Table 1.

Medications for Pain in Those With an AUD OR SUD

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Non-narcotic medications						
Acetaminophen	COX inhibitor	325–1,000 mg every 4–6 h PRN maximum 1 g every 4 h and 4 g/d from all sources	Mild pain, fever	Headache, nausea or vomiting, rash	Anaphylaxis, hepatotoxicity, renal tubular necrosis, nephropathy, anemia, thrombocytopenia	Caution in the setting of hepatic disease, chronic alcohol use, renal impairment, hypersensitivity
Aspirin	COX inhibitor, reduces prostaglandin and thromboxane A2 synthesis, anti-inflammatory, affects platelet aggregation	325–650 mg every 4–6 h PRN, maximum 4 g/d	Mild pain, arthritis, fever	Nausea, vomiting, abdominal pain, constipation or diarrhea, dizziness, tinnitus, hyperuricemia, ecchymosis	Blood cell dyscrasias, anaphylaxis, angioedema, bleeding, GI bleeding and perforation, ulcer, nephrotoxicity, hepatotoxicity, Reye syndrome	GI bleeding, G6PD deficiency, uncontrolled HTN, pregnancy starting at 30 wk gestation, alcohol use, renal or hepatic impairment, gout
NSAIDs (ibuprofen, naproxen, celecoxib, meloxicam, Voltaren, indomethacin, others)	Blocks prostaglandin synthesis through COX-1 and COX-2 inhibition	Oral, gel, topical patch	Mild-to-moderate pain, fever, osteoarthritis, rheumatoid arthritis, others	Dyspepsia, nausea, abdominal pain, rash, pruritus, ecchymosis, dizziness, AST or ALT elevation	GI bleeding and perforation, edema, HTN, congestive heart failure, stroke, thrombotic events, renal impairment, nephritis, nephrotic syndrome, chronic kidney disease, SJS, TEN	Renal impairment, interactions with numerous medications[12]
Lidocaine **- Postherpetic neuralgia**	Blockade of voltage-gated sodium channels leading to reversible block of action potential propagation	Various dosing, maximum 4.5 mg/kg/dose, 300 mg/total dose; patch, regional, infiltration, peripheral, or central nerve block	Arrhythmias; local, regional, and spinal anesthesia	Tremor, confusion, hypotension, lightheadedness, dizziness, nausea, vomiting, anxiety, hallucinations, drowsiness, lethargy	CNS toxicity, seizures, respiratory or cardiac arrest, bradycardia, heart block, arrhythmia, hypotension, anaphylaxis	Cardiac impairment, elderly, caution in renal impairment, hepatic impairment, antiarrhythmic, lowers seizure threshold, bradycardia
Capsaicin topical **- Diabetic neuropathy, neuropathic pain with postherpetic neuralgia**	Exact mechanism unknown, selectively binds TRPV1 receptors, degenerates cutaneous nociceptive neurons, substance P depletion	Cream 0.025%, 0.075%, apply TID to QID	Musculoskeletal pain	Burning, erythema, hyperalgesia	Severe burns, neurotoxicity	Avoid use on skin that is damaged, broken, or irritated
Over-the-counter agents						
S-adenosyl-methionine (SAMe)	DNA methylation	200 mg by mouth BID up to 800 mg by mouth BID, TID dosing	Treatment-resistant depression (TRD), pain disorders, chronic fatigue syndrome, osteoarthritis, low back and knee pain, fibromyalgia, cognition, dementia	Nausea, diarrhea, dry mouth, headache, anxiety, restlessness, insomnia	Mania	Generally viewed as safe
Magnesium oxide	Inhibits calcium influx via NMDA receptor blockade	Oral, IV, intrathecal 400 mg by mouth QHS	Headache prevention, perioperative and postoperative pain, dysmenorrhea, neuropathic pain, postherpetic neuralgia, neuropathy	Diarrhea, GI upset, weakness, nausea, and vomiting		Generally viewed as safe

(continued)

Table 1 (continued).

