the receptors in the nervous system. However, how it has therapeutic effects is unknown

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Vyleesi (bremelanotide)

- Adverse effects: nausea, flushing, injection site reactions, headache, vomiting, cough, fatigue, hot flush, paresthesia, dizziness, nasal congestion
- Warnings/precautions
 - Increase in blood pressure and decrease in heart rate
 - Focal hyperpigmentation
 - Nausea

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Vyleesi (bremelanotide)

- Drug interactions
 - May decrease gastric emptying
 - Naltrexone

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Infectious Disease

- Nuzyra (omadacycline) for community acquired pneumonia or bacterial skin/skin structure infections
- Xenleta (lefamulin) for community acquired bacterial pneumonia in adults
- Seysara (sarecycline) for moderate to severe acne vulgaris
- Fetroja (cefiderocol) for complicated UTIs by multi-drug resistant gram-negative bacteria

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Infectious Disease

- Aemcolo (rifamycin) for traveler's diarrhea caused by non-invasive strains of *E. coli*
- Pretomanid in combination with linezolid and bedaquiline for MDR tuberculosis
- Xofluza (baloxavir marboxil) for acute uncomplicated influenza

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Other Interesting Approvals

- Mental Health
 - Zulresso (brexanolone) injection for postpartum depression
 - Spravato (esketamine) nasal spray for treatment resistant depression
- Sickle Cell Anemia
 - Oxbryta (voxelotor) prevents the binding of deoxygenated sickle hemoglobin
 - Adakveo (crizanlizumab-tmca) reduces frequency of vaso-occlusive crisis

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Cancer Agents

- Vitakvi (larotrectinib sulfate): NTRK*gene fusion positive solid tumors
- Xospata (gilteritinib fumarate): acute myeloid leukemia with FLT3 mutations
- Daurismo (glasdegib maleate): acute myeloid leukemia
- Lobrena (loratinib): metastatic non-small cell lung cancer (ALK+)
- Piqray (apelsib): advanced or metastatic breast cancer (HR+, HER2-, PIK3CA mutated)

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Cancer Agents

- Zykadia (ceritinib): metastatic non-small cell lung cancer (ALK+)
- Balversa (erdafatinib): locally advanced or metastatic urothelial carcinoma
- Talzena (talazoparib): locally advanced or metastatic breast CA (HER2- and abnormal BRCA gene)
- Xpovio (selinexor): relapsed or refractory multiple myeloma
- Nubeqa (darolutamide): non-metastatic castration-resistant prostate cancer

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Cancer agents

- Turalio (pexidartinib): tenosynovial giant cell tumor
- Rozlytrek (entrectinib): non-small cell lung cancer (ROS1+) or solid tumors with NTRK fusion
- Brukinsa (zanubrutinib): mantle cell lymphoma
- Padcev (enfortumab vedotin-ejfv): bladder and urinary tract cancer
- Ayvakit (avapritinib): gastro-intestinal stromal tumor who have PDGFRA exon 18 mutation
- Tazverik (tazemetostat): epithelioid sarcoma

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NEW FORMULATIONS

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New Formulations

- Sympazan: clobazam oral film
- Bryhalinda: halobetasol proprionate
- Nayzilam: nasal midazolam
- Valtoco: nasal midazolam
- Slynd: drospirenone
- Tolsura: itraconazole- SUBA
- Ezallor: rosuvastatin sprinkles
- Licart: diclofenac epolamine patch
- Inbrija: levodopa inhaled

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New Formulations

- Tosymra: sumatriptan nasal
- Gloperba: colchicine oral solution
- Jatenzo: testosterone undecanoate capsule
- Avaclyr: acyclovir ointment
- Lotemax SM: loteprednol etabonate
- Qmiiz ODT: meloxicam
- Ortikos: budesonide ER
- Katerzia: amlodipine suspension

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New formulations

- Baqsimi: glucagon nasal powder
- Harvoni: ledipasvir/sofosbuvir pellets
- Sovaldi: sofosbuvir pellets
- Absorica: isotretinoin
- Arazlo: tazarotene lotion
- Riomet ER: metformin ER suspension
- Rybelsus: oral semaglutide
- Amzeeq: topical minocycline

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Mental Health Reformulations

- Brixadi: buprenorphine weekly/monthly injections
- Evekeo ODT: amphetamine sulfate
- Adhansia XR: methylphenidate
- Drizalma: duloxetine sprinkles
- Secuado: asenapine patch

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BIOSIMILARS

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Biosimilar Approvals

- Truxima (rituximab-abbs)
- Ruxience (rituximab-pvvr)
- Herzuma (trastuzumab-pkrb)
- Ontruzant (trastuzumab-dttb)
- Trazimera (trastuzumab-qyyp)
- Kanjinti (trastuzumab-anns)
- Eticovo (etanercept-ykro)

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Biosimilar Approvals

- Zirabev (bevacizumab-bvzr)
- Hadlima (adalimumab-bwwd)
- Abrilada (adalimumab-tmca)
- Ziextenzo (pegfilgrastim-bmez)
- Avsola (infliximab-axxq)

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NEW COMBINATIONS

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New Combinations

- Qternmet XR: dapagliflozin, metformin, saxagliptin
- Trijardy XR: empagliflozin, linagliptin, metformin
- Rocklatan: latanoprost, netarsudil dimesylate
- Duaklir pressair: acridinium bromide, formoterol fumarate
- Dovato: dolutegravir sodium, lamivudine
- Duobrii: halobetasol propionate, tazarotene
- Bijuva: estradiol, progesterone
- Talicia: amoxicillin, omeprazole magnesium, rifabutin

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Assessment Question

1. Which of the following medications is a novel medication for postpartum depression?
 - a) **Zulresso**
 - b) Xolair
 - c) Zirabev

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Assessment Question

2. What is the indication for Wakix?
- a) Skin and skin structure infections
 - b) Hypoactive sexual desire disorder
 - c) Excessive daytime sleepiness

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Assessment Question

3. Which of the following medications has a black box warning for serious infections, malignancies and thrombosis?
- a) Yupelri
 - b) Rinvoq
 - c) Motegrity

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Assessment Question

4. Which of the following is purported benefit of Jatenzo?
- a) Oral dosing
 - b) No inadvertent testosterone exposure
 - c) All of the above