BRIEF MEDICATION PRESCRIBING DIRECTIONS

Overview

Our early clinical experience as psychiatric consultants in collaborative care revealed a need for standardized medication instructions for Primary Care Providers (PCPs) and Behavioral Health Providers (BHPs). Based on this need, we developed a collection of medication prescribing protocols for commonly prescribed psychotropic medications used for treating adult patients. The protocols are succinct and tailored to the outpatient setting. We developed these prescribing protocols by reviewing and integrating information from several sources: our clinical experience in collaborative care; each medication's FDA labels (accessible at https://dailymed.nlm.nih.gov/dailymed/index.cfm); the published literature; and practice guidelines including reviewing the Agency for Healthcare Research and Quality National Guideline Clearinghouse.

Protocols were organized into three sections: dosing information, monitoring, and general information.

Dosing information: Designed to make prescribing treatment with medications straightforward by listing prescribing instructions on a week-by-week basis, including requirements for baseline lab work, if needed. The dosing protocol includes a **starting dose**, an **initial target dose**, a **typical dosage range**, and a **maximum dose,** where appropriate. Where appropriate, dosing instructions are listed for multiple indications and for off-label use. With some medications, an FDA recommended tapering protocol is listed. In most case, general tapering recommendations are provided.

Monitoring: Designed to emphasize the importance of tracking metabolic parameters, QTc prolongation, as well as drug levels when available.

General information: The longest of the three sections and includes information about medications thought to be clinically relevant to the prescribers. Information in this section includes:

- Mechanism of action—describes the commonly accepted mechanism of action of a drug recognizing that our understanding of how a psychotropic medication works is often incomplete.
- FDA indications— lists FDA indications for a medication.

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- Off-Label indications—describes well-accepted and often evidence-based off-label uses for a medication.
- Pharmacokinetics—lists the T½ for a medication from the FDA label information, when available. Primarily includes information about the parent compound, but where appropriate (e.g., fluoxetine) includes information about metabolites.
- **Common Side Effects**—lists common side effects by percentage, when available, from label information on the FDA website. In general, the side effect is listed if it occurs at a frequency above 5%, is twice placebo, or is clinically relevant. In medications with multiple indications (e.g., Abilify), side effects are listed for more than one indication for the most common uses of the medication.
- **Black Box Warning**—summarizes the black box information for a medication.
- **Contraindications**—summarizes the contraindications for a medication. For all medications, a known hypersensitivity is a contraindication.
- Warning and Precautions—lists *specific* medication-related warnings and precautions found in the FDA label information together with clinically significant medication concerns where appropriate.
- Metabolism/Pharmacogenomics—lists information about metabolism and significant pharmacogenomics concerns as mentioned in the FDA label or in the research literature, e.g., the use of fluoxetine in CYP2D6 poor metabolizers.
- Significant drug-drug interactions—lists significant drug-drug interactions. Given the complexity of drug-drug interactions with some medications in some individuals, it may be appropriate to consult with a pharmacist before prescribing a medication.
- Reproductive potential, Pregnancy, Lactation — As of June 2015, Pregnancy Categories for medications (A, B, C, D, X) are no longer used by FDA to communicate risk. New FDA Classification of risks and benefits associated with medication treatment include considering an individual's status in three categories:
    - **1) Females and Males of Reproductive Potential –** Includes when pregnancy test or contraception is required or recommended; or effects on fertility such as valproate (PCOS)
    - **2) Pregnancy –** Also includes labor and delivery. Consider risks in terms of A) Obstetric, B) Congenital, C) Neonatal, and D) Child long-term neurodevelopmental. Consider need to increase dose of certain medications with advancing pregnancy.
    - **3) Lactation –** Most psychotropic medications are secreted in breastmilk. Consider concentration of medication in breastmilk and safety of medications during breastfeeding. For some individuals, consider prioritizing sleep over breastfeeding, due to risk of mood episode recurrence associated with poor sleep.
- Dosage information—lists the available medication forms, e.g., tablet vs. capsule, etc.

- Generic Available—reports whether a generic form of a medication is available.
- Cost—medication cost (accessible at https://www.goodrx.com/) is reported in four categories: Inexpensive (¢) < $20, moderately expensive ($) $20-100, expensive ($$) $101-250, and very expensive ($$$) > $250

ANTIDEPRESSANT MEDICATIONS

AMITRIPTYLINE (ELAVIL)

DOSING INFORMATION: ***Initiation for depression****:* Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start**: 25-50 mg qHS (10-25 mg qHS in the elderly). Week 2 and beyond: Increase dose by 25-50 mg (10-25 mg in the elderly) per day each week, if tolerated, to an **Initial Target Dose** of 75 mg qHS (50 mg qHS in the elderly). **Typical Dosage Range**: 75-150 mg/day (50-100 mg qHS in the elderly). **Max Dose:** 300 mg/day (150 mg qHS in the elderly). ***Initiation for insomnia (off-label):*** Start 10 mg qHS**;** increase in 10-25 mg qHS increments, if tolerated; **Typical Dosage Range**: 10-50 mg qHS. ***Initiation for pain (off-label):*** Start 10 mg qHS**;** increase in 10-25 mg qHS increments; **Typical Dosage Range**: 10-50 mg qHS. **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING**:** EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range (amitriptyline + nortriptyline): 100-250 ng/ml; Toxic: >500 ng/ml. Blood draw timed to achieve a trough level.

GENERAL INFORMATION: **Mechanism of Action**: TCA: serotonin > NE reuptake inhibitor. **FDA Indications**: Depression. **Off-Label Indications:** pain (doses up to 100 mg); second-line RX for PTSD. **Pharmacokinetics:** T½: 9-27 hrs. **Common Side Effects (MDD):** Sedation, anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation—more so than nortriptyline); orthostatic hypotension, weight gain, sexual side effects, headache. **Black Box Warning:** Increased SI in patients <25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping Elavil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Elavil within 14 days of stopping a MAOI, use with cisapride due to the potential for increased QT interval and increased risk for arrhythmia, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, serotonin syndrome, orthostatic hypotension, cardiac dysrhythmia, QTc prolongation, seizures, manic switch, hepatic changes, decreased blood cell count, hyperthermia**,** increased intraocular pressure, urinary retention, SIADH. **Metabolism/Pharmacogenomics**: Metabolized by 2D6 to less active metabolites and by 2C19 to

nortriptyline. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine), and with medications that affect QTc; check all drug-drug interactions before prescribing. **Dosage Form:** Tablet**. Generic available:** Yes. **Cost**: **¢. FDA label from dailymed.nlm.nih.gov, dated 4.13.16**

BUPROPION (WELLBUTRIN, FORFIVO, APLENZIN, ZYBAN)

DOSING INFORMATION: **Wellbutrin-IR:** Week 1: Baseline blood pressure. **Start IR**: 100 mg bid. Week 2: Increase to 100 mg tid, if tolerated (single dose should not exceed 150 mg). **Wellbutrin-SR**: Week 1: Baseline blood pressure: **Start SR**: 150 mg qAM. Week 2: Increase to an **Initial Target Dose** of 150 mg bid, if tolerated. **Wellbutrin-XL**: Week 1: Baseline blood pressure. **Start XL**: 150 mg qAM. Week 2: Increase to 300 mg qAM, if tolerated. **Note:** Aplenzin has a different titration. **Typical Dosage Range:** 300-450 mg/day. **Max Dose:** 400-450 mg qday. **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize risk of relapse.

MONITORING**:** Blood pressure. Reports of false-positive urine immunoassay screening tests for amphetamines have been reported in patients taking bupropion, consult lab if needed.

GENERAL INFORMATION: Wellbutrin has a novel mechanism of action (weak dopamine and NE reuptake inhibitor; stimulant like effect). **FDA Indications:** Major depressive disorder, season affective disorder (prophylaxis), and smoking cessation. **Off-Label Indications:** Second line RX for ADHD. **Pharmacokinetics:** T½ = 21 hr. **Common Side effects (XL-MDD):** Headache (34%), dry mouth (26%), >5 lb. weight loss (23%), insomnia (20%), nausea (13%), constipation (9%), anxiety (7%), flatulence (6%). **Black Box Warning:** Increased SI in patients < 25 y/o. Increased risk of neuropsychiatric symptoms and suicidality in patients taking bupropion for smoking cessation. **Contraindications:** Seizure disorder, current or prior diagnosis of bulimia or anorexia nervosa, abrupt discontinuation of alcohol or benzodiazepines, use of a MAOI within 14 days of stopping Wellbutrin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Wellbutrin within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, increased risk of seizures, use in patients with a history of traumatic brain injury, potential for hepatotoxicity and hepatic impairment, increased agitation and insomnia, hypertension, decreased appetite and weight, activation of psychosis, potential for renal impairment.. **Pharmacogenetics:** Metabolized by 2B6. **Significant drug-drug interactions:** Inhibitor of 2D6; check all drug-drug interactions before prescribing. **Dosage Form:** Tablet (do not cut, crush or chew). **Generic available:** IR, SR, XL; Cost: **$. FDA label information from FDA label from dailymed.nlm.nih.gov for bupropion dated 9.1.2017.**

CITALOPRAM (CELEXA)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults and baseline QTc in all patients.

Start: 10 mg qday. Week 2: Increase dose to 20 mg qday, if tolerated. Week 3 and beyond: Consider further titration upward to the **Initial and Typical Target Dose** of 40 mg qday as tolerated (except in older adults and 2C19 poor metabolizers where the initial and typical target dose is 20 mg qday). **Max Dose:** 40 mg qday (20 mg qday in older adults and 2C19 poor metabolizers). **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
MONITORING: Weight, consider posttreatment BMP to rule out hyponatremia in older adults consider EKG to measure QTc with dose increases in all patients.
GENERAL INFORMATION: **Mechanism of Action:** Highly selective serotonin reuptake inhibitor. **FDA Indications:** Depression. **Other Indications:** Anxiety disorders. **Pharmacokinetics:** T½= 35 hrs. **Common Side effects (MDD):** Nausea (21%), dry mouth (20%), somnolence (18%), sexual side effects/ejaculatory dysfunction (6%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping Celexa, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Celexa within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, QTc prolongation and torsade de pointes, activation of hypomania/mania, serotonin syndrome, discontinuation symptoms, abnormal bleeding, hyponatremia, seizures. It is recommended that citalopram should not be used in patients with congenital long QTc syndrome, bradycardia, hypokalemia or hypomagnesemia, recent acute myocardial infarction, or uncompensated heart failure or used in combination with drugs that prolong the QTc. **Metabolism/Pharmacogenomics:** Primarily metabolized by 2C19 & 3A4 with 2D6 playing a less significant role. Use caution with 2C19 and 2D6 poor metabolizers. **Significant drug-drug interactions:** Weak 2D6 inhibitor; check all drug-drug interactions before prescribing. **Dosage Form:** Oral solution, Tablet. **Generic available:** Yes. **Cost**: **¢. FDA label information from Drugs @FDA for Celexa dated 6.14.17.**

CLOMIPRAMINE (ANAFRANIL)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start**: 25 mg qHS—should be given with food and dose may be divided to limit GI effects. Week 2: increase to 50 mg qHS. Week 3: increase to 75 mg qHS. Week 4: increase dose to an **Initial Target Dose** of 100 mg qHS. **Max Dose:** 250 mg/day. **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 150-300 ng/ml; Toxic > 500 ng/ml. Blood draw timed to achieve a trough level, goal approximately 12 hours after last dose.

