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Overview of approved psychiatric medications 2008-2023: A systematic review

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Abstract

Objective: The purpose of this systematic review is to enumerate the psychiatric medications approved by the Food and Drug Administration (FDA) over the past 15 years, from 2008 to 2023, and describe their mechanism of action, approved indications, dosing ranges, and adverse effects.

Methods: Studies published from 2008 to 2023 were identified from the PubMed database, using the keywords: 'psychiatric' OR 'psychopharm*" AND 'medic*' OR 'pharm*'. An independent focused analysis was conducted, and a consensus was reached on the studies for approved medications to be included in this systematic review. Key findings were derived from the full-text and tables of the selected studies.

Results: From 2008-2023, the FDA approved 118 medications including: 26 for Schizophrenia, 12 for Bipolar Disorders, 16 for Depressive Disorders, two for Anxiety Disorders, one for Feeding and Eating disorders, 13 for Sleep-Wake Disorders, five for Sexual Dysfunctions, 16 for Substance Use Disorders, six for Neurocognitive Disorders, and 18 for Neurodevelopmental Disorders (specifically, Attention-Deficit/Hyperactivity Disorder, ADHD), in addition to three for Psychiatric Medication-Related Movement Disorders. It is important to note that 37 out of the 118 medications were New Drug Application (NDA) approvals by the FDA, i.e., they have not been previously approved for another indication. We also noted that nine medications were discontinued by the manufacturer, with no reported safety or effectiveness concerns. Over the past fifteen years, several novel treatment approaches and modalities have been introduced, such as monoclonal antibodies for the treatment of Alzheimer's Disease, very long-acting injectable antipsychotic drugs, targeting the glutamate neurochemical system for depression and depressive symptoms in other disorders, medications for conditions without any previously approved medicines (e.g., Binge Eating Disorder), and tablets with sensors to monitor treatment adherence. Of note, no new medications were approved from 2008-2023 for: Anxiety Disorders (with the exception of two extended-release preparations of previously approved agents), Obsessive-Compulsive Disorder, Trauma- and Stressor-Related Disorders, Dissociation Disorders, Somatic Symptom Disorders, and Disruptive, Impulse-Control, and Conduct Disorders.

Conclusion: Approved psychiatric medications from 2008-2023 show substantial promise in the treatment of psychiatric conditions. More than 100 psychiatric medications were approved over the past 15 years for the major psychiatric conditions including a combination of newly introduced medications and new indications and drug formulations for already approved medications. It behooves psychiatric clinicians to keep up to date with this ever evolving and fast changing field. As the overview article, this manuscript will be followed by in-depth, disorder-based descriptions of approved medications, as well as those currently under development in Phase III.

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Keywords: Psychiatric medications; FDA-approved; Psychiatric Disorders; Schizophrenia, Bipolar; Depression; Anxiety; Insomnia; Narcolepsy; Sexual Dysfunctions; Substance Use Disorders; Neurocognitive Disorders; ADHD; Tardive Dyskinesia

1. Introduction

The past 15 years have witnessed significant progress in the development and introduction of new medications for psychiatric disorders. Psychiatric medications go through a lengthy process in order to obtain Food and Drug Administration (FDA) approval (Reichert, 2003). However, the utilization of approved medications remains substantially variable largely due to lack of familiarity by clinicians with new agents (Prosser and Walley, 2006) as well as concerns about the costs and benefits of new formulations and/or derivatives of existing medications (Aronson et al., 2020). This systematic review examines the psychiatric medications approved in the past 15 years (between 2008 to 2023) and describes, in detail, their mechanism of action, indication for both labeled and off-label uses, evidence for efficacy, dosing, adverse effects and considerations with regards to practical implementation (e.g., cost). The purpose is to provide prescribers with a practical and informative review of recently approved psychiatric medications to help clinicians become familiar with these medications, particularly those that currently might be underutilized, and to understand their advantages and disadvantages over those they prescribe most frequently.

2. Methods

FDA-approved psychiatric medication studies published from 2008 until 2023 were identified from the PubMed database, using the keywords: 'psychiatric' OR 'psychopharm*" AND 'medic*' OR 'pharm*' AND 'FDA-approv*'. The authors conducted a focused analysis independently and reached a consensus on the medications to be included in this systematic review. Key findings were derived from the full-text and tables of the selected studies.

3. Results

3.1. Overview

Psychiatric medications which received FDA approval in the past 15 years from 2008 to 2023 are described in detail. We organized the list of medications by psychiatric disorder according to the nomenclature of the Diagnostic and Statistical Manual 5th edition (DSM-5-TR, APA, 2022), then listed the medications alphabetically. A summary table is presented for each diagnostic category, containing each medication's generic and trade names (with added notation if being tested as an adjunctive therapy), year of approval, mechanism of action, route of administration, dosage, and notes for clinicians (including effects on sedation, weight/lipids, extrapyramidal symptoms, sexual dysfunction, and potential QTc prolongation). As the overview article, this manuscript will be followed by disorder-based manuscripts containing more in-depth descriptions of approved medications and those currently under development in Phase III, which will describe their mechanisms of action, indications, evidence, adverse effects and practical implementation (e.g., cost).

Table 1 Approved medications by psychiatric disorder in the past 15 years

Disorder	N	Approved medications/Approval Year
Schizophrenia	26	Aripiprazole (Abilify Asimtufii), 2023 Aripiprazole (Abilify Maintena), 2013 Aripiprazole Lauroxil (Aristada), 2015 Aripiprazole (Aristada Initio), 2018 Aripiprazole ODT (generic Abilify Discmelt), 2015 Aripiprazole tablets with sensor (Abilify MyCite), 2017 Asenapine SL (Saphris), 2009 * Asenapine Transdermal (Secuado), 2021 Brexpiprazole (Rexulti), 2015 * Cariprazine (Vraylar), 2015 * Clozapine Suspension (Versacloz), 2013 Dexmedetomidine SL (Igalmi), 2022

		Iloperidone (Fanapt), 2009 * Loxapine inhalation (Adasuve), 2012 Lumateperone Tosylate (Caplyta), 2019 * Lurasidone (Latuda), 2010 * Olanzapine Pamoate (Zyprexa Relprevv), 2009 Olanzapine + Samidorphan (Lybalvi), 2021 Paliperidone Extended release (Invega), 2009 Paliperidone Palmitate (Invega Sustenna), 2009 Paliperidone Palmitate (Invega Trinza), 2019 Paliperidone Palmitate (Invega Hafyera), 2021 Pimavanserin (Nuplazid), 2016 (for psychotic symptoms in Parkinson Disease) * Risperidone SC (Perseris), 2019 Risperidone SC (Uzedy), 2023 Risperidone IM (Rykindo), 2023
Medication-Induced Movement Disorders	3	Amantadine Extended-Release (Osmolex ER), 2018 Deutetrabenazine Extened-Release (Austedo XR), 2023 * Valbenazine (Ingrezza), 2017 *
Bipolar Disorders	12	Aripiprazole (Abilify Asimtufii), 2023 Aripiprazole (Abilify Discmelt), 2015 Aripiprazole tablets with sensor (Abilify MyCite), 2017 Asenapine SL (Saphris), 2009 * Cariprazine (Vraylar), 2017 * Dexmedetomidine SL (Igalmi), 2022 Lumateperone Tosylate (Caplyta), 2021 * Lurasidone (Latuda), 2018 Olanzapine + Samidorphan (Lybalvi), 2021 Quetiapine Extended-Release (Seroquel XR), 2008 Risperidone IM (Rykindo), 2023 Valproic Acid Delayed-Release (Stavzor), 2008 (discontinued in 2013) †
Depressive Disorders	16	Brexanolone (Zulresso), 2019 * Brexipiprazole (Rexulti), 2015 * Bupropion hydrobromide (Aplenzin), 2008 Buproprion hydrochloride (Forfivo XL), 2011 Cariprazine (Vraylar) (as an adjunct), 2022 Desvenlafaxine (Pristiq), 2008 * Dextromethorphan-bupropion (Auvelity), 2023 Duloxetine (Drizalma Sprinkle), 2019 Esketamine Nasal spray (Spravato), 2020 * Gepirone Extended-Release (Exxua), 2023 * Levomilnacipran (Fetzima), 2011 * Quetiapine Extended-Release (Seroquel XR), 2009 (as adjunct) Trazodone ER (Oleptro), 2010 Vilazodone (Viibryd), 2009 * Vortioxetine (Trintellix), 2013 * Zuranolone (Zurzuvae), 2023 *