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Antidepressants						
TCAs						
Amitriptyline **- Depression**	Tertiary amine TCA inhibits serotonin and norepinephrine reuptake	10–25 mg by mouth QHS, up to 150 mg by mouth QHS	Off label: diabetic neuropathy, migraine headache prophylaxis, postherpetic neuralgia fibromyalgia	Sedation, nausea, vomiting, constipation, dry mouth, blurry vision, palpitations, tachycardia, weight gain, rash, urinary retention	HTN, syncope, arrhythmias, QTc prolongation, MI, stroke, tardive dyskinesia, blood cell dyscrasias, hallucinations, psychosis, mania, depression, suicidality, serotonin syndrome, transaminitis, paralytic ileus, withdrawal symptoms if abruptly discontinued	Can monitor for therapeutic drug levels, efficacy may take weeks, ECG if cardiac disease, suicidality, behavioral changes, CYP2D6 (primary) 1A2, 2C19, active metabolites including nortriptyline
Nortriptyline **- Depression**	Secondary amine TCA Active metabolite of amitriptyline	10–25 mg by mouth QHS, up to 150 mg by mouth QHS	Off label: chronic pain, neuropathy, postherpetic neuralgia	Sedation, nausea, vomiting, constipation, dry mouth, blurry vision, palpitations, tachycardia, weight gain, rash, urinary retention, increased appetite, tachycardia, confusion, restlessness	HTN, syncope, arrhythmias, QTc prolongation, MI, stroke, tardive dyskinesia, blood cell dyscrasias, hallucinations, psychosis, mania, depression, suicidality, serotonin syndrome, transaminitis, paralytic ileus, withdrawal symptoms if abruptly discontinued	Similar cautions and monitoring as amitriptyline; lower sedation, hypotension, and anticholinergic side effects compared with tertiary amines (amitriptyline)
SNRIs						
Duloxetine **- MDD, GAD** **- Diabetic neuropathy** **- Fibromyalgia** **- Chronic musculoskeletal pain**	SNRI	20–30 mg by mouth daily, up to 60 mg by mouth BID, often dosed BID for pain disorders	Off label: chemotherapy-induced peripheral neuropathy and stress urinary incontinence	Headache, nausea, weight loss, abdominal pain, somnolence, fatigue, nausea, vomiting, dizziness, sexual dysfunction, agitation, elevated blood pressure, urinary hesitancy, ALT or AST elevation	Withdrawal syndrome, mania, depression, suicidality, serotonin syndrome, seizures, SIADH, liver enzymes, hypotension, bleeding, SJS, EM, hyponatremia	Doses >60 mg/d are rarely more effective for depression; creatinine clearance <30, hepatic disease, cirrhosis, abrupt withdrawal, elderly
Venlafaxine **- MDD, GAD, social anxiety disorder, panic disorder**	SNRI also inhibits dopamine reuptake	75–225 mg by mouth/d, typical dose 150 mg ER by mouth/d	Off label: migraine prophylaxis, diabetic neuropathy, fibromyalgia, PTSD, OCD, ADHD, premenstrual dysphoric disorder	Headache, nausea constipation, diarrhea, weight loss, sexual dysfunction, decreased libido, abnormal dreams	Hypomania/mania, suicidality, serotonin syndrome, SIADH, bleeding, blood cell dyscrasias, SJS, TEN, EM, hyponatremia, seizures, HTN, arrhythmia, QT prolongation, Torsades de pointes, pancreatitis, hepatotoxicity, withdrawal syndrome	Doses >225 mg may increase blood pressure; liver CYP2D6 (primary) 3A4, active metabolite desvenlafaxine
Desvenlafaxine **- MDD**	SNRI and dopamine reuptake	50–100 mg by mouth/d, maximum 200 mg by mouth/d	Off label: neuropathic pain, moderate-to-severe menopausal vasomotor symptoms	Headache, nausea constipation, dry mouth, diarrhea, weight loss, sexual dysfunction, decreased libido, abnormal dreams, hyperlipidemia, anxiety, vertigo, yawning	EPS, SIADH, HTN, serotonin syndrome, mania, hypomania, depression exacerbation, suicidality, hypersensitivity reaction, SJS, glaucoma, seizures, SIADH, hyponatremia, withdrawal syndrome	CYP3A4 (minor)

(continued)

Table 1 (continued).