GENERAL INFORMATION: **Mechanism of Action**: TCA, tertiary amine: serotonin >> NE reuptake inhibitor. **FDA Indications:** OCD. **Off-Label Indications:** Depression. **Pharmacokinetics:** T½: 32 hr. **Common Side Effects (OCD):** dry mouth (84%), somnolence (54%), dizziness (54%), tremor (54%), headache (52%), constipation (47%), ejaculation failure (42%), fatigue (39%), nausea (33%), increased sweating (29%), dyspepsia (22%), libido change (20%), impotence (20%), weight gain (18%), nervousness (18%), abnormal vision (18%), micturition disorder (14%), increased appetite (11%), paresthesia (9%), memory impairment (9%), anxiety (9%), rash (8%), vomiting (7%), twitching (7%), flatulence (6%), impaired concentration (5%), depression (5%). **Black Box Warning:** increased SI in patients <25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping Anafranil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Anafranil within 14 days of stopping a MAOI, use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk**,** highly lethal in overdose**,** activation of hypomania/mania, serotonin syndrome, seizures, orthostatic hypotension, caution in patients with known cardiovascular disease, neuropsychiatric symptoms, caution and monitoring in patients with liver disease, decreased blood cell count, hyperthermia, sexual dysfunction, weight gain, caution in patients with hyperthyroidism/thyroid supplementation, increased intraocular pressure, a history of narrow-angel glaucoma, urinary retention, with tumors of the adrenal medulla, or with impaired renal function, discontinuation syndrome. Potentially prolongs QTc so caution is advised in patients with cardiovascular disease. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 to less active metabolites and by 2C19 to active metabolites. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use with caution with 2D6 inhibitors (e.g., fluoxetine and paroxetine); check all drug-drug interactions before prescribing. **Dosage Form:** Capsule. **Generic available:** Yes. **Cost**: **$$**. **FDA label information from Drugs @FDA for Anafranil dated 10.26.12.**

DESIPRAMINE (NORPRAMIN)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start**: 25-50 mg qday (10-25 mg in older adults); May be given at night. Week 2 and beyond: Increase dose by 25-50 mg per day each week to and **Initial Target Dose** of 100 mg (50 mg for older adults), if tolerated. **Typical Dosage Range**: 100-200 mg (50-100 mg for older adults), **Max Dose:** 300 mg (150 mg older adults). **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 115-250 ng/ml; Toxic > 500 ng/ml. Blood draw timed to achieve a trough level, goal approximately 12 hours after

last dose.
GENERAL INFORMATION: Mechanism of Action: TCA, secondary amine: NE >> serotonin reuptake inhibitor. **FDA Indications**: Depression. **Off-Label Indications:** ADHD, neuropathic pain. **Pharmacokinetics:** T½ is highly variable with a mean of 30 hr. **Common Side effects (MDD):** Anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation—least of the group of TCAs), weight gain, GI upset, sexual side effects, somnolence, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:**Use of a MAOI within 14 days of stopping Norpramin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Norpramin within 14 days of stopping a MAOI, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk**,** highly lethal in overdose, activation of hypomania/mania, serotonin syndrome, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, increased SIADH. Use with extreme caution in patients with cardiovascular disease, with a family history of sudden death, cardiac dysrhythmias, or cardiac conduction disturbances, with a history of urinary retention or glaucoma, with thyroid disease, or with a history of seizures. **Metabolism/Pharmacogenomics:** Metabolized by 2D6 and 2C19 (minor). Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use with caution with 2D6 inhibitors (e.g., fluoxetine and paroxetine) and with medications that affect the QTc interval; Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost**: ¢. **FDA label information from Drugs @FDA for Norpramin dated 11.19.2012.**

DESVENLAFAXINE (PRISTIQ)

DOSING INFORMATION: Week 1: Obtain blood pressure and weight. Consider BMP for baseline sodium in older adults. **Start**: 50 mg qday. **Initial Target and Typical Dose**: 50 mg qday. **Max Dose:** No evidence of additional benefit for doses greater than 50 mg. **Discontinuation**: Gradual rather than abrupt discontinuation. Reduce dose to 25mg po daily for duration depending on length of treatment, need to reduce risk of relapse, and need to minimize withdrawal symptoms.
MONITORING: Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA Indications:** MDD. **Off-Label Indications:** None. **Pharmacokinetics:** T½ = 11 hr. **Common Side effects (MDD):** Nausea (22%), dizziness (13%), hyperhidrosis (10%), insomnia (9%), constipation (9%), decreased appetite (5%), specific male sexual function disorders (4%).
Black Box Warning: Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 7 days of stopping Pristiq, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Pristiq within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening/suicide risk, serotonin symptoms or NMS, elevated blood pressure, abnormal bleeding, narrow angle glaucoma, hypomanic/manic switch, discontinuation syndrome, seizure, hyponatremia, interstitial lung disease and

eosinophilic pneumonia. **Metabolism/Pharmacogenomics:** Primarily metabolized by conjugation. Minor metabolism by 3A4. **Significant drug-drug interactions:** Minimal; potential for abnormal bleeding with NSAIDs or anticoagulants; check all drug-drug interactions before prescribing. . **Dosage Form:** Tablet (Do not cut, crush or chew). **Generic available:** No. **Cost:** $. **FDA label information from Drugs @FDA for Pristiq dated 11.29.2017.**

DOXEPIN (SINEQUAN, SILENOR)

DOSING INFORMATION: **Initiation for Anxiety and Depression (doxepin):** Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start (doxepin)**: 25-50 mg qHS (10-25 mg qHS in older adults). Week 2 and beyond: Increase dose by 25-50 mg qHS per day each week to an **Initial Target Dose** of 75 qHS (50 mg qHS for older adults), if tolerated. **Typical Dosage Range**: 75-150 mg qHS (50-100 mg qHS for older adults). **Max Dose:** 300 mg/day (up to 150 mg in single dose and a total of 150 mg/day in the elderly). **Initiation for Insomnia (Silenor):** 6 mg qHS (3 mg qHS for older adult). Alternatively, can use doxepin oral solution (10 mg/ml) 0.6 ml qHS (0.3 ml qHS for older adult). OF NOTE: Should not be taken within 3 hours of a meal. **Discontinuation** (for depression-anxiety): 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action**: Sedating TCA tertiary amine: serotonin/NE reuptake inhibitor. **FDA Indications**: Depression and/or anxiety, insomnia. **Off-Label Indications:** Chronic pain, uticaria. **Pharmacokinetics:** T½ = 6-8 hrs; major metabolite 24-52 hr. **Common Side effects (MDD):** Sedating and anticholinergic (blurred vision, urinary retention, dry mouth, constipation), orthostatic hypotension, weight gain, sexual side effects, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping doxepin, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of doxepin within 14 days of stopping a MAOI, use in patients with glaucoma or a tendency to urinary retention. **Warnings and Precautions:** Clinical worsening and suicide risk**,** highly lethal in overdose, abnormal thinking and behavioral changes (e.g., sleep driving), serotonin syndrome, orthostatic hypotension, cardiac dysrhythmia, QTc prolongation, seizures, hypomanic/manic switch, hepatic changes, decreased blood cell count, hyperthermia**,** increased intraocular pressure, urinary retention, SIADH. **Metabolism/Pharmacogenomics**: Metabolized by 2D6 and 2C19 and to a lesser extent by 1A2 and 2C9. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine) and medications that affect QTc; check all drug-drug interactions before prescribing. **Dosage Form:** Capsule, Tablet (Silenor), Oral solution. **Generic available:** Yes; **Cost:** doxepin ¢, Silenor $$. **FDA label from dailymed.nlm.nih.gov, Rev. 10.07**

(doxepin) and from Drugs @FDA 1.4.2018 (Silenor).

DULOXETINE (CYMBALTA)

DOSING INFORMATION: Week 1: Obtain blood pressure and weight. Consider BMP for baseline sodium in older adults. **Start**: 30 mg qday. Week 2: Increase dose to the **Initial and Typical Target Dose** of 60 mg qday or 30 mg bid, if tolerated. **Max Dose:** 120 mg qday (little evidence that higher doses are beneficial). **Discontinuation**: 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
***MONITORING*:** Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA Indications:** MDD, GAD, diabetic peripheral neuropathic pain, fibromyalgia; chronic musculoskeletal pain. **Off-Label Indications:** Second-line ADHD, other pain, other anxiety. **Pharmacokinetics:** T½ = 12 hrs. **Common Side effects (MDD & GAD):** nausea (25%), dry mouth (15%), diarrhea (10%), constipation (10%), fatigue (10%), dizziness (10%), somnolence (10%), insomnia (10%), decreased appetite (7%), hyperhidrosis (6%), vomiting (5%), agitation (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:**Use of a MAOI within 14 days of stopping Cymbalta, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Cymbalta within 14 days of stopping a MAOI, use in patients with uncontrolled narrow angle glaucoma. **Warnings and Precautions:** Suicidality, hepatotoxicity (should not be prescribed in patients with substantial alcohol use or evidence of chronic liver disease), orthostatic hypotension and syncope, serotonin syndrome, abnormal bleeding, severe skin reactions, discontinuation symptoms, manic switch, seizures, increased BP, use with 1A2 inhibitors or thioridazine, hyponatremia, hepatic insufficiency and severe renal impairment, use caution in patient with controlled narrow-angle glaucoma and with slow gastric emptying, elevation in fasting blood glucose and HbA_{1C}, urinary hesitance and retention. **Metabolism/ Pharmacogenomics**: Metabolized by 1A2 and 2D6. **Significant drug-drug interactions:** 2D6 inhibitor. Avoid co-administration with potent 1A2 inhibitors (e.g., fluvoxamine); and use cautiously with 2D6 inhibitors (e.g., fluoxetine and paroxetine). Potential for abnormal bleeding with NSAIDs or anticoagulants; Check all drug-drug interactions before prescribing. **Dosage Form:** Capsule (Do not cut, crush or chew). **Generic available:** Yes. **Cost:** $. **FDA label information from Drugs @FDA for Cymbalta dated 1.9.2018.**

ESCITALOPRAM (LEXAPRO)

***DOSING INFORMATION*:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults). **Start**: 5 mg qday. Week 2: Increase dose to an **Initial Target Dosage** of 10 mg qday, if tolerated. **Typical Dosage Range**: 10-20 mg qday. **Max:** 20 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and

relapse.
***MONITORING*:** Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Highly selective serotonin reuptake inhibitor; S-enantiomer of the racemic derivative of citalopram. **FDA Indications:** MDD (acute and maintenance), GAD. **Off-Label Indications:** Other anxiety disorders. **Pharmacokinetics:** T½ = 27-32 hrs. **Common Side effects (MDD):** nausea (15%), ejaculation disorder (9%), insomnia (9%), somnolence (6%), fatigue (5%), sweating increased (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping escitalopram, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of escitalopram within 14 days of stopping a MAOI. Concomitant use with pimozide. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, discontinuation symptoms, seizures, hypomanic/manic switch, hyponatremia, abnormal bleeding. **Metabolism/Pharmacogenomics:** Primarily metabolized by 2C19 & 3A4. **Significant drug-drug interactions:** Weak 2D6 inhibitor; Use caution when coadministered with drugs metabolized by 2D6. Check all drug-drug interactions. **Dosage Form:** Oral solution, Tablet. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Lexapro dated 5.18.17.**

FLUOXETINE (PROZAC, SARAFEM)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start**: 10 mg qday. Week 2: Increase dose to an **Initial Target Dose** of 20 mg qday (for geriatric patients, a lower initial dose or longer dosing interval is recommended and in bulimia the initial target dosage is 60 mg qday), if tolerated. Week 4 and beyond: Consider further dose increases in 10-20 mg qday increments, as needed and tolerated. **Typical Dosage Range**: 20-60 mg qday. **Max:** 80 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
***MONITORING*:** Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Selective serotonin reuptake inhibitor. **FDA Indications:** MDD (acute and maintenance), OCD, panic disorder, bulimia nervosa, premenstrual dysphonic disorder. **Off-Label Indications:** Other anxiety, fibromyalgia. **Pharmacokinetics:** T½ parent = 4-6 days, active metabolite = 4-16 days. **Common Side effects (MDD):** nausea (21%), insomnia (16%), nervousness (14%), somnolence (13%), anxiety (12%), diarrhea (12%), anorexia (11%), dry mouth (10%), tremor (10%), asthenia (9%), sweating (8%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Known hypersensitivity reaction to fluoxetine. Use of a MAOI within 5 weeks of stopping fluoxetine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of fluoxetine within 5 weeks of stopping a MAOI. Do not use pimozide or Thioridazine with fluoxetine. **Warnings and Precautions:** Clinical worsening and suicide risk, increased suicidality, serotonin syndrome, allergic

reactions and rash, manic switch, seizures, altered appetite and weight, abnormal bleeding, hyponatremia**,** anxiety and insomnia, QT prolongation, long half-life. **Metabolism/ Pharmacogenomics:** Primarily metabolized by 2D6**.** Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Potent 2D6 inhibitor; Use significant caution when coadministered with drugs metabolized by 2D6 (e.g., TCAs). Check all drug-drug interactions before prescribing. **Dosage Form:** Oral solution, Capsule, Tablet. **Cost: ¢ Generic available:** Yes, Inexpensive. **FDA label information from Drugs @FDA for Prozac dated 7.26.2013.**