Anxiety Disorders	2	Duloxetine (Drizalma Sprinkle), 2019 Lorazepam Extended-Release (Loreev XR), 2021
Feeding and Eating Disorders	1	Lisdexamfetamine dimesylate (Vyvanse), 2015
Sleep-Wake Disorders	13	Daridorexant (Quiviviq), 2022 * Doxepin (Silenor), 2010 Lemborexant (Dayvigo), 2019 * Pitolisant (Wakix), 2019 * Sodium oxybate (Zyrem), 2017 * Sodium oxybate + other oxybate salts (Xywav), 2020 Sodium oxybate Extended-Release (Lumryz), 2023 Solriamfetol (Sunosi), 2019 * Suvorexant (Belsomra), 2014 * Tasimelteon (Hetlioz), 2014 * Zolpidem Tartrate SL (Edluar), 2009 Zolpidem Tartrate SL (Intermezzo), 2011 (discontinued in 2013) † Zolpidem Tartrate Oral Spray (Zolpimist Spray), 2008
Sexual Dysfunctions	5	Avanafil (Stendra), 2012 * Bremelanotide (Vyleesi), 2019 * Eroxon topical gel (over the counter), 2023 * Flibanserin (Addyi), 2015 * Vardenafil ODT (Satxyn), 2010
Substance-Related Disorders	16	Buprenorphine Implant (Probuphine), 2016 (discontinued in 2020) † Buprenorphine Injection (Sublocade), 2017 Buprenorphine and Naloxone buccal film (Bunavail), 2014 (discontinued in 2020) † Buprenorphine and Naloxone SL (Cassipa), 2018 (discontinued in 2020) † Buprenorphine + Naloxone SL (Zubsolv), 2013 Buprenorphine Transdermal (Butrans Patch), 2010 Buprenorphine XR, (Brixadi), 2023 Lofexidine (Lucemyra), 2018 * Naltrexone injection (Vivitrol), 2010 Nalmefene hydrochloride injection (Revex), 2022 * Nalmefene nasal spray (Opvee), 2023 Naloxone injection (Evzio), 2014 (discontinued in 2020) † Naloxone injection (Zimhi), 2021 Naloxone nasal spray (Narcan), 2015 Naloxone nasal spray (Kloxxado), 2021 Naloxone nasal spray (RiVive), 2023
Neurocognitive Disorders	6	Aducanumab (Aduhelm), 2021 (to be discontinued in 2024) *, † Brexpiprazole (Rexulti), 2023 Donepezil transdermal (Adlarity), 2022 Lecanemab (Leqembi), 2023 * Memantine Extended-Release (Namenda XR), 2010 Memantine + Donepezil (Namzaric), 2014

Neurodevelopmental Disorders: ADHD	19	Amphetamine ODT (Adenys XR-ODT), 2016 Amphetamine Salts Extended- Release (Mydayis), 2017 Amphetamine (Evekeo), 2012 Amphetamine ODT (Evekeo ODT), 2019 Amphetamine suspension (Dynavel XR), 2015 Clonidine Extended-Release (Kapvay), 2010 Dextroamphetamine Transdermal (Xesltrym), 2022 Guanfacine Extended- Release (Intuniv), 2009 Lisdexamfetamine dimesylate (Vyvanse), 2008 for Adult ADHD Methylphenidate (Adhansia XR), 2019 (discontinued in 2022) † Methylphenidate (Aptensio XR), 2015 Methylphenidate ODT (Cotempla XR ODT), 2017 Methylphenidate (Jornay PM), 2018 Methylphenidate (QuilliChew ER), 2015 Methylphenidate Extended-Release (Relexxii), 2022 Methylphenidate suspension (Quillivant XR), 2012 Serdexmethylphenidate + dexmethylphenidate (Azstarys), 2021 Viloxazine (Qelbree), 2021 *

***** New Drug Application approved by the FDA (i.e., medication has not been previously approved for another indication). † Discontinued by the manufacturer, with no reported safety or effectiveness concerns.

3.2. Schizophrenia

From 2008 to 2023, 26 medications were approved for the treatment of Schizophrenia, in a variety of capsule/tablet (10), orally disintegrating tablet (1), sublingual (2), transdermal (1), and inhalable (1) formulations, in addition to 11 long-acting injectable (LAI) preparations with 9 for intramuscular administration (IM), 1 for subcutaneous (SC) use, and 1 for SC or IM use.

Table 2 Summary descriptions of 2008-2023 approved medications for Schizophrenia

Name, **Year approved**	**Mechanism** **of Action**	**Route and Dose**	**Notes to clinicians including effects on sedation, weight/lipids, extrapyramidal tract, prolactin, and QTc**
Aripiprazole (Abilify Asimtufii), 2023	Dopamine 2 (D2) receptor partial agonist, Serotonin 5-HT1A receptor partial agonist and 5-HT2A receptor antagonist	IM Injection 960 mg every 2 months	Weight gain, and akathisia.
Aripiprazole (Abilify Maintena), 2013	D2 receptor partial agonist, 5-HT1A receptor partial agonist, and 5-HT2A receptor antagonist	IM Injection 400 mg monthly	Weight gain (≥7% from baseline):17% vs. 7% placebo (PBO). Sedation: 5% vs. 1% PBO. Low risk for Prolonged QTc. Akathisia: 11% vs. 4% PBO, and injection site pain: 5% vs. 1% PBO.
Aripiprazole lauroxil (Aristada), 2015	D2 receptor partial agonist, 5-HT1A receptor partial agonist, and 5-HT2A receptor antagonist	IM Injection 441 or 882 mg, monthly, and 1064 mg bimonthly	Weight gain (>7% from baseline): 10% (441 mg), 9% (882 mg) vs. 6% (PBO) No sedation difference from PBO.
Aripiprazole (Aristada Initio), 2018	D2 receptor partial agonist, 5-HT1A receptor partial	IM Injection 674 mg plus a single dose of 30 mg oral	Low risk for Prolonged QTc.