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Milnacipran **- Fibromyalgia**	SNRI	12.5 mg by mouth/d x 1, then 12.5 mg by mouth BID x 2 d, then to 50 mg by mouth BID over 1 wk, maximum 200 mg/d	Off label: MDD	Headache, nausea constipation, dry mouth, dizziness, weight loss, sexual dysfunction, decreased libido, ALT or AST elevated, paresthesias, tremor, chest discomfort, urinary retention, urinary hesitancy	EPS, SIADH, HTN, serotonin syndrome, mania, hypomania, depression exacerbation, suicidality, SJS, EM, cardiomyopathy, bleeding, hepatotoxicity, withdrawal syndrome	*Avoid in AUD or alcohol abuse*, hepatic impairment; creatinine at baseline, BP/HR at baseline; CrCL <50; avoid in chronic liver disease
Antiepileptic medications						
Topiramate **- Seizure disorders** **- Migraine headache prophylaxis**	Carbonic anhydrase inhibitor; positive allostatic modulator at $GABA_A$ receptors, increases chloride ion influx; GABA-mediated inhibition; AMPA/kainate	Dosage titration and varying doses from 50 mg up to 300 mg by mouth daily	Off label: AUD, cocaine use disorder, tobacco use disorder, PTSD, binge-eating disorder, weight loss	Brain fog/cognitive impairment bilateral upper and lower extremity paresthesia, hypoesthesia, weight loss, somnolence, fatigue, ataxia, taste changes, visual disturbances, nystagmus, tremor, anxiety, nervousness, depression, paresthesias, dysesthesias	Nephrolithiasis, metabolic acidosis, osteoporosis, osteomalacia, hyperammonemia, SJS, TEN, EM, may decrease effectiveness of oral contraceptives, folate deficiency, major congenital malformations	Creatinine at baseline, bicarbonate, signs and symptoms of depression, behavioral changes, suicidality Consider use in patients with chronic migraine headache, comorbid PTSD, binge-eating disorder, and to promote weight loss
Gabapentin **- Partial seizures** **- Postherpetic neuralgia**	Modulates GABAergic activity on voltage-gated calcium channels	300 mg by mouth TID or 600 mg by mouth TID	Off label: pain disorders: fibromyalgia, neuropathy/ neuralgia AUD, postacute protracted alcohol withdrawal (with anxiety and insomnia), moderate to severe menopausal vasomotor symptoms	Dizziness, somnolence, fatigue, peripheral edema, weight gain	Depression, suicidality, allergic reactions including SJS, TEN, EM, angioedema	Creatinine at baseline, signs and symptoms of depression, behavioral changes, suicidality; consider use in patients with comorbid pain disorders or alcohol withdrawal anxiety and insomnia, abuse potential
Pregabalin **- Diabetic neuropathy** **- Fibromyalgia** **- Seizures**	Binds to presynaptic voltage-gated calcium channels and decreasing calcium influx, decreasing release of excitatory neurotransmitters	Various dosing for IR and ER form; suggested starting dose for neuropathic pain is 50 mg by mouth TID, increasing to 300 mg/d within 1 wk of starting	Off label: chronic pain, GAD, social anxiety, bipolar disorder, insomnia, restless leg syndrome	Dizziness, somnolence, blurred vision, nausea, headache, constipation, impaired coordination, decreased platelets	Depression, suicidality, SJS, thrombocytopenia, rhabdomyolysis, abuse potential, withdrawal syndrome	Avoid in alcohol use, abuse potential; CrCL <30, renal impairment, angioedema, CNS depressant risk; structurally like GABA but does not bind to GABA receptors
Valproate **- Migraine headache prophylaxis** **- Bipolar disorder** **- Seizures**	Inhibits voltage-gated sodium channels	250–500 mg twice daily for migraine prophylaxis	Off label: diabetic peripheral neuropathy, postherpetic neuralgia, agitation and aggression related to traumatic brain injury	Headache, nausea/ vomiting, sedation, blood cell dyscrasias, dyspepsia, abdominal pain diarrhea, weight gain, transaminitis, blurry vision, tremor	Hepatotoxicity, pancreatitis, hyponatremia, pancytopenia, allergic reactions including SJS, TEN, anaphylaxis, psychosis, hallucinations, suicidality, hyperammonemia	Caution for use in those on lamotrigine or cross-tapering due to risk of serious skin reactions (SJS and TEN)

(continued)

Table 1 (continued).