FLUVOXAMINE (LUVOX): IR—IMMEDIATE RELEASE, CR—SUSTAINED RELEASE

DOSING INFORMATION: **Luvox IR:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start IR**: 50 mg qHS. Week 2: Increase to an **Initial Target Dose (IR)** of 100 mg qHS, if tolerated. Week 3-4 and beyond: Consider further increases in 50 mg increments qHS q3-4 weeks. **Luvox CR:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start CR**: 100 mg qHS, the **Initial Target Dose (CR)**. Week 3-4 and beyond: Consider further increases in 50 mg increments q3-4 weeks, if tolerated. **Typical Dosage Range (IR/CR)**: 100 mg-200 mg qHS. **Max Dose:** 300 mg/day. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
MONITORING: Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Selective serotonin reuptake inhibitor. **FDA Indications:** OCD. **Off-Label Indications:** Depression, other anxiety. **Pharmacokinetics:** T½ = 15-16 hr. **Common Side effects (OCD-IR):** Nausea (40%), somnolence (22%), insomnia (21%), asthenia (14%), dry mouth (14%), nervousness (12%), diarrhea (11%), dizziness (11%), dyspepsia (10%), abnormal ejaculation (8%), sweating (7%), anorexia (6%), vomiting (5%), tremor (5%), anxiety (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping fluvoxamine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of fluvoxamine within 14 days of stopping a MAOI. Coadministration of tizanidine, thioridazine, alosetron, pimozide, or ramelteon. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, important drug-drug interactions (SEE CONTRAINDICATIONS and DRUG-DRUG INTERACTIONS), discontinuation symptoms, abnormal bleeding, hypomanic/manic switch, seizures, hyponatremia. **Metabolism/Pharmacogenomics:** Primarily metabolized by 2D6**.** Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use with great caution in combination with other medications as fluvoxamine is a potent inhibitor of multiple P450 enzymes including 1A2, 2C9, 3A4, and 2C19 (ASLO SEE CONTRAINDICATIONS). Fluvoxamine is a relatively weak 2D6 inhibitor. Use fluvoxamine with caution with 2D6 inhibitors; OF NOTE: tobacco induces the metabolism of fluvoxamine —consider dosage adjustment when starting or stopping tobacco; Check all drug-drug interactions and ***CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION***. **Dosage Form:** Capsule (Do not cut, crush or chew), Tablet**. Generic available:** IR: Yes; CR: Yes. **Cost:** IR **¢,** CR **$. FDA label information from Drugs**

@FDA for Luvox dated 2.21.2017.

IMIPRAMINE (TOFRANIL IR, TOFRANIL PM)

DOSING INFORMATION: **Tofranil IR:** Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start IR**: 25-50 mg qHS (10-25 mg in older adults). Week 2 and beyond: Increase dose by 25-50 mg per day each week to **initial target dosage (IR)** of 75 mg qHS (50 mg in older adults), if tolerated. **Typical Dosage Range (IR)**: 75-150 mg qHS (50-100 mg qHS in older adults). **Max (IR):** 300 mg (up to 150 mg in single dose and 150 mg max dose in older adults). **Tofranil-PM**: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start PM**: 75 mg qHS, the **Initial Target Dose (PM)** (25-50 mg qHS in older adults—use Tofranil at these dosages). Week 4-6 and beyond: Increase dose in 25-50 mg per day increments as needed and tolerated. **Typical Dosage Range (PM)**: 75-150 qHS. (50-100 mg qHS for older adults). **Max (PM):** 300 mg/day (150 mg in older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Measure serum trough goal approximately 12 hours after last dose with defined therapeutic range: 150-300 ng/ml; Toxic >500 ng/ml.

GENERAL INFORMATION: **Mechanism of Action:** TCA tertiary amine: serotonin > NE reuptake inhibitor. **FDA Indications**: Depression. **Off-Label Indications:** Second-line PTSD. **Pharmacokinetics:** T½ = 8-20 hrs; desipramine (active metabolite) highly variable with a mean of 30 hr. **Common Side effects (MDD):** Anticholinergic (moderate in the group of TCAs), weight gain, GI upset, sexual side effects, somnolence, headache. **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping imipramine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of imipramine within 14 days of stopping a MAOI. Acute recovery period after MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, serotonin syndrome, photosensitization, activation of psychosis, hypomanic/manic switch, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, blood glucose dysregulation, increased intraocular pressure, urinary retention, narrow angle glaucoma, SIADH. Per FDA, use with extreme caution in patients with cardiovascular disease, with a history of urinary retention or glaucoma, with thyroid disease, with a history of seizures, or on clonidine or similar agents. Caution in patients with significant hepatic or renal disease. **Metabolism/Pharmacogenomics**: Metabolized by 2D6 to less active metabolites and by 2C19 to desipramine. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with strong 2D6 inhibitors (e.g., fluoxetine and paroxetine), and with medications that affect QTc; check all drug-drug

interactions. **Dosage Form:** Capsule, Tablet. **Generic available:** Yes for both Tofranil and Tofranil-PM. Cost: Tofranil **¢,** Tofranil-PM **$**. **FDA label for Tofranil from dailymed.nlm.nih.gov, Rev. 9.2009. FDA label information from Drugs @FDA for Tofranil-PM dated 10.26.2012**

MIRTAZAPINE (REMERON)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start**: 15 mg qHS (7.5 mg qHS in older adults). Week 2: Increase to an **Initial Target Dose** of 30 mg qHS (15 mg qHS in older adults), if tolerated. **Typical Dosage Range**: 30-45 mg qHS (15-30 mg qHS in older adults). **Max Dose:** 45 mg qHS (30 mg qHS in older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
MONITORING: Weight, lipids. Consider posttreatment BMP to rule out hyponatremia in older adults.
GENERAL INFORMATION: **Mechanism of Action:** Central pre-synaptic alpha$_2$-adrenergic antagonist effects, which results in increased release of norepinephrine and serotonin. **FDA Indications:** MDD. **Off-Label Indications:** Other anxiety, neuropathic pain, insomnia, anti-nausea effect (similar mechanism to odansetron). **Pharmacokinetics:** T½ = 26 hrs (females), 37 hrs (males). **Common Side effects (MDD):** Somnolence (54%), dry mouth (25%), increased appetite (17%), constipation (13%), weight gain (12%), dizziness (7%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping mirtazapine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of mirtazapine within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, agranulocytosis (avoid in immunocompromised), discontinuation symptoms, akathisia/psychomotor restlessness, hyponatremia, increased cholesterol/triglycerides, dizziness, increased appetite/weight gain, transaminase elevations, seizures.
Metabolism/Pharmacogenomics: Metabolized by 1A2, 2D6, and 3A4. **Significant drug-drug interactions:** Use caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine). Check all drug-drug interactions before prescribing. **Dosage Form:** Orally Disintegrating Tablet, Tablet. **Generic available:** Yes. **Cost: ¢**. **FDA label information from Drugs @FDA for mirtazapine dated 4.11.2017.**

NORTRIPTYLINE (PAMELOR, AVENTYL)

DOSING INFORMATION: Week 1: Baseline EKG (if any history of cardiac disease, history of arrhythmias, or over 65 y/o), pulse, HR, weight. Consider BMP for baseline sodium in older adults. **Start**: 25 mg qHS (10 mg qHS in older adults). Week 2 and beyond: Increase dose by 25-50 mg qHS (10 mg qHS in older adults) each week to an **Initial Target Dose** of 75 mg qHS (30 mg qHS for older adults), if tolerated. **Typical Dosage Range**: 75-100 mg qHS (30-50 mg qHS in older adults). **Max Dose:** 150 mg qHS (75 mg qHS in

older adults). **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
***MONITORING*:** EKG (pretreatment, initial, and annual—if any history of cardiac disease, history of arrhythmias or over 65 y/o), pulse, HR, weight. Consider posttreatment BMP to rule out hyponatremia in older adults. Blood test for serum level available with defined therapeutic range: 50-150 ng/ml; toxic >500 ng/ml. The FDA recommends testing serum levels in adults in doses above 100 mg qHS. Blood draw timed to achieve a trough level, goal approximately 12 hours after last dose.
***GENERAL INFORMATION:* Mechanism of Action:** TCA, secondary amine: NE > serotonin reuptake inhibitor. Generally better tolerated than other TCAs. **FDA Indications:** Depression. **Off-Label Indications:** neuropathic pain (doses up to 75 mg). **Pharmacokinetics:** T½: highly variable 16-90+ hr. **Common side effects (MDD):** Sedation, anticholinergic side effects (blurred vision, urinary retention, dry mouth, constipation), orthostatic hypotension, weight gain, nausea, headache, sexual side effects. **Black Box:** Increased SI in patients <25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping Pamelor, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Pamelor within 14 days of stopping a MAOI, or use during the acute recovery period after a MI. **Warnings and Precautions:** Clinical worsening and suicide risk, highly lethal in overdose, hypomanic/manic switch, serotonin syndrome, orthostatic hypotension, QTc prolongation, hepatic changes, decreased blood cell count, hyperthermia, urinary retention, SIADH, use in patients with cardiovascular disease, who have glaucoma or a history of urinary retention, with a history seizures, or with hyperthyroidism; use with quinidine. **Metabolism/Pharmacogenomics**: Metabolized by 2D6 to less active metabolites. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** use caution with strong 2D6 inhibitors (e.g., fluoxetine), and with medications that affect QTc; check all drug-drug interactions. **Dosage Form:** Capsules, Oral solution. **Generic available:** Yes. **Cost: ¢. FDA label information from Drugs @FDA for Pamelor dated 6.18.2016.**

PAROXETINE (PAXIL CR, PAXIL, PEXEVA): IR: PAXIL, PEXEVA; CR: SUSTAINED RELEASE
***DOSING INFORMATION:* Paxil IR:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start IR**: 10 mg qday. Week 2: Increase to an **Initial Target Dose (IR)** of 20 mg qday (40 mg qday for OCD), if tolerated. Week 4 and beyond: Consider further increases as needed in 10 mg qday per week increments as tolerated. **Typical Dosage Range (IR): 20-60 mg qday. Max Dose (IR): 60 mg qday. Paxil CR:** Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start CR**: 25 mg qday (the **Initial Target Dose**). Week 4 and beyond: Consider further increases as needed in 12.5 mg qday per week increments. **Usual Dosage Range (CR): 25-62.5 mg qday. Max Dose (CR)** CR: 62.5 mg qday. **Discontinuation:** *Often problematic*. Incremental decrease in the daily dose by 10mg/day at weekly intervals.
***MONITORING*:** Weight. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: **Mechanism of Action:** Selective serotonin reuptake inhibitor, with anticholinergic properties. **FDA Indications:** GAD, MDD, OCD, Panic Disorder, PTSD, PMDD, Social anxiety disorder. **Pharmacokinetics:** T½ = 21 hrs. **Common Side effects (MDD-IR):** Nausea (26%), somnolence (23%), dry mouth (18%), asthenia (15%), constipation (14%), dizziness (13%), insomnia (13%), sexual side effects (13%), diarrhea (12%), tremor (8%), decreased appetite (6%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 4 weeks of stopping Paxil, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Paxil within 4 weeks of stopping a MAOI. Concomitant use with pimozide or thioridazine. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, teratogenic effects, seizures, discontinuation syndrome, drug-drug interactions, use with tamoxifen, akathisia, abnormal bleeding, hyponatremia, bone fracture. **Metabolism/Pharmacogenomics**: Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Strong 2D6 inhibitor. Use caution with drugs metabolized by 2D6 (e.g., TCAs); check all drug-drug interactions. **Dosage Form:** Oral solution, Tablet, Coated Tablet (Do not cut, crush or chew). **Generic available:** IR: Yes; CR: yes, Cost: IR **¢;** CR **$**. **FDA label information from Drugs @FDA for Paxil dated 1.17.2017.**