	agonist, and 5-HT2A receptor antagonist	aripiprazole for initiation	Akathisia: 5% (441 mg), 7% (882 mg) vs. 4% PBO, and injection site pain: 4% (441 mg), 5% (882 mg), vs. 2% PBO, Insomnia: 3% (441 mg), 4% (882 mg) vs. 2% PBO.
Aripiprazole ODT (generic Abilify Discmelt), 2015	D2 receptor partial agonist, 5-HT1A receptor partial agonist, and 5-HT2A receptor antagonist	Orally disintegrating tablet 15-20 mg daily	Akathisia.
Aripiprazole tablets with sensor (Abilify MyCite)	D2 receptor partial agonist, 5-HT1A receptor partial agonist, and 5-HT2A receptor antagonist	Oral 15-20 mg	Akathisia.
Asenapine SL (Saphris), 2009	Antagonist at D2 and 5-HT2A receptors	Sublingual 5 mg-10 mg twice daily	Akathisia, somnolence, and extrapyramidal side effects.
Asenapine transdermal (Secuado), 2021	Antagonist at D2 and 5-HT2A receptors	Transdermal 3.8 mg-7.6 mg/24 hours	Weight gain (>7% from baseline): 5.5% (5-10 mg bid) vs. 0.4% PBO, sedation: 23% (5-10 mg bid) vs. 5% PBO, Moderate effect on QTc, in addition to tiredness, dizziness, somnolence, and insomnia.
Brexpiprazole (Rexulti), 2015	Partial agonist at D2 and 5-HT1A receptors	Oral 2-4 mg daily	Akathisia, somnolence, and weight gain.
Cariprazine (Vraylar), 2015	Partial agonist at D2, D3, and 5-HT1A receptors, and antagonist at 5-HT2A receptors	Oral 1.5 mg-4.5 mg daily	Akathisia, insomnia.
Clozapine Suspension (Versacloz), 2013	Antagonist at 5-HT2A, 5-HT2C, D1, and D4 receptors	Oral 12.5 -900 mg daily	QT prolongation, sedation, weight gain, dyslipidemia, and risk of severe neutropenia. Only available through REMS program.
Dexmedetomidine sublingual (Igalmi), 2022	Alpha-2 adrenergic receptor agonist	Sublingual 120 ug-180 ug daily	Somnolence, hypotension, bradycardia, withdrawal symptoms, arrhythmia and QTc prolongation.
Iloperidone (Fanapt), 2009	D2 and 5-HT2A receptor antagonist	Oral 6 -12 mg twice daily	QTc prolongation, weight gain, and sedation.
Loxapine (Adasuve), 2012	Antagonist at D1, D2 and 5-HT2 receptors	Inhalation powder 10 mg, once per day maximum.	Sedation (12%) Only available at approved facilities under FDA-required REMS program (black box warning for bronchospasm).
Lumateperone Tosylate (Caplyta), 2019	5-HT2A and D2 receptor antagonist	Oral 42 mg daily	Sedation (24%). Low frequency of EPS, weight gain, prolactin changes, and QTc prolongation.
Lurasidone (Latuda), 2010	D2 and 5-HT2A receptor antagonist	Oral 40 -80 mg daily	Weight gain, and somnolence.

Olanzapine Pamoate (Zyprexa Relprevv), 2009	D2 and 5-HT2A receptor antagonist	IM 150-300 mg every 2 weeks or 300-405 mg every 4 weeks	Weight gain, and sedation.
Olanzapine and Samidorphan (Lybalvi), 2021	Samidorphan is an opioid antagonist (to prevent olanzapine's effect on weight and metabolism)	Oral 5 mg/10 mg to 20 mg/10 mg	Insomnia, increased ALT and increased CPK.
Paliperidone Extended release (Invega), 2009	D2 and 5HT2A receptor antagonist; also, antagonist at alpha-1 and alpha-2 and H1 histamine receptors	Oral 3 – 12 mg daily	Akathisia, insomnia, EPS.
Paliperidone Palmitate (Invega Sustenna), 2009	D2 and 5HT2A receptor antagonist	IM 234 mg initial dose, then 156 mg on day 8, and then 234 mg monthly	Akathisia, insomnia, EPS.
Paliperidone Palmitate (Invega Trinza), 2019	D2 and 5HT2A receptor antagonist	IM 273 -819 mg every 3 months	Akathisia, insomnia, and EPS.
Paliperidone Palmitate (Invega Hafyera), 2021	D2 and 5HT2A receptor antagonist	IM Extended-release Injection 1,092 mg/3.5 mL or 1,560 mg/5 mL, every 6 months	Akathisia, insomnia, and EPS.
Pimavanserin (Nuplazid), 2016 for psychotic symptoms in Parkinson Disease	5 HT2A inverse agonist/antagonist	Oral 20 mg daily	Sedation
Risperidone SC (Perseris), 2018	D2 and 5HT2A receptor antagonist	SC or IM, long-acting injection 75 – 100 mg once per month	Akathisia, and weight gain.
Risperidone SC (Uzedy), 2023	D2 and 5HT2A receptor antagonist	SC Extended-release Injection 50 - 150 mg monthly or 150-250 mg bimonthly	Akathisia, and weight gain.
Risperidone IM (Rykindo), 2023	D2 and 5HT2A receptors antagonist	IM50 mg every 2 weeks	Akathisia, and weight gain.

Abbreviations: D1, D2, D3, D4 = Dopamine receptors; 5HT1A, 5HT2A = Serotonin receptors; H = Histamine receptors; GABA = Gamma Amino Butyric Acid receptors; IM = Intramuscular; IN = Intranasal; IV = Intravenous; SC = subcutaneous

3.2.1. Medications for psychiatric medication-related movements disorders

From 2008 to 2023, 3 medications were approved for the treatment of movement disorders associated with psychiatric medication, all for oral use.

Table 3 Summary descriptions of the medications for psychiatric medication-related movements disorders

Name, Year Approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Amantadine (Osmolex ER), 2018	Increase dopamine release and dopamine reuptake blocker, weak NMDA receptor antagonist	Oral 129 -322 mg daily	Somnolence, and possible QTc prolongation.
Deutetrabenazine Extended-Release (Austedo XR), 2023	Reversible inhibitor of vesicular monoamine transporter -2 (VMAT-2), causing depletion of dopamine from nerve terminals ‡	Oral 12 -48 mg once daily	Increased risk of QT interval prolongation, depression, sedation, and akathisia
Valbenazine (Ingrezza), 2017	Reversible inhibitor of VMAT-2 ‡	Oral 40 -80 mg daily	Increased risk of QT interval prolongation, depression, sedation, and akathisia

‡ Novel mechanism of action

3.3. Bipolar disorders

From 2008 to 2023, 12 medications were approved for the treatment of Bipolar Disorder including 10 medications in a variety of enteral formulations including tablet/capsule (7), orally disintegrating tablets (1), and sublingual (2), and 2 long-acting injectable formulations (LAI) for intramuscular (IM) use.