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Carbamazepine **- Neuropathy** **- Neuralgia**	Blocks voltage-gated sodium channels; exact mechanism unknown in trigeminal neuralgia	200–400 mg twice daily, max 1,200 mg daily	Off label: restless leg syndrome, bipolar disorder, seizure disorder	Nausea/vomiting, constipation, dizziness, ataxia, HTN, hyponatremia, dry mouth, pruritus, blurry vision, tremor, rash, HTN, tremor, hyponatremia, speech disturbance	Suicidality, male infertility, serious dermatologic reactions, anaphylaxis, blood cell dyscrasias, aplastic anemia, hyperammonemia, agranulocytosis, SIADH, hepatotoxicity, arrhythmia, AV block, syncope, SJS, TEN, EM, syncope, angioedema, pancreatitis	CYP1A2, 2C8, 3A4 (primary); many cytochrome interactions and inducer CYP3A4 inhibition; caution in those with elevated AST/ALT
Oxcarbazepine **- Partial seizures**	Blocks voltage-sensitive sodium channels, exact mechanism unknown	300–1,200 mg by mouth BID, starting with 300 mg by mouth BID and increasing by 300 mg daily every 3 d as tolerated	Off label: neuropathy/ neuralgia, trigeminal neuralgia, bipolar disorder	Dizziness, sedation, ataxia, headache, confusion, nausea, abdominal pain, diarrhea, constipation, rash, hyponatremia, somnolence, fatigue	Suicidality, SIADH, anaphylaxis, SJS, TEN, EM, pancreatitis; hematologic side effects are rare	10-keto derivative of carbamazepine; causes fewer rashes and is typically better tolerated than carbamazepine; hyponatremia may be more common in oxcarbazepine; may decrease efficacy of oral contraceptives
Lamotrigine **- Bipolar I disorder maintenance** **- Seizure disorders** **- Lennox-Gastaut syndrome**	Selectively inhibits voltage-gated sodium channels, stabilizes presynaptic neuronal membranes, inhibits presynaptic glutamate and aspartate release	Start 25 mg daily, increase by 25 mg/ d weekly, usual dose 100 mg daily migraine prophylaxis, up to 200–400 mg daily divide daily to BID, valproate inhibits the metabolism of lamotrigine	Off label: migraine with aura prophylaxis, diabetic neuropathy, fibromyalgia, bipolar depression, mood stability in personality disorders	Dizziness, vertigo, headache, ataxia, nausea, vomiting, blurry vision, diarrhea, constipation, dyspepsia, abdominal pain, xerostomia, amenorrhea, rash, fatigue, tremor, fever, anxiety, mood lability, edema, impaired concentration, irritability, depression	Suicidality, worsening depression, severe rash, SJS, TEN, angioedema, severe or life-threatening hypersensitivity reaction, blood cell dyscrasias, aseptic meningitis, hepatic failure, arrhythmia, tubulointerstitial nephritis	Caution in pregnancy: possible risk of teratogenicity, CrCL <50, renal impairment, hepatitis impairment, heart failure, arrhythmia or cardiac disease, Cr at baseline, ECG at baseline in patients over age 60 y
Lacosamide **- Adjunctive therapy of seizure disorders**	Stabilizes voltage-gated sodium channels	Start 50 mg by mouth BID x 3 wk, may increase by 100 mg/d/wk, up to 100–200 mg by mouth BID	Off label: diabetic neuropathy	Dizziness, vertigo, headache, ataxia, nausea, blurry vision, nystagmus, diarrhea, tremor, depression, somnolence, pruritis	Suicidality, psychosis, hypersensitivity, SJS, TEN, blood cell dyscrasias, abuse potential ECG PR prolongation, AV block, bradycardia, ventricular arrhythmia, atrial fibrillation	*Avoid alcohol use, abuse potential* CrCL <30, mild-moderate hepatic impairment: decrease maximum dose by 25%; avoid severe impairment, cardiovascular disease, cardiac conductivity
Opioid pain medications						
Tramadol **- Pain moderate to severe, acute, and chronic**	μ-opioid receptor agonist, also SNRI	Start: IR: 25 mg by mouth in the morning, up to 50–100 mg by mouth every 4–6 PRN Chronic: 100–300 mg ER by mouth daily	Off label: depression, premature ejaculation	Dizziness, headache, nausea, vomiting, diarrhea, constipation, dyspepsia, pruritis, flushing, insomnia, xerostomia	Suicidal ideation, risk of seizures especially at high doses and when co-prescribed other serotoninergic medications and antidepressants, or general anesthetic, serotonin syndrome, sleep apnea, anaphylaxis, SJS, TEN, hypotension, syncope, QT prolongation	*Abuse potential, misuse*, alcohol or drug intoxication, risks with concomitant use with benzodiazepines or other CNS depressants, serotonin syndrome, neonatal opioid withdrawal Avoid when the CrCl <30, MAO inhibitor within 2 wk, cardiac disease, QT prolongation, ventricular arrhythmia, seizure risk, head injury