SERTRALINE (ZOLOFT)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start**: 25 mg qday. Week 2: Increase to an **Initial Target Dose** of 50 mg qday, if tolerated. Week 4 and beyond: Consider further increases in dose if needed and tolerated, in 25 mg qday per week increments. **Typical Dosage Range: 50-200 mg qday. Max Dose:** 200 mg qday. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.
***MONITORING*:** Weight. Consider posttreatment BMP to rule out hyponatremia in older adults. OF NOTE: False-positive urine immunoassay screening tests for benzodiazepines have been reported in patients taking sertraline.
GENERAL INFORMATION: **Mechanism of Action:** Selective serotonin reuptake inhibitor. **FDA Indications:** MDD, OCD, panic disorder, PTSD, social phobia, PMDD. **Off-Label Indications:** Other anxiety. **Pharmacokinetics:** T½ = 26 hrs. **Common Side effects (MDD):** Nausea (26%), diarrhea (18%), dry mouth (16%), insomnia (16%), somnolence (13%), dizziness (12%), tremor (11%), fatigue (11%), increased sweating, (8%), ejaculation failure (7%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 4 weeks of stopping Zoloft, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Zoloft within 4 weeks of stopping a MAOI. Concomitant use with pimozide. **Warnings and Precautions:** Clinical worsening and suicide risk, hypomanic/manic switch, serotonin symptoms, weight loss, seizure, discontinuation symptoms, abnormal bleeding, altered platelet function, hyponatremia, weak uricosuric effect, angle closure glaucoma. **Metabolism/Pharmacogenomics**: Metabolized by multiple P450 enzymes with 2C19 having the greatest pharmacogenetic and drug-drug interaction evidence. Use

caution with 2C19 poor metabolizers. **Significant drug-drug interactions:** Weak 2D6 inhibitor. Use caution with drugs metabolized by 2D6 (e.g., TCAs); check all drug-drug interactions. **Reproductive potential/pregnancy/lactation:** Usual first-line SSRI antidepressant during pregnancy and lactation. **Dosage Form:** Oral solution, Tablet. **Generic available:** Yes. **Cost**: **¢. FDA label information from Drugs @FDA for Zoloft dated 2.1.2013.**

VENLAFAXINE (EFFEXOR - IR: IMMEDIATE RELEASE; ER/ XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Effexor XR:** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start XR**: 75 mg qday (37.5mg for panic disorder). Week 2: Increase to the **Initial Target Dose (XR)** of 150 mg qday, if tolerated. OF NOTE, the initial target dose for social phobia is 75 mg qday and the initial target dose for neuropathic pain is 225 mg qday. Week 4 and Beyond: Consider further increases in 75 mg/day increments every 2 weeks as needed and tolerated. **Typical Dosage Range (XR): 150-300 mg/day. Max Dose (XR):** 300 mg qday. **Effexor IR:** Week 1: Baseline blood pressure, weight. Consider BMP for baseline sodium in older adults. **Start IR**: 37.5 mg bid (37.5 qday with panic disorder). Week 2: Increase to the **Initial Target Dose** of 75 mg bid, if tolerated. OF NOTE, the initial target dose for social phobia is 37.5 mg bid qday and the initial target dose for neuropathic pain is 112.5 mg bid. Week 3 and Beyond: Can consider further increases in 75 mg/day increments every 7 days as needed and tolerated. **Typical Dosage Range (IR):** 150-300 mg/day. **Max Dose IR:** 375 mg/day. **Discontinuation:** *Often problematic*. 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

***MONITORING*:** Blood pressure, weight. Consider posttreatment BMP to rule out hyponatremia in older adults

GENERAL INFORMATION: **Mechanism of Action:** Serotonin/Norepinephrine Reuptake Inhibitor (SNRI). **FDA Indications:** GAD, MDD, Panic Disorder, Social Anxiety Disorder. **Off-Label Indications:** Neuropathic pain, other anxiety. **Pharmacokinetics:** T½ = 5 hrs and 11 hrs (active metabolite). **Common Side effects (MDD, XR):** Nausea (31%), dizziness (20%), somnolence (17%), insomnia (17%), abnormal ejaculation (16%), sweating (14%), dry mouth (12%), nervousness (10%), anorexia (8%), constipation (8%), abnormal dreams (7%), tremor (5%), blurry vision (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 14 days of stopping Effexor, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Effexor within 14 days of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, sustained hypertension, elevations in systolic and diastolic blood pressure, seizures, mydriasis/ narrow angle glaucoma, discontinuation symptoms, insomnia and nervousness, weight loss and decreased appetite, abnormal bleeding, serum cholesterol elevation, interstitial lung disease and eosinophilic pneumonia. **Metabolism/Pharmacogenomics**: Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Limited drug-drug interactions, Low protein binding, check all drug-drug interactions before prescribing. **Dosage Forms:** Tablet, Capsule, Coated Tablet (Do not cut, crush or

chew). **Generic available:** IR/ER: Yes. **Cost**: IR/ER ¢. **FDA label information from Drugs @FDA for venlafaxine dated 12.8.2016.**

ANXIOLYTICS & HYPNOTIC MEDICATIONS

ALPRAZOLAM (IR: IMMEDIATE RELEASE; XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Anxiety Disorders:** Consider CBC and LFTs (see *MONITORING*); **Xanax IR:** *Week 1:* **Start IR**: 0.25 to 0.5 mg tid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for anxiety symptoms. *Week 2 and beyond:* Increase dose as needed and tolerated to the minimally effective dose. **Typical Dosage Range IR**: 0.5 to 1 mg tid. **Max Dose IR:** 4 mg/day. **Panic Disorder**: Consider CBC and LFTs (see *MONITORING*); **Xanax IR:** *Week 1:* **Start IR**: 0.5 mg tid. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for anxiety symptoms; *Week 2 and beyond:* Increase dose as needed and tolerated in 0.5-1 mg/day increments each week to the minimally effective dose. **Typical Dosage Range IR**: 4-6 mg/day. **Max Dose IR:** 9 mg/day. **Xanax XR (Panic Disorder):** *Week 1:* **Start XR**: 0.5-1mg qAM. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms; *Week 2 and beyond:* Increase dose as needed and tolerated in 0.5-1 mg/day increments each week to the minimally effective dose. **Typical Dosage Range (XR):** 3-6 mg/day. **Max Dose XR:** 6 mg/day. **Discontinuation:** Uniquely problematic withdrawal syndrome; Recommended taper of no more than 0.5 mg every 3 days; Doses above 4 mg/day may need slower taper of 10% per month. OF NOTE: Alprazolam concentrations may be reduced by up to 50% in smokers compared to non-smokers.
***MONITORING*:** Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.
GENERAL INFORMATION: **Mechanism of action**: enhances activity of GABA (benzodiazepine). **FDA Indications:** Panic Disorder; Anxiety disorders; Short-term use for anxiety symptoms. **Other Indications:** Insomnia. **Pharmacokinetics:** T½ = 11 hrs; Onset: Rapid. **Common Side effects (IR—panic disorder):** Drowsiness (77%), impaired coordination (40%), memory impairment (33%), increased appetite (33%), cognitive disorder (29%), weight gain (27%), constipation (26%), dysarthria (23%), weight loss (23%), decreased libido (14%), micturition difficulties (12%), increased libido (8%), sexual dysfunction (7%). **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. **Contraindications:** Use in patients with acute narrow angle glaucoma. Coadministration with ketoconazole or itraconazole. **Warning/Precautions:** Dependence and withdrawal reactions, including seizures, status epilepticus, interdose symptoms, CNS depression and impaired performance, risk of fetal harm, use with CYP 3A inhibitors, weak uricosuric effect, respiratory depression, sleep apnea/COPD, physical and psychological dependence, abuse potential, use in the elderly and in patients with liver disease, paradoxical reactions.
Metabolism/Pharmacogenomics: **Metabolized by CYP3A**. **Significant drug-drug interactions:** Use with caution with potent 3A

inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort)—see also under contraindications; Use with caution with other sedative/hypnotics. Check all drug-drug interactions. **Breastfeeding:** Excreted in breast milk/Not Recommended. **Dosage Form:** Tablet, Oral dissolving tablet, Oral solution, Coated Tablet (Do not cut, crush or chew). **Generic available:** IR/XR**:** Yes. Cost: IR ¢, XR $. **FDA label information from Drugs @FDA for alprazolam dated 6.6.2017. FDA label information from Drugs @FDA for alprazolam dated 6.6.2017.**

BUSPIRONE (BUSPAR)

DOSING INFORMATION: Week 1: Baseline weight. Consider BMP for baseline sodium in older adults. **Start**: 7.5 mg bid. Week 2: Increase to an **Initial Target Dose** of 15 mg bid, if tolerated; Consider further increases as needed and tolerated. **Typical Dose Range**: 15 mg bid to 30 mg bid mg. **Max Dose:** 30 mg bid. OF NOTE: Time frame for improvement similar to SSRIs and other antidepressants. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
MONITORING*:** Weight. Consider posttreatment BMP to rule out hyponatremia in older adults. ***GENERAL INFORMATION: **Mechanism of Action:** Not specifically known; high affinity for serotonin (5-HT1A) receptors and moderate affinity for dopamine (D2) receptors; Not related to benzodiazepines and does not affect GABA binding. **FDA Indications:** Anxiety **Other Indications:** Depression augmentation. OF NOTE: BuSpar may be helpful for reversing SSRI/SNRI induced sexual dysfunction. **Pharmacokinetics:** T½: 2-3 hrs. **Common Side effects (Anxiety):** Dizziness (12%), nausea (8%), headache (6%), nervousness (5%). **Black Box Warning:** None. **Contraindications**: **Warnings/Precautions**: Use of a MAOI within 14 days of stopping BuSpar, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of BuSpar within 14 days of stopping a MAOI, use in patients with severe hepatic or renal impairment, potential restlessness syndrome (e.g., akathisia). **Metabolism/Pharmacogenomics**: **Metabolized by CYP3A4**. **Significant drug-drug interactions:** Use cautiously when co-administered with potent 3A inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Avoid grapefruit juice. Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for BuSpar dated 5.25.2016**

CLONAZEPAM (KLONOPIN)

DOSING INFORMATION: *Week 1:* Consider CBC and LFTs (see *MONITORING*); **Start**: 0.25 mg bid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for anxiety symptoms. *Week 2:* Increase dose as needed and tolerated to the **Typical Initial and Target Dosage** of 0.5 mg bid. Can give more of dose at qHS to target insomnia, or if causing excessive daytime sedation. *Week 3 and beyond:* Can consider further increases as needed and tolerated however most individuals experience reduced effectiveness and

more side effects at higher doses. **Max Dose:** 4 mg/day. **Rapid Discontinuation:** 0.125 mg bid every 3 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month.
***MONITORING*:** Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.
GENERAL INFORMATION: **Mechanism of action**: enhances activity of GABA (benzodiazepine). **FDA Indications:** Panic disorder. **Other Indications:** GAD, Social phobia. **Pharmacokinetics:** T½ 30-40 hrs; Onset: intermediate (1-4 hrs). **Common Side effects (Panic Disorder):** Somnolence (37%), dizziness (8%), upper respiratory tract infection (8%), depression (7%), abnormal coordination (6%), ataxia (5%). **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. . **Contraindications:** Patients with clinical or biochemical evidence of significant liver disease, acute narrow angle glaucoma. **Warning/Precautions**: Cognitive/motor impairment, suicidal behavior/ideation, risk of fetal harm, withdrawal symptoms, respiratory depression, sleep apnea/COPD, worsening of seizures, need for periodic blood counts and liver function tests (see above under MONITORING) physical and psychological dependence, abuse potential, use in the elderly, increased salivation, caution in renally impaired patients, paradoxical reaction. **Metabolism/Pharmacogenomics**: **Metabolized by CYP3A**. **Significant drug-drug interactions:** Use with caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Use caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet, Oral dissolving tablet. **Generic available:** Yes. Cost: ¢. **FDA label information from Drugs @FDA for clonazepam dated 10.23.2017.**