Table 4 Summary descriptions of the newly approved medications in Bipolar and Related Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on sedation, weight/lipids, extrapyramidal tract, prolactin, and QTc**
Aripiprazole (Abilify Asimtufii), 2023	Partial agonist at D2 and 5-HT1A receptors, 5-HT2A receptor antagonist	IM Injection 960 mg every 2 months	Weight gain, and akathisia.
Aripiprazole (generic Abilify Discmelt), 2015	Partial D2 agonist and 5-HT1A receptors, and 5-HT2A receptor antagonist	Orally disintegrating 15-20 mg daily	Akathisia.
Aripiprazole tablets with sensor (Abilify MyCite), 2017	Partial D2 agonist and 5-HT1A receptors, and 5-HT2A receptor antagonist	Oral 15-20 mg	Akathisia.
Asenapine sublingual (Saphris) for Bipolar, 2015	Antagonist at D2 and 5-HT2A. receptors	Sublingual 5 mg-10 mg twice daily	Akathisia, somnolence, and extrapyramidal side effects.
Cariprazine (Vraylar) for Bipolar depression, 2017, for Bipolar mania and mixed, 2019	Partial agonist at D2, D3, and 5-HT1A receptors, and antagonist at 5-HT2A receptors	Oral 1.5 mg-4.5 mg daily	Akathisia, insomnia.
Dexmedetomidine (Igalmi), 2022	Alpha-2 adrenergic receptor agonist	Sublingual 120 ug-180 ug daily	Somnolence, hypotension, bradycardia, withdrawal symptoms, arrhythmia and QTc prolongation.

Lumateperone Tosylate (Caplyta), 2021	5-HT2A and D2 receptor antagonist	Oral 42 mg	Sedation (24%). Low frequency of EPS, weight gain, prolactin changes, and QTc prolongation.
Lurasidone (Latuda), 2018	Dopamine D2 and serotonin 5-HT2A receptor antagonist	Oral 40-80 mg daily	Weight gain, somnolence.
Olanzapine + samidorphan (Lybalvi), 2021	Opioid receptor antagonist used to prevent olanzapine's effect on weight and metabolism	Oral 5 mg/10 mg to 20 mg/10 mg	Insomnia, increased ALT and increased CPK.
Quetiapine Extended-Release (Seroquel XR), 2008	Antagonist at 5-HT2A and D2 receptors	Oral 50 -600 mg daily	Daytime sedation, weight gain, dyslipidemia.
Risperidone IM (Rykindo), 2023	D2 and 5HT2A receptor antagonist	IM 50 mg every 2 weeks	Akathisia, and weight increase.
Valproic Acid Delayed-Release (Stavzor), 2008, discontinued in 2013	Precise mechanism unknown; inhibits voltage-gated sodium channels	Oral 750 mg starting dose, not to exceed 60 mg/kg/day daily	Somnolence, weight gain, and tremor.

Abbreviations: D1, D2, D3, D4 = Dopamine receptors; 5HT1A, 5HT2A = Serotonin receptors; H = Histamine receptors; GABA = Gamma Amino Butyric Acid receptors; IM = Intramuscular; IN = Intranasal; IV = Intravenous; SC = subcutaneous

3.4. Depressive disorders

From 2008 to 2023, 16 medications were approved for the treatment of Depressive Disorders including oral tablets (14), intranasal (1), and intravenous (IV) administration (1).

Table 5 Summary descriptions of the newly approved medications in Depressive Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on sedation, weight/lipids, sexual dysfunction and QTc**
Brexanolone (Zulresso), 2019 for Postpartum depression	GABA-A receptor modulator ‡	Intravenous infusion (continuous) 60-90 µg per kilogram per hour for 60 hours.	Headache, dizziness, and somnolence. Schedule IV drug.
Brexpiprazole (Rexulti), 2015	D2 and 5-HT1A partial agonist, and 5-HT2A receptor antagonist	Oral 1-3 mg daily	Akathisia, somnolence, and weight gain.
Bupropion hydrobromide (Aplenzin), 2008	Noradrenergic and dopaminergic reuptake inhibitor	Oral 174 mg-522 mg in the morning	This form contains a technology that allows steady release of bupropion over 24 hours. Side effects include insomnia, weight loss, no sexual dysfunction, and no effects on QTc.
Bupropion hydrochloride (Forfivo XL), 2011	Noradrenergic and dopaminergic reuptake inhibitor	Oral 450 mg in the morning	This form contains 450mg in one extended-release tablet. Side effects include insomnia, weight loss, no sexual dysfunction, and no effects on QTc.

Cariprazine (Vraylar) as adjunct for MDD, 2022	Partial agonist at D2, D3, and 5-HT1A receptors, and antagonist at 5-HT2A receptors	Oral 1.5-4.5 mg/day	Akathisia, insomnia.
Desvenlafaxine (Pristiq), 2008	Serotonin - norepinephrine reuptake inhibitor	Oral 50-400 mg daily	Sedation, sexual dysfunction, decreased appetite
Dextromethorphan + bupropion (Auvelity), 2023	Dextromethorphan prodrug for dextrorphan) is an NDMA receptor antagonist and non-selective serotonin reuptake inhibitor; ‡ bupropion is noradrenergic and dopaminergic reuptake inhibitor	Oral 45 mg dextromethorphan + 105 mg bupropion once daily then increase to twice daily after 3 days	Somnolence, sexual dysfunction.
Duloxetine (Drizalma Sprinkle), 2019	Serotonin - norepinephrine reuptake inhibitor	Oral 30-60 mg daily	Sedation, nausea, and constipation.
Esketamine nasal spray (Spravato), 2020 for treatment refractory depression	NMDA receptor antagonist ‡	Intranasal 56 mg-84 mg 1-2 times weekly	Needs office monitoring for BP elevation, dissociation. Schedule III drug.
Gepirone Extended-Release (Exxua), 2023	Partial 5-HT1A receptor agonist	Oral 18.2-72.6 mg daily	QTc prolongation, and weight gain.
Levomilnacipran (Fetzima), 2009	Serotonin - norepinephrine reuptake inhibitor	Oral 40 mg-120 mg daily	Monitor for BP elevation. Dose-related effects included sexual side effects and urination difficulty.
Quetiapine Extended-Release (Seroquel XR), 2009 (as adjunct in MDD)	5-HT2A and D2 receptor antagonist	Oral 50-300 mg daily	Daytime sedation, weight gain, dyslipidemia.
Trazodone ER (Oleptro), 2010	5-HT2A and 5-HT2B receptor antagonist, - HT1A receptor partial agonist and reuptake inhibitor	Oral 150-375 mg daily	Daytime sedation, QTc prolongation, sexual dysfunction, and priapism (which was not reported in initial studies not powered to detect it).
Vilazodone (Viibryd), 2011	5-HT reuptake inhibitor and 5-HT1A receptor partial agonist	Oral 20-40 mg daily with food	Very low frequency of sexual side effects.
Vortioxetine (Trintellix), 2013	Nonselective serotonin reuptake inhibitor; 5-HT1A receptor agonist, 5-HT1B receptor partial agonist; 5-HT3 and 5-	Oral 5-20 mg daily	Very low frequency of sexual side effects.

	HT7 receptor antagonist. ‡		
Zuranolone (Zurzuvae), 2023 for Postpartum depression	GABA receptor modulator ‡	Oral 30-50 mg nightly	Sedation

‡ Novel mechanism of action

Abbreviations: D2, D3, D4 = Dopamine receptors; 5HT = Serotonin receptors; H = Histamine receptors; GABA = Gamma Amino Butyric Acid receptors; NMDA = N-methyl-D-aspartate receptor; IM = Intramuscular; IN = Intranasal; IV = Intravenous; SC = subcutaneous

3.5. Anxiety disorders

From 2008 to 2023, 2 medications were approved for the treatment of Anxiety disorders, both for oral use.