(continued)

Table 1 (continued).

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Tapentadol **- Pain moderate to severe, acute and chronic** **- Diabetic peripheral neuropathic pain**	μ-opioid receptor agonist, also SNRI	50–100 mg by mouth every 4–6 h PRN		Dizziness, headache, somnolence, fatigue, lethargy, nausea, vomiting, dyspepsia, constipation, diaphoresis, pruritus, insomnia, anxiety	Respiratory depression, confusion, coma, hallucinations, seizures, tachycardia, agitation, tremor, miosis, dyspnea, atrial fibrillation; risk of seizures especially at high doses and when co-prescribed other serotoninergic medications and antidepressants, or general anesthetic, serotonin syndrome, sleep apnea, anaphylaxis, SJS, TEN, hypotension, syncope, QT prolongation	Abuse potential, misuse, alcohol or drug intoxication, risks with concomitant use with benzodiazepines or other CNS depressants, serotonin syndrome, neonatal opioid withdrawal Avoid when CrCl <30, hepatic impairment, MAO inhibitor within 2 wk, pulmonary impairment, seizure risk, head injury
Buprenorphine + naloxone **- OUD**	Opioid partial agonist	Dosing for OUD: dosage escalation starting with 2 mg/0.5 mg SL x 1, up to 8/2 mg SL on first day, up to 16 mg SL daily, usual maintenance dose 4 mg/1 mg–24 mg/6 mg SL daily	OUD, AUD: off label, adjunct in OUD	Headache, insomnia, anxiety, dizziness, depression, vertigo, rigors, vomiting, pain, withdrawal symptoms	Hepatotoxicity, misuse and dependency, adrenal insufficiency, respiratory depression, central sleep apnea, anaphylaxis, QT interval prolongation, withdrawal	Moderate-to-severe hepatic disease, consider buprenorphine monotherapy Consider use in patients with OUD and comorbid AUDs
Muscle relaxants						
Baclofen (see below)						
Carisoprodol **- Musculoskeletal pain, acute**	Centrally acting muscle relaxant	250–350 mg by mouth TID and QHS for up to 2–3 wk, taper gradually		Dizziness, drowsiness, headache	EM, angioedema, seizures, hypotension, syncope, blood cell dyscrasias	Abuse, dependency, withdrawal symptoms; caution renal impairment, hepatic impairment, seizure history or seizure risk, substance use history
Cyclobenzaprine **- Muscle spasm**	SNRI, centrally acting muscle relaxant	15–30 mg by mouth/d up to 3 wk		Dizziness, drowsiness, sedation, fatigue, constipation, dyspepsia, nausea, anxiety, confusion	Psychosis, seizures, stroke, myocardial infarction, arrhythmia, hypersensitivity, anaphylaxis	Caution in use with benzodiazepines or other CNS depressants, serotonin syndrome, alcohol use, myocardial infarction, hepatic impairment, elderly, cardiac conduction disturbance, arrhythmia, MAO inhibitor in 2 wk
Methocarbamol **- Muscle spasm**	Centrally acting muscle relaxant	1,000 mg by mouth QID, start 1,500 mg by mouth QID for 2–3 d, other dosing for IM or IV route		Dizziness, somnolence, nausea, vomiting, headache, hypotension, lightheadedness, urticaria, pruritus, rash	Seizures, syncope, bradycardia, anaphylaxis	Caution in use with benzodiazepines or other CNS depressants, alcohol use; seizure disorder, elderly, renal impairment
Tizanidine **- Spasticity**	Binds to central alpha-2 adrenergic receptors, centrally acting muscle relaxant	2 mg by mouth x 1, may repeat every 6–8 PRN, up to 3 doses/24 h, may increase by 2–4 mg/dose every 1–4 d, taper dose if prolonged, high dose use		Dizziness, somnolence, hypotension, nausea, vomiting, constipation, bradycardia, blurry vision, nervousness, hallucinations	Hallucinations, syncope, hepatotoxicity, bradycardia, withdrawal symptoms, SJS, anaphylaxis, exfoliative dermatitis	Caution in use with benzodiazepines or other CNS depressants, alcohol use; caution in breastfeeding, abrupt withdrawal, elderly patients, CrCl <25, hepatic impairment