DIAZEPAM (VALIUM)

DOSING INFORMATION: *Week 1:* Consider CBC and LFTs (see *MONITORING*); **Start**: 5 mg bid. OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. *Week 2:* Increase dose as needed and tolerated by 5-10 mg/day increments per week to the minimally effective dose; Can give more of dose at qHS to target insomnia, or if causing excessive daytime sedation. **Typical Dosage Range**: 10-20 mg/day. **Max Dose:** 40 mg/d. **Rapid Discontinuation:** 10% of total dose every 3-4 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month.
***MONITORING*:** Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.
GENERAL INFORMATION: **Mechanism of action**: Enhances activity of GABA (benzodiazepine). **FDA Indications:** Anxiety disorder, Acute alcohol withdrawal. **Pharmacokinetics:** T½ up to 48 hrs, active metabolite: up to 100 hours; Onset: immediate (1-1.5 hrs). **Common Side effects (Anxiety):** Drowsiness, fatigue, muscle weakness, ataxia. **Black Box Warning:** Concomitant use of

benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. . **Contraindications:** Myasthenia gravis, severe respiratory insufficiency, severe hepatic insufficiency, sleep apnea syndrome, acute narrow angle glaucoma. **Warning/Precautions**: Cognitive/motor impairment, suicidal behavior/ideation, risk of fetal harm, withdrawal symptoms, respiratory impairment, hepatic insufficiency, worsening of seizures, physical and psychological dependence, abuse potential, use in the elderly, paradoxical reaction, psychotic patients. **Metabolism/Pharmacogenomics**: Metabolized by CYP3A4 and 2C19 to active metabolites and largely eliminated by glucuronidation. Use caution in 2C19 poor metabolizers. **Significant drug-drug interactions:** Use with a great deal of caution with potent 3A inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort) as well as with 2C19 inhibitors; Check all drug-drug interactions before prescribing. **Significant drug-drug interactions:** Check all drug-drug interactions. Use with caution with other sedative/hypnotics. **Dosage Form:** Tablet, Oral solution. **Generic available:** Yes. Cost: **¢. FDA label information from Drugs @FDA for diazepam dated 1.12.2018.**

ESZOPICLONE (LUNESTA)

DOSING INFORMATION: *Week 1:* **Start**: 1 mg qHS. *Week 2:* Consider an increase in dose to 2mg or 3 mg qHS if clinically indicated if tolerated. **Typical Dosage Range**: 1-3 mg qHS (1-2 mg qHS in patients who are elderly, hepatically impaired, or taking a 3A4 inhibitor). **Max Dose:** 3 mg qHS (2 mg qHS in patients who are elderly, hepatically impaired, or taking a 3A4 inhibitor). OF NOTE: Do not take immediately after a meal—much less effective. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

***MONITORING*:** None indicated.

GENERAL INFORMATION: **Mechanism of action**: Non-benzodiazepine hypnotic that acts at the GABA receptor complex. **FDA Indications:** Treatment of insomnia. **Pharmacokinetics:** T½ = 6 hrs. **Common Side effects (2 mg, Insomnia):** headache (21%), unpleasant taste (17%), somnolence (10%); dry mouth (5%). **Black Box Warning:** None. **Contraindications**: **Warnings/Precautions:** Need to evaluate for co-morbid diagnoses, severe anaphylactic/anaphylactoid reaction, abnormal thinking, behavioral changes and complex behaviors (e.g., "sleep driving", "sleep eating" and hallucinations), withdrawal effects (monitor for tolerance, abuse, and dependence), cognitive/motor impairment, use in the elderly, use in patients with hepatic impairment, impaired respiratory function, impaired drug metabolism or hemodynamic responses. **Metabolism/Pharmacogenomics**: Metabolized by 3A4 and 2E1. **Significant drug-drug interactions:** Use with caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort); Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet. **Generic available:** Yes. **Cost**: **$. FDA label information from Drugs @FDA for Lunesta dated 5.30.2017**.

HYDROXYZINE PAMOATE (VISTARIL), HYDROXYZINE HYDROCHLORIDE (ATARAX)

DOSING INFORMATION: *Week 1:* **Start**: 25 mg q6 hrs. *Week 2:* Increase if needed and tolerated to the **Initial Target Dose** of 50 mg q6 hrs. *Week 3:* Can consider further increases in dose in 25 mg q6 hr increments, if needed and tolerated. OF NOTE: Can start at 50 mg q6 hrs and titrate up to 100 mg q 6hr more quickly, if needed. **Typical Dosage Range**: 50-100 mg q6hs. **Max Dose:** 400 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
***MONITORING*:** None indicated.
GENERAL INFORMATION: **Mechanism of action**: Antihistamine (H_1-receptor). **FDA Indications:** Anxiety. **Non-FDA Indications:** Insomnia. **Pharmacokinetics:** T½ 20-25 hrs. Onset within 15 to 30 minutes. **Common Side effects:** Drowsiness; dry mouth. **Black Box Warning:** None. **Contraindications: Use in early pregnancy. Use in patients with a prolonged QT interval. Warning/Precautions:** Use with caution in patients with risk factors for QT prolongation/Torsade de Pointes. Use with other CNS depressants, cognitive/motor impairment, use in elderly patients. **Metabolism/Pharmacogenomics**: Metabolized in the liver. Specific pathways are unknown. **Significant drug-drug interactions:** Caution is recommended during the concomitant use of drugs known to prolong the QT interval. Check all drug-drug interactions before prescribing. **Significant drug-drug interactions:** Use with caution with sedatives/hypnotics. Check all drug-drug interactions before prescribing. May potentiate effects of meperidine and barbiturates. **Dosage Form: Generic available:** Yes. **Cost**: ¢. **FDA label information from dailymed.nlm.nih.gov for Atarax dated 6.2006. FDA label information from Drugs @FDA for Vistaril dated 11.14.2017.**

LORAZEPAM (ATIVAN)

DOSING INFORMATION: *Week 1:* Consider CBC and LFTs (see *MONITORING*); **Start**: 0.5 mg bid; OF NOTE: Scheduled dosing is typically more effective than PRN dosing for control of anxiety symptoms. *Week 2:* Increase dose as needed and tolerated to the **Initial Target Dose** of 1 mg bid. Can give more of the dose at qHS to target insomnia or if causing excessive daytime sedation. *Week 3 and beyond:* Consider further increases as needed and tolerated to the minimally effective dose. **Typical Target Dose**: 1-3 mg bid. **Max Dose:** 10 mg/day**. Rapid discontinuation:** 10% every 3 days. **Extended Discontinuation** (e.g., after months/years of use): 10% per month.
***MONITORING*:** Consider UTOX if abuse/diversion is a concern. Per FDA: "periodic" blood counts and liver-function tests are recommended for patients on long-term therapy.
GENERAL INFORMATION: **Mechanism of action**: enhances activity of GABA (benzodiazepine). **FDA Indications:** Anxiety disorders; Short-term use for anxiety symptoms or anxiety associated with depressive symptoms. **Other Indications:** Insomnia (1-4 mg qHS). **Pharmacokinetics:** T½ = 12 hrs; Onset: intermediate (2 hrs)**;** OF NOTE: no active metabolites, so safer in liver disease. **Common Side effects (Anxiety):** Sedation (15.9%), dizziness (6.9%), weakness (4.2%), unsteadiness (3.4%). **Black Box Warning:** Concomitant use of

benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. . **Contraindications**: Acute narrow-angle glaucoma. **Warning/Precautions:** Cognitive/motor impairment, suicidal behavior/ideation, worsening of depression, risk of fetal harm, withdrawal symptoms, respiratory depression, caution in patients with sleep apnea/COPD, with hepatic insufficiency and/or encephalopathy, and in the elderly, physical and psychological dependence, abuse potential, paradoxical reaction. **Metabolism/Pharmacogenomics**: Largely eliminated by glucuronidation. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions. **Dosage Form:** Oral solution, Tablet, IV. **Generic available:** Yes. **Cost: ¢. FDA label information from Drugs @FDA for lorazepam 12.1.2016.**

TRAZODONE (DESYREL [IR], OLEPTRO [ER])

DOSING INFORMATION: Initiation for insomnia (off-label): **Start:** 25-50 mg qHS (the initial target dose)**;** increase in 25-50 mg qHS per week increments, if tolerated; typical dose 50-200 mg qHS. **Discontinuation:** 25% per week to 25% per month depending on length of treatment in order to minimize withdrawal symptoms and relapse.

MONITORING: Weight; Monitor for orthostatic hypotension in elderly and other vulnerable populations.

GENERAL INFORMATION: **Mechanism of Action:** Serotonin reuptake inhibitor. **FDA Indications:** Depression. **Other Indications:** Insomnia, depression augmentation. **Pharmacokinetics:** T½ = 10 hrs. **Common Side effects:** Drowsiness (41%), dry mouth (34%), dizziness/lightheadedness (28%), headache (20%), blurred vision (15%), nausea/vomiting (13%), constipation (8%), skin condition/edema (5%), fatigue (6%), weight loss (6%), diarrhea (5%), musculoskeletal aches/pains (5%), tremors (5%), weight gain (5%), syncope (5%). **Black Box Warning:** Increased SI in patients < 25 y/o. **Contraindications:** Use of a MAOI within 4 weeks of stopping trazodone, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of trazodone within 4 weeks of stopping a MAOI. **Warnings and Precautions:** Clinical worsening and suicide risk, serotonin syndrome, hypomanic/manic switch, QT prolongation, use in patients with heart disease (e.g., recent MI), orthostatic hypotension and syncope, abnormal bleeding, **priapism**, hyponatremia, discontinuation syndrome. **Metabolism/Pharmacogenomics**: 3A4. **Significant drug-drug interactions:** Use caution with potent 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and enzyme inducers (e.g., carbamazepine and St. John's wort). Check all drug-drug interactions. **Dosage Form:** Tablet (IR), capsule (ER). **Generic available:** IR**:** Yes; ER: No. Cost: IR ¢. ER $$. **FDA label for trazodone from dailymed.nlm.nih.gov, Rev. 7.31.2017.**

ZALEPLON (SONATA)

DOSING INFORMATION: *Week 1:* **Start**: 10 mg qHS the **Initial Target and Typical Dose** (5 mg qHS for low-weight individuals, older adults, or individuals with hepatic impairment) **Max Dose:** 20 mg qHS (10 mg qHS for elderly, debilitated, hepatically impaired

patients). OF NOTE: Very short acting. Should not be taken with or immediately after a meal due to decreased efficacy.
Discontinuation: Taper slowly to minimize withdrawal symptoms.
***MONITORING*:** None indicated.
GENERAL INFORMATION: **Mechanism of action**: Non-benzodiazepine hypnotic that acts at the benzodiazepine receptor (GABA-A). **FDA Indications:** Short-term treatment of insomnia. **Pharmacokinetics:** T½ = 1 hr. **Common Side effects (Insomnia):** Abdominal pain (6%). **Black Box Warning:** None. **Contraindications**: **Warnings/Precautions:** Need to evaluate for co-morbid diagnoses, abnormal thinking, behavioral changes and complex behaviors (e.g., "sleep driving", "sleep eating" and hallucinations), severe anaphylactic/anaphylactoid reaction, worsening of depression or suicidal thinking, withdrawal effects (monitor for tolerance, abuse, and dependence), CNS depressant effects with cognitive/motor impairment, use in the elderly, use in patients with hepatic impairment, impaired respiratory function, impaired drug metabolism or hemodynamic responses. **Metabolism/Pharmacogenomics**: Metabolized by aldehyde oxidase and to a lesser extent by 3A4. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Pregnancy:** Category C. **Dosage Form:** Capsule. **Generic available:** Yes. Cost: ¢. **FDA label information from Drugs @FDA for Sonata dated 11.17.2016.**

ZOLPIDEM (AMBIEN, AMBIEN CR, INTERMEZZO)