Table 6 Summary descriptions of the newly approved medications in Anxiety Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on sedation, weight/lipids, sexual dysfunction and QTc**
Duloxetine (Drizalma Sprinkle), 2019 for Generalized Anxiety Disorder	Serotonin - norepinephrine reuptake inhibitor	Oral 30-60 mg daily	Sedation, nausea, and constipation.
Lorazepam Extended-Release (Loreev XR)	Positive allosteric modulator of GABA-A receptors	Oral 1-10 mg daily	Sedation, high risk of misuse (Schedule IV drug).

3.6. Feeding and eating disorders

From 2008 to 2023, 1 medication was approved for the treatment of Feeding and Eating disorders, for oral use.

Table 7 Summary descriptions of the newly approved medications in Feeding and Eating Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on sedation, weight/lipids, dependence risk and others**
Lisdexamfetamine dimesylate (Vyvanse), 2015 for Binge Eating Disorder	Prodrug converted to dextroamphetamine	Oral 50-70 mg daily	High risk of misuse (Schedule II drug). Side effects include weight loss, insomnia.

3.7. Sleep-wake disorders

From 2008 to 2023, 13 medications were approved for the treatment of Sleep-Wake disorders including a variety of formulations including oral tablets (7), oral solution (3), and sublingual (2) use, and 1 oral spray formulations.

Table 8 Summary descriptions of the newly approved medications in Sleep-Wake Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Daridorexant (Quiviviq), 2022 for Insomnia	Dual orexin receptor antagonist ‡	Oral 25-50 mg nightly	Daytime sedation, though shorter half-life than other DORAs. Low abuse liability; Schedule IV drug.
Doxepin (Silenor), 2010 for Insomnia	Serotonin -norepinephrine reuptake inhibitor	Oral 3-6 mg within 30 minutes of bedtime	Daytime sedation
Lemborexant (Dayvigo), 2019 for Insomnia	Dual orexin receptor antagonist ‡	Oral 5-10 mg nightly	Daytime sedation. Low abuse liability; Schedule IV drug
Pitolisant (Wakix), 2019 for Narcolepsy and Cataplexy	Antagonist/inverse agonist at histami-3 receptors ‡	Oral 4.45 mg-17.8 mg nightly	Risk of QTc prolongation
Sodium oxybate (Xyrem), 2017 for Narcolepsy and Cataplexy	Sodium salt of gamma-hydroxybutyrate (GHB); ‡ mechanism not known	Oral solution 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later up to 6-9 g/night	Sedation. Schedule III drug with high abuse potential and only available through REMS program.
Sodium oxybate + other oxybate salts (Xywav), 2020 for Narcolepsy and Cataplexy	Sodium salt of gamma-hydroxybutyrate (GHB); ‡ mechanism not known	Oral solution 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later up to 6-9 g/night	Sedation. Schedule III drug with high abuse potential and only available through REMS program. Contains significantly less sodium than Xyrem.
Sodium oxybate Extended-Release (Lumryz), 2023 for Narcolepsy and Cataplexy	Sodium salt of gamma-hydroxybutyrate (GHB); ‡ mechanism not known	Oral solution 6-9 g nightly	Sedation. Schedule III drug with high abuse potential and only available through REMS program.
Solriamfetol (Sunosi), 2019 for Excessive daytime sleepiness due to OSA or Narcolepsy	Norepinephrine-dopamine reuptake inhibitor	Oral 150-300 mg nightly	Low to moderate abuse potential; Schedule IV drug.
Suvorexant (Belsomra), 2014 for Insomnia	Dual orexin receptor antagonist ‡	Oral 10 mg within 30 minutes of bedtime; could be increased to 20 mg daily	Daytime sedation. Low abuse liability; Schedule IV drug
Tasimelteon (Hetlioz), 2014 for Non-24 Sleep Wake Disorder and	Melatonin receptor agonist ‡	Oral 20 mg nightly, not with food	Somnolence.

Smith-Magenis Syndrome Sleep Disturbance			
Zolpidem Tartrate Sublingual (Edluar), 2009 for Insomnia	Positive allosteric modulator of GABA-A receptors	Sublingual 10 mg at bedtime	Daytime sedation, potential for dependence and misuse, Schedule IV drug
Zolpidem Tartrate SL (Intermezzo), 2011 for Insomnia, discontinued in 2013	Positive allosteric modulator of GABA-A receptors	Sublingual 1.75 mg as needed once per night	Daytime sedation, potential for dependence and misuse, Schedule IV drug
Zolpidem Tartrate Oral Spray (Zolpimist Spray), 2008 for Insomnia	Positive allosteric modulator of GABA-A receptors	Oral Spray 10 mg (two sprays) nightly	Daytime sedation, potential for dependence and misuse, Schedule IV drug

‡ Novel mechanism of action

3.8. Sexual dysfunctions

From 2008 to 2023, 5 medications were approved for the treatment of Sexual Dysfunctions in a variety of oral tablet (2), orally diintegrating tablet (1), gel (1), and subcutaneous injectable (1) formulations.

Table 9 Summary descriptions of the newly approved medications in Sexual Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Avanafil (Stendra), 2012 for Male Erectile Disorder	Phosphodiesterase (PDE) -5 inhibitor	Oral 50 mg-200 mg 30 min before sexual activity	Fast absorption and onset of action relative to other PDE-5 inhibitors
Bremelanotide (Vyleesi), 2019 for Female Desire/Arousal Disorder	Melanocortin (MC)-1 and -2 receptor agonist ‡	SC Injection 1.75 mg-3.5 mg 45 minutes before sexual activity	Acute increase in blood pressure and decrease in heart rate; high incidence of nausea, hyperpigmentation
Eroxon OTC gel, 2023 for Male Erectile Disorder	Nerve endings stimulation ‡	Gel One local application 20 minutes before sexual activity	FDA approved in US, however only available in EU and UK as of early 2024
Flibanserin (Addyi), 2015 for Female Desire/Arousal Disorder	5HT-1A receptor agonist and 5HT-1A receptor antagonist ‡	Oral 100 mg nightly	Increases risk of severe hypotension and syncope; alcohol use contraindicated; only available through REMS program
Vardenafil ODT (Staxyn), 2010 for Male Erectile Disorder	PDE-5 inhibitor	Orally disintegrating tablet 10 mg PO as needed 60 min before sexual activity	Associated with small increases in QTc

‡ Novel mechanism of action

3.9. Substance-related and addictive disorders

From 2008 to 2023, 16 medications were approved for the treatment of Substance Use Disorders, in a variety of oral (1), sublingual (2), intranasal (IN) (4), intramuscular (IM) (1), subcutaneous (SC) (2), buccal (1), transdermal (1), and subdermal (1) formulations, in addition to 1 medication for SC, IV, or IM use and 2 medications for SC or IM use.