(continued)

Table 1 (continued).

Medications and FDA indications	Mechanism of action	Typical dose	Indication/evidence	Common side effects	Serious reactions	Caution/other information
Emerging medications or medications of interest/concern						
Baclofen **- Muscle relaxant used to treat spasticity**	$GABA_B$ receptor antagonist	Begin with 5 mg by mouth TID, titrating up 5–10 mg/d every 3 d, most trials 30–80 mg by mouth daily	Antispasmodic, muscle spasms and pain in multiple sclerosis, AUD, hiccups - Approved for AUD treatment in France	Drowsiness, dizziness, confusion, headaches, urinary frequency, fatigue	CNS depression, respiratory depression, ataxia, depression, hallucinations, autonomic dysregulation	Creatinine at baseline
Cannabis	Cannabinoid		Off label: cancer pain, neuropathic pain, seizure disorder, muscle spasticity, appetite stimulation, treatment of nausea/vomiting			Caution in use with benzodiazepines or other CNS depressants, alcohol use, opioid use, or in those with alcohol use disorder or substance use disorder
Cannabidiol	Cannabinoid	2.5 mg/kg/dose twice daily up to 20 mg/kg/d	Rare pediatric seizure disorders	Somnolence, diarrhea, decreased appetite, and weight loss, vomiting, abdominal discomfort, gastroenteritis, fever, fatigue, insomnia, decreased platelets, increased eosinophils, sialorrhea	Hepatotoxicity, CNS depression, respiratory failure	Liver enzymes, total bilirubin, depression and suicidality, behavioral changes *Limited evidence of efficacy and low quality

Abbreviations: ALT = alanine aminotransferase, AMPA = α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, AST = aspartate aminotransferase, AUD = alcohol use disorder, BID = twice daily, CNS = central nervous system, COX = cyclooxygenase, EM = erythema multiforme, ER = extended release, GABA = γ-aminobutyric acid, GI = gastrointestinal, HTN = hypertension, IM = intramuscular, IR = immediate release, IV = intravenous, NSAID = nonsteroidal anti-inflammatory drug, OUD = opioid use disorder, PRN = as needed, QHS = every night, QID = 4 times/d, SIADH = syndrome of inappropriate antidiuretic hormone secretion, SJS = Stevens–Johnson syndrome, SL = sublingual, SNRI = serotonin-norepinephrine reuptake inhibitor, TCA = tricyclic antidepressant, TEN = toxic epidural necrolysis, TID = 3 times daily.