DOSING INFORMATION: **Ambien (Ambien CR):** *Week 1:* **Men Start**: 5-10 mg qHS (**CR:** 6.25-12.5 mg qHS); **Women Start**: Ambien 5 mg qHS (**CR:** 6.25 mg); **Elderly, debilitated, or hepatically impaired Start**: 5 mg (B: 6.25 mg qHS). *Week 2:* Assess for side effects. **Typical Target Dose**: 5-10 mg qHS (Ambien CR 6.25-12.5 mg qHS). **Max Dose:** 10 mg qHS (**CR**: 12.5mg qHS). OF NOTE: Short acting. Should not be taken with or immediately after a meal due to decreased efficacy.
***MONITORING*:** None indicated.
GENERAL INFORMATION: **Mechanism of action**: Non-benzodiazepines hypnotic that acts at the benzodiazepine receptor (GABA-A agonist). **FDA Indications:** Short-term treatment of insomnia. **Pharmacokinetics:** T½ = 2.6 hrs. **Common Side effects (Insomnia):** Drowsiness (8%), dizziness (5%). **Black Box Warning:** None. **Contraindications**: **Warnings/Precautions:** CNS depressant effects with cognitive/motor impairment including next day impairment, need to evaluate for co-morbid diagnoses, severe anaphylactic/anaphylactoid reaction, abnormal thinking, behavioral changes and complex behaviors (e.g., "sleep driving", " sleep eating" and hallucinations), worsening of depression or suicidal thinking, withdrawal effects (monitor for tolerance, abuse, and dependence), respiratory depression. **Metabolism/Pharmacogenomics**: Metabolized by multiple P450 enzymes. **Significant drug-drug interactions:** Use with caution with other sedative/hypnotics. Check all drug-drug interactions before prescribing. **Dosage Form:** Oral solution, Tablet, Sublingual. **Generic available:** Yes. Cost: ¢. **FDA label information from Drugs @FDA for zolpidem 3.13.2017.**

ADHD MEDICATIONS

ATOMOXETINE (STRATTERA)

DOSING INFORMATION: *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems) and screen for psychosis and bipolar disorder; Baseline HR, BP and consider EKG; **Start**: 40 mg qAM. *Week 2:* Increase to 80 mg qAM (or 40 mg bid, the **Initial Target and Typical Dose**), if tolerated. *Week 4-6:* Assess for side effects; can consider further increase to 100 mg/day if still symptomatic. **Max Dose:** 100 mg qAM. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

MONITORING: BP and HR at baseline, 1 month, then every 6 to 12 months; hepatic function tests if signs of liver dysfunction.

GENERAL INFORMATION: **Mechanism of action**: Selective norepinephrine reuptake inhibitor. **FDA Indication:** ADHD. **Pharmacokinetics:** T½ = 5.2 hrs. **Common Side effects (ADHD):** nausea (26%), dry mouth (20%), decreased appetite (16%), insomnia (15%), fatigue (10%), constipation (8%), dizziness (8%), somnolence (8%), erectile dysfunction (8%), abdominal pain (7%), urinary hesitation, (6%) and irritability (5%). **Black Box Warning:** Increased risk of suicidal ideation in children or adolescents, monitor closely. **Contraindications:**. Use of a MAOI within 14 days of stopping atomoxetine, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Strattera within 14 days of stopping a MAOI**,** narrow angle glaucoma, pheochromocytoma, severe cardiovascular disorders. **Warnings/Precautions:** Suicidal ideation**,** severe liver injury, serious cardiovascular events, emergent cardiovascular symptoms, effects on blood pressure and heart rate including hypertension, tachycardia, orthostatis and syncope, emergent psychotic or manic symptoms—screening for bipolar disorder is recommended, aggressive behavior/hostility, possible severe allergic reactions including anaphylaxis, urinary hesitancy and retention, priapism, use in patients receiving potent 2D6 inhibitors (e.g., fluoxetine or paroxetine) or who are know to be 2D6 poor metabolizers as dosage adjustments may be necessary. **Metabolism/Pharmacogenomics**: Metabolized by 2D6. Use with caution and consider alternatives to atomoxetine in 2D6 poor metabolizers. **Significant drug-drug interactions:** Use with great caution and consider alternatives to Strattera when considering use with 2D6 inhibitors (e.g., fluoxetine or paroxetine); Check all drug-drug interactions and ***CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION***. **Dosage Form:** Capsule. **Generic available:** No. **Cost:** **$$**. **FDA label information from Drugs @FDA for Strattera dated 12.3.2015**.

D-AMPHETAMINE AND L-AMPHETAMINE SALTS (ADDERALL IR: IMMEDIATE RELEASE; XR: SUSTAINED RELEASE)

DOSING INFORMATION: **Adderall IR:** *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; Screen for bipolar disorder; **Start IR**: 5 mg qAM and 5 mg qPM (use intervals of 4-6 hours between doses—can take earlier in the afternoon if insomnia results). *Week 2:* Increase to 10 mg qAM and 5 mg qPM, if needed and tolerated. *Week 3 and beyond:* Consider further increases in 5 mg qday per week increments, if tolerated, until treatment of symptoms or max dose is reached. **Adderall XR:** *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; Screen for bipolar disorder. **Start XR**: 10 mg qAM. *Week 2:* Consider increase to 20 mg qAM, if needed and tolerated. *Week 3 and beyond:* Consider further increases in 10 mg qAM increments per week, if tolerated, until treatment of symptoms, or max dose is reached. **Typical Target Dose (IR/XR)**: Lowest effective individualized dose. **Usual Max Dose (IR/XR):** 40 mg/day. Patients taking divided doses of IR (for example twice a day) may be switched to Adderall XR at the same total dailt dose taken once daily.

***MONITORING*:** BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern.

GENERAL INFORMATION: **Mechanism of action**: CNS stimulant. **FDA Indication: IR**: ADHD in children, narcolepsy. **XR**: ADHD in children and adults. **Pharmacokinetics:** T½ = 10-13 hrs. **Common Side effects (ADHD, XR):** Dry mouth (35%), loss of appetite (33%), insomnia (27%), headache (26%), weight loss (10%), nausea (8%), anxiety, (8%), dizziness (7%), tachycardia (6%), diarrhea (6%), urinary tract infections (5%). **Black Box Warnings: High potential for abuse/dependence**; Misuse may cause sudden death and serious cardiovascular adverse events. **Contraindications:** Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma, agitated states, history of drug abuse, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Adderall within 14 days of stopping a MAOI. **Warnings/Precautions:** Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems,** increased blood pressure, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, seizures, peripheral vasculopathy including Raynaud's phenomenon, visual disturbance, may worsen tics, potential for abuse of dependence. CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. **Metabolism/Pharmacogenomics**: Metabolized by 2D6. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet (IR), Capsule (XR). **Generic available: IR/XR:** Yes. Cost: **$**. **FDA label information from Drugs @FDA for Adderall XR dated 10.14.2016**. **FDA label information from Drugs @FDA for Adderall XR dated 10.4.2017**.

David Harrison, MD, PhD & Anna Ratzliff, MD, PhD

LISDEXAMFETAMINE (VYVANSE)

DOSING INFORMATION: *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start**: 30 mg qAM. *Week 2:* Increase dose in weekly increments of 10 mg-20 mg, if tolerated, until treatment of symptoms or max dose is reached. **Typical Target Dose**: 50mg-70mg/day. **Usual max dose:** 70 mg/day.
***MONITORING*:** BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern.
GENERAL INFORMATION: **Mechanism of action**: CNS stimulant. **FDA Indication:** ADHD in children and adults. **Pharmacokinetics:** T½ = < 1 hour (pro-drug for dextroamphetamine T½= 10 hrs). **Common Side effects (ADHD):** Decreased appetite (27%), insomnia (27%), dry mouth (26%), diarrhea (7%), nausea (7%), anxiety (6%) and anorexia (5%). **Black Box Warnings:** CNS stimulants have a high potential for abuse/dependence; Assess for risk of abuse prior to and after prescribing. **Contraindications:** Concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Vyvanse within 14 days of stopping a MAOI.
Warnings/Precautions: Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems,** blood pressure and heart rate increases, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, peripheral vasculopathy including Raynaud's phenomenon, potential for abuse of dependence. CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients.
Metabolism/Pharmacogenomics: Converted to dextroamphetamine in the blood. Dextroamphetamine metabolized by 2D6.
Significant drug-drug interactions: Check all drug-drug interactions before prescribing. **Dosage Form:** Capsule. **Generic available:** No.
Cost: $$. FDA label information from Drugs @FDA for Vyvanse dated 1.19.2018.

METHYLPHENIDATE (IMMEDIATE RELEASE (IR): RITALIN, METHYLPHENIDATE SUSTAINED RELEASE (SR): METADATE ER, METHYLIN ER, RITALIN SR; METADATE CD, RITALIN LA, CONCERTA, DAYTRANA-PATCH, QUILLIVANT XR)

DOSING INFORMATION: **Ritalin IR:** *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start IR**: 5 mg qAM and 5 mg qPM (preferably before meals; use intervals of 4-6 hours between doses; can take earlier in the afternoon if insomnia results). *Week 2:* Increase dose to 10 mg qAM and 5 mg qPM, if needed and tolerated. *Week 3 and beyond:* Consider further increase in dose in 5 mg/day per week increments, if tolerated, until treatment of or max dosage is reached. **Ritalin SR:** *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac

abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start SR**: 10 mg qAM (preferably before meals). *Week 2:* Consider increase to 20 mg qAM, if needed and tolerated. *Week 3 and beyond:* Consider further increase in dose in 10 mg increments qday per week, if tolerated until treatment of symptoms or max dose is reached. **Concerta:** *Week 1:* Evaluate cardiovascular risk (e.g., presence of structural cardiac abnormalities or other serious heart problems); Baseline HR, BP and consider EKG; **Start Concerta**: 18 mg qAM. *Week 2:* Increase dose to 36 mg qAM if needed and tolerated; *Week 3 and beyond:* Consider further increases in 18 mg qday per week increments, if tolerated, until treatment of symptoms or max dose is reached. **Daytrana:** Patch; Special dosing (see FDA guidelines). **Typical Target Dose (IR/SR/Concerta)**: Lowest effective individualized dose. **Usual Max Dose (IR/SR):** 60 mg/day (**Concerta** 72 mg/day).

***MONITORING*:** BP and HR at baseline, 1 month, then every 6 to 12 months; Signs of aggressive behavior or hostility; Consider UTOX if abuse/diversion is a concern. Per FDA: "Periodic CBC, differential, and platelet counts are advised during prolonged therapy."

GENERAL INFORMATION: **Mechanism of action**: CNS stimulant. **FDA Indication:** ADHD; Narcolepsy. **Pharmacokinetics:** T½ for Concerta: 3.5 hrs (others vary). **Common side effects (ADHD, Concerta):** Decreased appetite (25%), headache (22%), dry mouth (14%), nausea (13%), insomnia (12%), anxiety (8%), weight decreased (7%), irritability (6%), and hyperhidrosis (5%), tachycardia (5%). **Black Box Warnings:** Caution in use in patients with history of drug or alcohol dependence. Chronic abusive use can lead to tolerance and psychological dependence including abnormal behavior. **Contraindications:** Marked anxiety, tension, and agitation, glaucoma, tics or a family history or diagnosis of Tourette's syndrome, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of methylphenidate within 14 days of stopping a MAOI. **Warnings/Precautions:** Serious cardiovascular events (death, stroke, and myocardial infarction)—**stimulant drugs should not be used in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems,** blood pressure and heart rate increases, adverse psychiatric events (may worsen pre-existing psychosis or bipolar disorder or trigger the emergence of new psychotic or manic symptoms—screening for bipolar disorder is recommended), monitor for aggressive behavior, seizures, **priapism**, visual disturbance, tics, peripheral vasculopathy including Raynaud's syndrome, GI obstruction with preexisting GI narrowing, hematologic monitoring advised (see above under MONITORING). CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. **Metabolism/Pharmacogenomics**: Primarily metabolized by de-esterification. **Significant drug-drug interactions:** May inhibit the metabolism of Coumadin, anticonvulsants and some antidepressant, e.g., TCAs and SSRIs. Check all drug-drug interactions before prescribing. **Significant drug-drug interactions: Dosage Form:** Tablet, Capsule Extended Release, Patch, Solution, Suspension, Tablet Chewable. **Generic available: IR/ER. Cost: IR $, ER $$. FDA label information from Drugs @FDA for Concerta dated 1.5.2017**.