Table 10 Summary descriptions of the newly approved medications in Substance-Related and Addictive Disorders

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Buprenorphine Implant (Probuphine), 2016 for Opioid Use Disorder, discontinued in 2020	Partial mu agonist/weak kappa receptor antagonist	Subdermal Implant 74.2 mg / 6 months	Risk of severe withdrawal; Schedule III drug.
Buprenorphine Injection (Sublocade), 2017 for Opioid Use Disorder	Partial mu receptor agonist/weak kappa receptor antagonist	SC 300 mg / month for two months, then 100 mg / month maintenance	Risk of severe withdrawal; Schedule III drug.
Buprenorphine + Naloxone buccal film (Bunavail), 2014 for Opioid Use Disorder, discontinued in 2020	Partial mu receptor agonist/weak receptor kappa antagonist + opioid antagonist	Buccal film 2.1 mg / 0.3 mg to 12.6 mg / 2.1 mg daily	Risk of severe withdrawal; Schedule III drug.
Buprenorphine + Naloxone SL 16 mg / 4 mg (Cassipa), 2018 for Opioid Use Disorder, discontinued in 2020	Partial mu receptor agonist/weak receptor kappa antagonist + opioid antagonist	Sublingual 16 mg / 4 mg daily (brand name is high, single dose)	Risk of severe withdrawal; Schedule III drug.
Buprenorphine + Naloxone (Zubsolv), 2013 Opioid Use Disorder	Partial mu receptor agonist/weak receptor kappa antagonist + opioid antagonist	Sublingual 1.4 mg / 0.36 mg to 11.4 mg/ 2.9 mg daily	Risk of severe withdrawal; Schedule III drug.
Buprenorphine Transdermal (Butrans Patch), 2017 for Opioid Use Disorder	Partial mu receptor agonist/weak receptor kappa antagonist + opioid antagonist	Transdermal 5-20 mcg/hour; replace every 7 days	Risk of severe withdrawal; Schedule III drug.
Buprenorphine XR, (Brixadi) 2023 for Opioid Use Disorder	Partial mu receptor agonist/weak receptor kappa antagonist + opioid antagonist	SC (weekly) 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, and 32 mg/0.64 mL (monthly) 64 mg/0.18 mL, 96 mg/0.27 mL, and 128 mg/0.36 mL.	Injection site pain/infection; risk of severe withdrawal and dependence, Schedule III drug
Lofexidine (Lucemyra), 2018 for Opioid Withdrawal	Alpha-2 adrenergic agonist	Oral 2.4-3.2 mg daily	Risk of hypotension, bradycardia, and syncope; QT interval prolongation; daytime sedation
Naltrexone extended-release injectable (Vivitrol), 2010 for Alcohol and Opioid Use Disorder	Mu opioid receptor antagonist	IM 380 mg monthly	Approved for Opioid use disorder (originally approved for alcohol use disorder since 2006) Injection site pain/infection, risk of precipitated withdrawal, and symptoms of endogenous opioid blockade (i.e. nausea, chills, and joint pain)

Nalmefene injection (Revex), 2023 for Opioid Overdose	Mu opioid receptor antagonist	IV, IM and SC 0.1-1 mcg/kg/dose opioid reversal postop OR 0.5 mg/70kg/dose for opioid overdose	Injection site pain/infection and acute symptoms of endogenous opioid blockade (i.e. nausea, chills, and joint pain)
Nalmefene nasal spray (Opvee), 2023 for Opioid Overdose	Mu opioid receptor antagonist	IN 2.7 mg per device every 2-5 minutes	Much longer duration of action (up to 8h) than intranasal naloxone; may be best indicated in overdose of long-acting opioid agonists.
Naloxone injection (Evzio), 2014 for Opioid Overdose, discontinued in 2020	Opioid receptor antagonist	IM or SC 2 mg /0.4 mL	May result in precipitating acute opioid withdrawal.
Naloxone injection (Zimhi), 2021 for Opioid Overdose	Opioid receptor antagonist	IM or SC 5 mg/0.5 mL	Contains 1 mg more naloxone than Narcan per spray
Naloxone 4 mg nasal spray (Narcan), 2015 for Opioid Overdose	Opioid receptor antagonist	IN 4 mg/spray	Over the counter, as of March 2023
Naloxone 8 mg nasal spray (Kloxxado), 2021 for Opioid Overdose	Opioid receptor antagonist	IN 8 mg/spray	Contains 4 mg more naloxone than Narcan per spray
Naloxone 3 mg nasal spray (RiVive), 2023 for Opioid Overdose	Opioid receptor antagonist	IN 3 mg/spray	Over the counter; least expensive naloxone product

3.10. Neurocognitive disorders

From 2008 to 2023, 6 medications were approved for the treatment of Neurocognitive Disorders, for a variety of oral (3), transdermal (1), and (2) intravenous (IV) use

Table 11 Summary descriptions of the newly approved medications in Neurocognitive disorders

Name, **Year approved**	**Mechanism** **of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Aducanumab (Aduhelm), 2021, to be discontinued in 2024	Monoclonal antibody targeting Beta-amyloid ‡	IV Infusion every 4 weeks titrated from 1 mg for doses 1and2, 3 mg for doses 3, 4, 6 mg for doses 5, 6, and 10 mg for doses 7+	Significant risk of amyloid-related imaging abnormalities-edema (ARIA), including ARIA-Edema (35%), ARIA-H microhemorrhages (19%), and ARIA-H superficial siderosis (15%).
Brexpiprazole (Rexulti), 2023 for Agitation associated with dementia due to Alzheimer's disease	D2 and 5-HT1A receptor partial agonist, and 5-HT2A receptor antagonist	Oral 0.5-2 mg daily NOT PRN	Sedation, akathisia, and weight gain. Increased incidence of cardiovascular adverse reactions (i.e. stroke, transient ischemic attack) in elderly patients with dementia-related psychosis.

Donepezil transdermal (Adlarity), 2022	Acetylcholinesterase inhibitor	Transdermal patch weekly delivering 5 mg or 10 mg daily	Application site reactions (itching, irritation, pain), headache (15%), muscle spasms (9%), insomnia (7%), abdominal pain (5%), constipation (5%), diarrhea (4%), risk of QTc prolongation, bradycardia, and seizures due to cholinomimetic activity.
Lecanemab (Leqembi), 2023	Antibody against Beta-amyloid ‡	IV 10 mg/kg every other week	Infusion-related reactions (20%) and amyloid related imaging abnormalities (ARIA), including ARIA-Edema (10%); possibly better safety profile than Aducanumab. Brain MRI prior to initiation, 5th, 7th, and 14th infusion.
Memantine Extended-Release (Namenda XR), 2010	Non-competitive NMDA receptor antagonist	Oral 7-28 mg daily	Headache, constipation, somnolence, confusion, and possible risk of QTc prolongation.
Memantine and Donepezil (Namzaric) Extended-Release, 2014	Combination of NMDA receptor antagonist and acetylcholinesterase inhibitor	Oral 7 mg / 10 mg to 28 mg / 10 mg Daily	Possible risk of QTc prolongation, bradycardia, somnolence, and seizures due to cholinomimetic activity.

‡ Novel mechanism of action

3.11. Neurodevelopmental disorders

*3.11.1. Attention deficit hyperactivity disorder **(ADHD)***

From 2008 to 2023, 18 medications and treatments were approved for the treatment of ADHD, for a variety of tablet/capsule (12), orally disintegrating tablet (3), transdermal (1), and suspension (2) formulations.

Table 12 Summary description of the newly approved medications in ADHD

Name, Year approved	**Mechanism of Action**	**Route and Dose**	**Notes to clinicians including effects on daytime sedation, dependence risk, and others**
Amphetamine ODT (Adenys XR-ODT), 2016	Monoamine reuptake inhibitor and releasing agent	Orally disintegrating tablet 6.3-18.8 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Amphetamine Salts Extended-Release (Mydayis), 2017	Monoamine reuptake inhibitor and releasing agent	Oral 12.5-50 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss. Up to 16 hours duration of action
Amphetamine (Evekeo), 2012	Monoamine reuptake inhibitor and releasing agent	Oral 5-60 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss. Racemic amphetamine product: greater levoamphetamine concentration may possibly lead to greater sympathomimetic effects

Amphetamine ODT (Evekeo ODT), 2019	Monoamine reuptake inhibitor and releasing agent	Oral 2.5-40 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Amphetamine suspension (Dynavel XR), 2015	Monoamine reuptake inhibitor and releasing agent	Oral 2.5-20 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Clonidine Extended-Release (Kapvay), 2010	Alpha-2 adrenergic agonist	Oral 0.1-0.4 mg nightly	Sedation, hypotension
Dextroamphetamine transdermal (Xelstrym), 2022	Monoamine reuptake inhibitor and releasing agent	Transdermal Patch 4.5 mg/9 hours up to 18 mg/9 hours daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Guanfacine Extended-Release (Intuniv), 2009	Selective alpha-2 adrenergic agonist	Oral 1-4 mg daily	Sedation, hypotension Greater selectivity for alpha-2 adrenergic receptors than clonidine; possibly better side effect profile
Lisdexamfetamine dimesylate (Vyvanse), 2008 for Adult ADHD	Prodrug converted to dextroamphetamine	Oral 50-70 mg daily	High risk of misuse (Schedule II drug). Side effects include weight loss, insomnia.
Methylphenidate (Adhansia XR), 2019, discontinued in 2022	Norepinephrine and dopamine reuptake inhibitor	Oral 10-60 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Methylphenidate (Aptensio XR), 2015	Norepinephrine and dopamine reuptake inhibitor	Oral 10-60 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Methylphenidate ODT (Cotempla XR ODT), 2017	Norepinephrine and dopamine reuptake inhibitor	Orally disintegrating tablet 17.3-51.8 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Methylphenidate (Jornay PM), 2018	Norepinephrine and dopamine reuptake inhibitor	Oral 20-100 mg nightly	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss. Taken at night; delayed-release mechanism for following day
Methylphenidate (QuilliChew ER), 2015	Norepinephrine and dopamine reuptake inhibitor	Oral 20-60 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Methylphenidate Extended-Release (Relexxii), 2022	Norepinephrine and dopamine reuptake inhibitor	Oral 18-72 mg daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.

Methylphenidate suspension (Quillivant XR), 2012	Norepinephrine and dopamine reuptake inhibitor	Oral 25 mg per 5 mL (5 mg/mL) daily	Schedule II drug with potential for abuse; sympathomimetic adverse effects, as well as weight loss.
Serdexmethylphenidate + dexmethylphenidate (Azstarys), 2021	Norepinephrine and dopamine reuptake inhibitor prodrug combination	Oral 26.1/5.2 mg to 52.3/10.4 mg daily	Schedule II drug combination with liability for abuse; sympathomimetic effects, including appetite suppression, may lead to weight loss.
Viloxazine (Qelbree), 2021	Norepinephrine reuptake inhibitor	Oral 100-200 mg daily	Somnolence; little effect on weight; no effect on QTc.

4. Discussion

This systematic review identified FDA-approved or the treatment of psychiatric and related disorders over the last 15 years (2008-2023) for a wide range of psychiatric disorders. 118 medications were identified, including: 26 for Schizophrenia, 12 for Bipolar Disorders, 16 for Depressive Disorders, two for Anxiety Disorders, one for Feeding and Eating disorders, 13 for Sleep-Wake Disorders, five for Sexual Dysfunctions, 16 for Substance Use Disorders, six for Neurocognitive Disorders, and 18 for Neurodevelopmental Disorders (specifically, Attention-Deficit/Hyperactivity Disorder, ADHD), in addition to three for Psychiatric Medication-Related Movement Disorders. It is important to note that 37 out of the 118 medications were New Drug Application (NDA) approvals by the FDA, i.e., they have not been previously approved for another indication. We also noted that nine medications were discontinued by the manufacturer, with no reported safety or effectiveness concerns. No new medications were approved for the following disorders: OCD, Trauma- and Stressor-Related Disorders, Dissociative Disorders, Somatic symptom disorders, and Disruptive, Impulse-Control, and Conduct Disorders.

Of note, there was a shift in schizophrenia management towards partial dopamine receptor agonism, as is the case with antipsychotics such as aripiprazole (Abilify), brexpiprazole (Rexulti), and cariprazine (Vraylar), as opposed to traditional dopamine receptor antagonism (Mohr et al., 2022). This direction reflects an evolving understanding of dopaminergic activity in the meso-cortical and mesolimbic pathways, with the aim to achieve improved symptomatology in both positive and negative symptom domains (Sonnenschein and Grace, 2020). Long acting injectable (LAI) medications with reduced dosing frequencies, show markedly greater treatment adherence compared to oral antipsychotics among patients with schizophrenia and schizoaffective disorder (Lachaine, 2015). New formulations of paliperidone palmitate, including Invega Trinza and Invega Hafyera, offer longer durations of action of 3 months and 6 months, respectively (Peters et al., 2023). In particular, Invega Hafyera, which was approved in late 2021, is the first, and only long-acting injectable antipsychotic that can be administered at a frequency of twice yearly (Peters et al., 2023). These new long-acting formulations offer additional treatment options to patients and clinicians, helping to combat the challenge of suboptimal medication adherence among patients with schizophrenia and similar conditions, especially when used as first line in addition to traditional conversion from oral formulations (Lachaine, 2015).

There were several other innovative advancements during this period, notably: a long-acting, monthly antipsychotic (risperidone/Perseris) subcutaneously rather than IM (Clark and Taylor, 2020), a sublingual alpha-2 adrenergic agonist indicated for agitation in Schizophrenia or Bipolar I or II Disorder (dexmedetomidine/Igalmi) (Smith et al., 2023), an antipsychotic with samidorphan, an added opioid agonist/antagonist to address olanzapine-induced weight gain (Lybalvi) (Monahan et al., 2022), and an antipsychotic (lumateperone tosylate/Caplyta) which, modulates glutamatergic signaling, with precognitive benefits in patients with Bipolar Disorder and Schizophrenia, in addition to 5-HT2A and D2 receptor antagonist activity (Greenwood et al., 2020). Moreover, a new form of aripiprazole tablet was introduced incorporating a sensor to monitor compliance (Abilify MyCite) (Cochran et al., 2022).

Furthermore, in the last few years, the first two medications were approved for postpartum depression, intravenous brexanolone (Zulresso) and oral zuranolone (Zurzuvae), which are neuroactive steroid GABA-A receptor modulators (Walkery et al., 2021). In addition, several opioid antagonists with various durations of action were introduced aimed at addressing the opioid overdose risk, including several nasal sprays (Narcan, Opvee, Kloxxado, and RiVive), and nalmefene (Revex), in addition to injectable, extended-release formulation of naltrexone (Vivitrol) for opioid use disorder (Skolnick, 2022).

Novel drugs for insomnia that were developed act on orexin receptors (known as dual orexin receptor antagonists), such as suvorexant (Belsomra), lemborexant (Dayvigo), and daridorexant (Quiviviq) (Xue et al., 2021). Pitolisant (Wakix), on the other hand, which promotes wakefulness by antagonizing histamine-3 receptors, is the first drug of its kind to be used in the treatment of narcolepsy (Li and Yang, 2020).