MISCELLANEOUS MEDICATIONS

NALTREXONE (ReVIA, DEPADE)

DOSING INFORMATION: Week 1: Obtain LFT's, pregnancy test in women, and urine toxicology testing as screening labs prior to initiation of naltrexone to assess for hepatic function. **Starting and Initial Target dose**: 50 mg qday. Week 4 and beyond: The dosage can then be increased in 4-6 weeks, as needed and tolerated, to 75 mg qday. Typical Dosage Range: 50-100 mg/day. **Max Dose:** 100 mg/day. OF NOTE: at least one large randomized controlled study (the COMBINE study) used 100 mg qday, which may be more effective. Naltrexone is not toxic to the liver at lower doses, however, it can become toxic if administered in larger quantities (300 mg qday) or taken in overdose.

MONITORING: Measure LFT's as screening labs prior to initiation of naltrexone to assess hepatic function and rule out acute hepatitis. If screening LFT's are normal, LFT's should be can be measured within 1-3 months or sooner if clinically indicated, and if non-concerning then measured annually. If screening LFT's are abnormal, rule out acute hepatitis or liver disease and consider monitoring LFT's q 1 month or sooner until they return to normal.

GENERAL INFORMATION: **Mechanism of action**: opiate antagonist. **FDA indications**: Opiate and alcohol dependence. **Off-label indication**: self-injurious behavior. OF NOTE: ***Naltrexone will cause opioid withdrawal; thus, it should not be used until the patient is opioid free for 7 to 10 days*****.** Self-reporting of abstinence from opioids in individuals with regular opioid usage should be verified by analysis of the patient's urine for absence of opioids. Patients treated with naltrexone should carry a card, for emergency medical care, in case they require treatment with an opioid analgesic. If there is any question of ongoing opioid use, perform a naloxone challenge test if naloxone available, or could administer naltrexone 25mg po once and observe for 90minutes for signs/symptoms of opioid withdrawal as assessed with a COWS measure. **Pharmacokinetics:** T½ = 4 hrs (naltrexone), 13 hrs (active metabolite). **Common Side effects (Alcohol Dependence):** nausea (10%), headache (7%). **Black Box Warning**: Naltrexone can cause hepatocellular injury when given in excessive doses and is contraindicated in acute hepatitis or liver failure. Use of naltrexone should be discontinued in the event of symptoms or signs of acute hepatitis. **Contraindications**: Patients receiving opioid analgesics, in opioid withdrawal, or dependent on opioids. Patients with acute hepatitis or liver failure. Any individual who has failed the naloxone/naltrexone challenge test or has a positive urine screen for opioids. **Warnings and Precautions**: Vulnerability to opioid overdose, precipitated opioid withdrawal, hepatotoxicity, depression and suicidality. Eosinophilic pneumonia, hypersensitivity reactions including anaphylaxis. **Patient education**: Patients should be warned of the risk of hepatic injury and advised to stop the use of naltrexone and seek medical attention if they experience symptoms of acute hepatitis. **Metabolism/Pharmacogenomics**:

Naltrexone is not metabolized by the P450 system; rather it is metabolized by the cytosolic enzyme dihydrodiol dehydrogenase. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet (IM available – see FDA http://www.accessdata.fda.gov/). **Generic Available:** Yes. **Cost:** $. **FDA label information from Drugs @FDA for Revia dated 2.8.2017**.

PRAZOSIN (MINIPRESS)

DOSING INFORMATION: *Week 1:* **Start**: 1 mg qHS increase to 2 mg qHS after 3-4 days. *Week 2:* Continue titration in 1 mg qHS increments every 3-4 days, if tolerated, until symptom remission, or max dose reached. **Typical Dosage Range**: 4-6 mg qHS. **Max Dose:** 10 mg qHS (in severe PTSD).
***MONITORING*:** Blood pressure at baseline and during treatment.
GENERAL INFORMATION: **Mechanism of action**: Antihypertensive (alpha-1 blocker). **Non-FDA Indication:** PTSD-related nightmares/night sweats. **Pharmacokinetics:** T½ = 2-3 hrs. **Common Side effects (Hypertension):** Dizziness (10%), headache (8%), drowsiness (8%), lack of energy (7%), weakness (6%), palpitations (5%), nausea (5%). **Black Box Warnings:** None listed. **Contraindications**: **Warnings/Precautions:** Syncope with loss of consciousness (occasionally associated with severe tachycardia), orthostatic hypotension, cataract surgery, dizziness or drowsiness may occur after first dose. **Metabolism/Pharmacogenomics**: Metabolized primarily by demethylation and conjugation. **Significant drug-drug interactions:** Taking with trazodone or Viagra may increase risk **priapism**. Check all drug-drug interactions. Check all drug-drug interactions before prescribing. **Dosage Form:** Capsules. **Generic available:** Yes. **Cost**: ¢. **FDA label information from Drugs @FDA for Minipress dated 4.17.2017**

NUTRITIONAL SUPPLEMENTS

OMEGA-3 FISH FATTY ACIDS

Omega-3 fish fatty acids added to antidepressant medication treatment has been associated with reducing depressive symptom beyond placebo and thus may be considered adjunctive treatment for major depression. A typical daily target dosage is 1500mg per day of omega-3 fatty acids (EPA + DHA) divided with food (J Sarris et al. Adjunctive Nutraceuticals for Depression: A Systematic Review and Meta-Analyses. American Journal of Psychiatry April 2016). EPA and DHA are naturally available in fish oil in a ratio of approximately 2:1. Recommended dosage of EPA + DHA is 1500mg per day and should be taken with food. Look on the label for the amount of EPA and DHA per serving AND total number of capsules per serving. Determine how many capsules to take to get to dose

of 1500mg of EPA + DHA per day. Based on emerging evidence, it appears that EPA is key for antidepressant efficacy. The best products are both protected from oxidation by the addition of Vit E and purified (filtered or distilled) to eliminate contaminants (pesticides and heavy metals). Premium brands include Nordic Naturals and Carlson. Therapeutic dosages can be purchased for as little as $8 per month (e.g., NatureMade Fish Oil available at Costco and Amazon).

S-ADENOSYL METHIONINE (SAMe)

SAMe is an evidence-based monotherapy and adjunctive treatment for unipolar depression (1) Freeman M, et al. Major Depressive Disorder: The APA Task Force Report. J Clin Psychiatry 2010;71:6 . 2) Sarris J, et al. Adjunctive Nurtaceuticals for depression: a systematic review and meta-analyses. Am J Psychiatry. 2016;173:575-587.). Treatment with SAMe with a starting dosage of 400 mg bid, which should be increased to 800 mg bid after four weeks if insufficiently effective and tolerated. Of note, SAMe is well tolerated and works quickly, cost is approx. $70-80/mo at 800 mg bid. For greatest efficacy SAMe should be foil wrapped and enterically coated. Nature Made SAMe is one example of a highly regarded brand of SAMe. Typically side effects are mild and can include insomnia, lack of appetite, constipation, nausea, sweating, dizziness, nervousness

MOOD STABILIZERS

CARBAMAZEPINE EXTENDED RELEASE (TEGRETOL XR; EQUETRO)

DOSING INFORMATION: Week 1**:** Check baseline labs (urine pregnancy test, CBC with differential, CMP—see below for guidelines regarding **individuals with ancestry across Asia**). Discuss birth control method with women of reproductive potential due to severe risk to fetus. **Avoid in pregnancy**. **Start**: 200 mg bid. Week 2-8: Check serum concentration as trough carbamazepine before the morning dose (approx. 12hrs after the last dose). If concentration is sub-therapeutic, increase dosage by 200 mg/day, if tolerated. This process is repeated weekly over 8 weeks due to autoinduction of metabolism. **Target Plasma Level:** Therapeutic levels: 4-12 mcg/ml (**Typical Dosage Range**: 600-1200 mg/day; **Max Dose**: 1600 mg/day). **Toxic concentration:** >15 mcg/ml. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING**:** Baseline labs: urine pregnancy test, CBC with differential, CMP. Monitoring of blood levels is recommended with the usual adult therapeutic drug levels between 4 and 12 mcg/ml. This medication induces autoinduction of metabolism, which is usually complete 3-5 weeks after initiation of a fixed carbamazepine regimen. Monitoring frequency (blood level & CBC with differential): Qweekly X 8 weeks, Q2 months X 2, and then q6 months. LFTs: q6 months.

GENERAL INFORMATION: **Mechanism of action**: Antiepileptic drug with mood stabilizer efficacy chemically related to tricyclic

antidepressants. **FDA Indications:** Bipolar I, acute manic and mixed episodes. **Pharmacokinetics:** T½ variable due to autoinduction; Initial: 35-40 hours Steady state: 12-17 hours. **Common Side effects (Equetro, Mania):** Dizziness (44%), somnolence (32%), nausea (29%), vomiting (18%), ataxia (15%), constipation (10%), pruritis (8%), dry mouth (8%), asthenia (8%), rash (7%), blurred vision (6%), speech disorder (6%). **Black Box Warnings:** (1) Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS). Estimated occurrence: 1 to 6 per 10,000 new users in countries w/ mainly Caucasian populations, but the risk in some Asian countries is estimated 10X higher and are associated with the presence of HLA-B*1502. **Individuals with ancestry across Asia and other high-risk patients should be screened for the presence of HLA-B*1502 prior to starting Equetro.** Discontinue, if these reactions occur. (2) Aplastic anemia and agranulocytosis. Obtain pretreatment hematological testing (SEE ABOVE). Discontinue if significant bone marrow depression develops. **Contraindications:** Bone marrow depression; concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), use of Equetro within 14 days of stopping a MAOI; concomitant use with nefazodone; concomitant use with delavirdine or other non-nucleoside reverse transcriptase inhibitors. **Warnings and Precautions:** Serious dermatologic reactions (SJS/TEN associated with HLA-B*1502 allele-as noted above, and hypersensitivity reactions associated with HLA-A*3101 allele—consider testing prior to treatment to reduce risk), aplastic anemia and agranulocytosis, drug reaction with eosinophilia and systemic symptoms, suicidal behavior and ideation, embryofetal toxicity, abrupt discontinuation and risk of seizure, hyponatremia, cognitive and motor impairment, hepatic porphyria, decreased antiviral effect of non-nucleoside reverse transcriptase inhibitors. **Metabolism/Pharmacogenomics**: **Metabolized by 3A4**. **Significant drug-drug interactions:** Equetro is a strong 3A4 inducer and is inhibited by many drugs include fluoxetine. Examples of interactions include with Warfarin (resulting in decreased Warfarin levels) and hormone contraceptives (resulting in reduced efficacy). Check all drug-drug interactions as they are common with this medication and ***RECOMMEND CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION.*** **Reproductive potential/pregnancy/lactation: Avoid in pregnancy due to association w/ increased risk of teratogenesis. Also need to inform women of reproductive potential of this risk. If used during lactation,** would recommend checking serum concentrationsin the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion among lactating women. **Dosage Form:** Capsule, Tablet. **Generic Available**: Yes; Equetro: No. **Cost:** Carbamazepine XR **$**. **FDA label information from Drugs @FDA for Equetro dated 4.6.2017**.

DIVALPROEX SODIUM (ER, STAVZOR (IR))

DOSING INFORMATION: **Depakote ER**: Week 1: Check baseline labs (urine pregnancy test, CBC for thrombocytopenia, coagulation tests, and liver function tests). Women of reproductive potential should use effective contraception while using divalproex due to severe risk to fetus. **Avoid in pregnancy**. **Start ER**: (extended-release) 500 mg qHS. Week 2: Check trough Depakote ER serum

concentration before, but as close to the dosing time as possible. If level is subtherapeutic, add 250-500 mg to qHS dose, if tolerated. Repeat weekly if needed to reach therapeutic serum concentration. **Target plasma level (ER):** 85 to 125 mcg/ml. **Usual Max Dose:** 60 mg/kg/day. **Formulation: Depakote DR** is a less preferable formulation due to increased side effect profile. If used, Depakote DR typically requires lower doses divided bid or TID and a trough plasma level of 50 to 125 mcg/ml. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

***ONGOING MONITORING*:** Weight, CBC, coagulation tests, and liver function tests are recommended before initiating therapy and at least q6 months.