We also noted the introduction of monoclonal antibodies into the market for Alzheimer's -type dementia, with drugs such as Lecanemab (Leqembi) and Aducanumab (Aduhelm). Though controversial, this signifies the entry of immunotherapy into the psychiatric pharmacological domain, a rising trend in all medical specialties (Usman et al., 2021). The maker of Aducanumab announced that it will be scheduled for discontinuation in 2024 for financial reasons (Kunz, 2024), although concerns about efficacy and cost likely undermined its commercial viability.

A number of new medications for the treatment of ADHD have been approved in the past 15 years, including new formulations of central nervous system stimulants and several non-stimulant medications. During this period, 14 new formulations of amphetamine and methylphenidate were approved, including several extended and delayed-release products, as well as a transdermal patch system and an ODT form of long-acting stimulant. In addition to previously approved atomoxetine, new non-stimulant medications, including viloxazine (Qelbree), a norepinephrine reuptake inhibitor, and alpha-2 adrenergic agonists, such as extended release guanfacine (Intuniv) and clonidine (Kapvay), provide treatment options for patients who might not be well-suited to stimulant treatment (Newcorn et al., 2022). A prescription ADHD treatment that was cleared by the FDA in 2020, is worth mentioning in this context even though it is non-pharmacological. EndeavorRx is a digital therapy software (Android or iOS compatible) video game leading to improved objective attention in children with ADHD ages 8-12, after using it for 25 minutes/day, 5 days/week, for at least 4 weeks. Additional FDA-cleared digital therapeutics available by prescription in psychiatry (Wang et al., 2023) include reSet for Substance Use Disorders (2016), reSet-O for Opioid Use Disorder (2018), Somryst for chronic insomnia using CBT for insomnia (2019), and Nightware for sleep disturbances in PTSD (2020).

Other advancements in the field have continued to mitigate barriers to medication administration through innovations in medication delivery and frequency of administration. For instance, Drizalma Sprinkle is a newly approved, delayed-release oral capsule formulation of duloxetine that may be swallowed or sprinkled on food. New formulations of asenapine, including a sublingual tablet (Saphris) (Citrome 2011) and transdermal system (Secuado) (Zhou et al., 2020), offer alternatives to oral tablets and intramuscular injection for the treatment of psychosis. We also see the first and currently only drug approved by the FDA for the treatment of binge eating disorder, lisdexamfetamine (Vyvanse), a prodrug converted to dextroamphetamine (Schneider et al., 2021).

Of note, several medications were approved for weight management from 2008-2023 which is of special interest to psychiatry given the risk of weight gain with some psychiatric medications and psychiatric disorders. The FDA approved oral combination of phentermine and topiramate (Qsymia) in 2012, oral combination of bupropion and naltrexone (Contrave) in 2014, oral phentermine that could be used up to 3 times/day before meals (Lomaira) in 2016 and daily subcutaneous MC4 agonist setmelanotide (Imcivree) in 2020. This era witnessed the development of Glucagon-like peptide-1 (GLP-1) receptor agonists for diabetes mellitus type 2 with significant impact on weight loss, such as weekly subcutaneous injection of semaglutide (Ozempic/ Wegovy) in 2017, and tirzepatide (Mounjaro in 2022), in addition to daily oral semaglutide (Rybelsus) in 2023. The FDA approved tirzepatide specifically for weight loss (Zipbound) in 2023.

No new medications were approved from 2008-2023, for anxiety disorders, except for two medications which were new formulations of previously approved medications (extended-release lorazepam and the sprinkle form of duloxetine). Notably missing from this list are new medications indicated for Obsessive Compulsive Disorder, Trauma- and Stressor-Related Disorders, Dissociative Disorders, Somatic Symptom Disorders, or Disruptive, Impulse-Control, and Conduct Disorders. During the 15-year period for which the review was conducted, we found that no new medications were approved for any of these conditions.

It should be noted that all such new medication options are just as subject to the same behavioral and psychological factors that have affected all previous psychiatric medication treatments. Medications are only as effective if patients are able and willing to take them consistently and as prescribed. Medication adherence remains an essential requirement for treatment effectiveness and remains dependent on such factors as patient beliefs, self-efficacy, perceived barriers, and social support (Holmes et al., 2014). The new medications continue to serve as vehicles for helping patients not only to reduce aversive symptoms, but also to assist them in pursuing meaningful life goals (Deegan et al., 2017). The new medications also continue to exist alongside psychotherapy in the treatment of psychiatric conditions, sometimes chosen as the sole treatment and sometimes used along with psychotherapy (Kamenov et al., 2017).

With the development of new advancements in psychotropic medications, it is important to examine the barriers which may curtail the prescription of novel medications by psychiatrists. Concrete examples of such barriers are reflected in this review. For example, Lecanemab (Leqembi) is expected to cost $26,500 per year, limiting its access to the general population (Burke et al., 2023). Moreover, the route of administration of Brexanolone, a novel medication indicated for postpartum depression, is intravenous only, limiting its use to medical facilities or other environments able to provide lengthy, scheduled infusions (Faden and Citrome, 2020). In general medicine, the uptake of an evidence-based intervention into clinical practice can take on average 17 years before it becomes part of a routine practice (Morris, 2011), though it remains unclear if such a delay extends to psychiatry as well. Studies have suggested a broad range of factors that affect the uptake of new medicines in healthcare (Medlinskiene et al., 2021). These include patient factors, prescriber factors (i.e. exposure to and interaction with pharmaceutical companies), medicine-level factors (such as the cost of new medicines and their safety profile), organization level factors (i.e. teaching status) and external environment-level factors (such as information sources, reimbursement, formulary conditions, and guidelines).

Strengths and Limitations

This systematic review displayed several strengths, such as its broad search strategy and inclusion of multiple medication classes which were systematically organized by disorder. This review also provided information on mechanism of action, evidence for uses, dosing and adverse effects. The result is a practical resource providing a concise summary of newly approved psychotropic medications in an objective format. In addition, by highlighting the mechanism of action and dosing, this review reflects new trends and developments within the field.

With regard to limitations, this systematic review is restricted to the 2008–2023-time frame. It is acknowledged that new medications are being continuously approved and recent or upcoming developments may not have been captured by this review. However, a second part of this review will be published containing the psychiatric medications in the drug development pipeline that were currently in or completed Phase 3 clinical trials up to the end of 2023.

5. Conclusion and future directions

New medications may only have a beneficial impact if adopted and used by clinicians to serve the general population. It appears that several medications listed in this review have not yet been widely adopted into clinical practice. In fact, this review may serve as the first introduction to these agents for clinicians who may have been unaware of newly approved treatments. Many barriers exist to the administration of, and ultimately adherence to psychotropic medications. This systematic review aims to aid in the adoption of new medications by providing an objective and practical guide of novel, newly approved medications for clinical use. In the rapidly evolving landscape of pharmacotherapy for psychiatric conditions, more studies and efforts are needed to better understand and address barriers to the adoption and wide clinical use of novel treatments. Efforts to promote innovation, development, and acceptance of new treatments are pivotal. Without such efforts, there may be a significant delay in the impact of new alternative treatments.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflicts of interest to report regarding the content of this systematic review.

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