GENERAL INFORMATION:* Mechanism of action**: Antiepileptic drug with mood stabilizer efficacy. **FDA Indications:** Bipolar I disorder, mania or mixed. **Off-Label Indications:** Bipolar I disorder, rapid cycling. **Pharmacokinetics:** T½ = 9-16 hrs. **Common side effects:** Somnolence (26%), dyspepsia (23%), nausea (19%), vomiting (13%), diarrhea (12%), dizziness (12%), abdominal pain (10%). **Black Box Warnings:** (1) Hepatotoxicity (usually during the first 6 months), (2) pancreatitis and (3) fetal risk particularly including neural tube defects, other major malformations, and decreased IQ. **Contraindications:** Hepatic disease or significant hepatic dysfunction, known mitochondrial disorders caused by mutations to DNA polymerase gamma, urea cycle disorders, pregnant patients treated for prophylaxis of migraine headaches. **Warnings and Precautions:** Hepatotoxicity, patients with known or suspected mitochondrial disease, birth defects, decreased IQ following in utero exposure, use in women of child bearing potential, pancreatitis, suicidal behavior or ideation, urea cycle disorders, thrombocytopenia, hyperammonemia, hyperammonemia and encephalopathy associated with concomitant topiramate use, hypothermia, multi-organ hypersensitivity reactions, interaction with carbapenem antibiotics, somnolence in the elderly, periodic drug plasma concentration monitoring, effect on ketone and thyroid function tests, effect of HIV and CMV replication, medication in the stool, Stevens-Johnson syndrome (~1:5000). **Metabolism/Pharmacogenomics**: Major metabolic pathways involve glucuronidation and beta-oxidation. **Significant drug-drug interactions:** Check all drug-drug interactions as they are common with this medication and ***CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION. OF NOTE: aspirin at antipyretic dosages can increase free valproic acid level up to 4X and both carbapenem antibiotics and carbamazepine can significantly increase the clearance of valproic acid. Also, hyperammonemia and encephalopathy are associated with concomitant topiramate use. **Reproductive potential/pregnancy/lactation: Avoid in pregnancy due to association w/ increased risk of teratogenesis/fetal risk, particularly neural tube defects, other major malformations, and decreased IQ. Also need to inform women of reproductive potential of this risk; should not be administered to woman of reproductive potential unless essential to management of medical condition. Use of effective contraception is essential in women of reproductive potential receiving treatment with divalproex. If used during lactation,** would recommend measuring serum concentrations in the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion among lactating women, as

well monitoring for excessive bleeding or bruising in the infant/toddler. Also consider periodically checking (e.g., q 6 months) the infant/toddler's platelets, LFTs, and coagulation tests. **Dosage Form:** Capsule, Coated Tablet (Do not cut, crush or chew), Solution. **Generic Available:** Yes (ER, DR). **Cost**: Divalproex IR: **$**; Divalproex ER **$$**. **FDA label information from Drugs @FDA for Depakote ER dated 10.18.2017.**

LAMOTRIGINE (LAMICTAL)

DOSING INFORMATION: Week 1 and 2: **Start:** 25 mg qday. Week 3 and 4: 50 mg qday, if tolerated. Week 5: 100 mg qday, if tolerated. Week 6: 200 mg qday, if tolerated (the **Initial Target and Typical Dose** as there is no compelling evidence of increased mood stabilization benefit at higher doses). Dosage will need to be adjusted for patients taking carbamazepine, phenytoin, phenobarbital, primidone, or valproate (see FDA guidelines). OF NOTE: Estrogen containing oral contraceptives increase metabolism of Lamictal such that target dose may need to be increased. Starter packs are available. **Restarting therapy after discontinuation**: If lamotrigine has been withheld for 3 days, restart according to initial dosing recommendations. **Non-urgent discontinuation:** Decrease by 50% per week (over at least 2 weeks).

***ONGOING MONITORING*:** Drug levels are not typically measured. Note: False positive urine drug tests for phencyclidine (PCP) have been reported.

GENERAL INFORMATION: **Mechanism of action**: Antiepileptic drug with mood stabilizer efficacy. **FDA Indications:** Bipolar Disorder, maintenance. **Off-Label Indications:** Bipolar, depression. **Pharmacokinetics:** T½ = 25 hrs. **Common side effects:** Nausea (14%), insomnia (10%), fatigue (8%), rhinitis (7%), abdominal pain (6%), constipation (5%), Vomiting (5%). **Black Box Warning:** For serious, life-threatening rashes requiring hospitalization and discontinuation of treatment (Stevens Johnson syndrome @ approx. 1: 1000). Nearly all cases of life-threatening rashes associated with lamotrigine have occurred within 2 to 8 weeks of treatment initiation. The risk of rash may also be increased by co-administration of lamotrigine with Depakote (valproic acid) exceeding the recommended initial dose of lamotrigine, or exceeding the recommended dose escalation for lamotrigine. Lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug related. **Contraindications**: **Warnings and Precautions:** Serious skin rashes, multiorgan hypersensitivity reactions and organ failure, blood dyscrasias, suicidal behavior and ideation, increased aseptic meningitis risk, dosage adjustments needed for oral contraceptives, withdrawal seizures, increased risk of status epilepticus, sudden unexplained death in epilepsy. **Metabolism/Pharmacogenomics**: Metabolized primarily by glucuronidation. **Significant drug-drug interactions:** Notable interactions decreasing lamotrigine levels include estrogen containing oral contraceptives (~50%), and carbamazepine (~40%). Valproate increases lamotrigine concentrations slightly more than two-fold. Check all drug-drug interactions before prescribing. **Reproductive potential/pregnancy/lactation: Oral contraceptives may decrease serum concentration of**

lamotrigine. Dosage Form: Tablet, Chewable, Oral Dissolving Tablet. **Generic Available:** Yes. Cost: ¢. **FDA label information from Drugs @FDA for Lamictal dated 5.12.2016.**

LITHIUM (LITHIUM CARBONATE, IR), LITHIUM-CONTROLLED RELEASE (LITHIUM ER, LITHOBID)

DOSING INFORMATION: Week 1: Check baseline labs (urine pregnancy, basic metabolic panel (baseline Cr), Ca^{2+}, CBC (for baseline WBC) TSH, EKG (for patients over 40 y/o). **Start (IR/ER)**: Lithium 300 mg bid or 600 mg qHS (may start with 300 mg/qHS, if the patient is less acute or sensitive to side effects, to increase tolerability). Week 2 and Beyond: Measure lithium concentration weekly (ideally 12 hours after the last dose) and as indicated and tolerated increase dose in 300 mg/day increments to target plasma level of 0.8-1.0 meq/L. **Typical Target Plasma Level and Dose:** Plasma level 0.8-1.0 meq/L which usually equates with daily dose of 1200-1800 mg. OF NOTE: For less severe conditions and for maintenance, a target plasma level between 0.6 and 0.8 may be desirable. **Dosing Schedule** should be determined by tolerability and compliance; Typically bid or qHS. **Formulation:** There are both immediate release and sustained release formulations. Nausea is more common with IR formulations and diarrhea with ER formulations. **Discontinuation:** Taper slowly (e.g., 25% per week) to minimize withdrawal symptoms and/or relapse.

ONGOING MONITORING*:** Measure lithium concentration 5-7 days after dose change (ideally 12 hours after last dose) and Q6 months when stable. Other labs: Baseline labs as above, Repeat at Q3 months X2 and Q6 months ***GENERAL INFORMATION: **Mechanism of action**: Natural salt with mood stabilizer efficacy. **FDA Indications:** Bipolar disorder, mania; bipolar disorder, maintenance. **Off-Label Indications:** Bipolar disorder, depression; depression augmentation; anti-suicide effect. **Pharmacokinetics:** T½ = ~24 hrs. **Common Side Effects:** Nausea, tremor, polyuria (related to nephrogenic diabetes insipidus) and thirst, weight gain, loose stools, cognitive impairment (sedation, including changes in memory, concentration, apathy, and decreased creativity). **Black Box Warning:** Toxicity can occur at levels close to therapeutic dosing: Mild symptoms occur at 1.5-2.5 meq/L (increase tremor, slurred speech, and increased lethargy), Moderate 2.5-3.5 meq/L (clonus, coarse tremors, worsening lethargy), and Severe above 3.5 meq/L which can be lethal. **Contraindications:** Significant renal impairment, significant cardiovascular disease, psoriasis, sodium depletion, dehydration, or debilitation. **Warnings and Precautions:** Lithium toxicity, unmasking of Brugada syndrome (disorder characterized by abnormal EKG findings and a risk of sudden death), renal effects (including long-term diminution of concentrating ability, morphologic changes), encephalopathic syndrome when coadministered with an antipsychotic, concomitant use with neuromuscular blocking agents, increased risk of hypothyroidism and hyperparathyroidism with long term use, drug-drug interactions (see below)**.** **Metabolism/Pharmacogenetics:** Excreted renally. **Significant drug-drug interactions:** Use with a great deal of caution with drugs that increase lithium levels including thiazide diuretics, NSAIDS (except aspirin), ACE-inhibitors, tetracyclines, metronidazole, potassium-sparing diuretics, and loop diuretics. Avoid or use alternatives with most calcium channel blockers. Increased risk of EPS and

neurotoxicity with 1st generation antipsychotics. Check all drug-drug interactions before prescribing. **Reproductive potential/pregnancy/lactation:: Associated w/ increased risk of teratogenesis (need to inform women of reproductive potential of this risk).** Cardiac malformations, including Epstein's anomaly (up to 2 additional cases per 100 births among pregnancies in women exposed to lithium during the first trimester compared with pregnancies in unexposed women with similar characteristics), are the primary risk of using lithium during the first trimester and risk seems dose-dependent. Would recommend consultation with an expert if considering lithium treatment during lactation. Lithium treatment during lactation requires special considerations such as assessing for toxicity in infant, measuring serum lithium concentration, BUN, creatinine, and TSH in infants, and close monitoring of lactating women. . **Dosage Form:** Capsule, Tablet, Coated Tablet (Do not cut, crush or chew). **Generic Available:** IR/ER: Yes. **Cost: $.**
FDA label information from Drugs @FDA for Lithobid and lithium carbonate dated 10.31.2017

ANTIPSYCHOTICS

ARIPIPRAZOLE (ABILIFY)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Mild; Metabolic Effects: Mild.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Major Depressive Disorder, Adjunctive: Start**: 2 mg qday (the **Initial Target Dose).** Continue for at least 2 weeks. Week 3: Consider further increase to 5 mg qday, if tolerated, and if still severely symptomatic. **Typical Dosage Range**: 2-5 mg qday. **Max Dose**: 10 mg qday. **Initiation for Schizophrenia: Start**: 7.5 mg qday. Week 2: increase dose to an **Initial Target Dose** of 15 mg qday, if tolerated. **Typical Dosage Range:** 15-30 mg qday. **Max Dose**: 30 mg qday, although there is little compelling evidence for benefit of doses above 15 mg qday. **Initiation for Bipolar Manic/Mixed Episode: Start**: 7.5-15 mg qday depending on episode severity. Week 2: Increase dose to an **Initial Target Dosage** between 15-30 mg qday depending on tolerability and response to Abilify. **Typical Dosage Range:** 15-30 mg qday**. Max Dose**: 30 mg qday. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
***ONGOING MONITORING*:** EKG at target dose (at least once to assess QTc). At 4 weeks: weight. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually ongoing: waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test. Repeat CBC in patients with previous low WBC.
GENERAL INFORMATION: Atypical antipsychotic/partial dopamine agonist. **FDA Indications:** Schizophrenia; Bipolar mania and mixed

episode (also as adjunctive to lithium and valproate); Major depressive disorder, adjunctive; Irritability associated with autism (pediatrics). **Off-Label Indications:** PTSD/OCD augmentation. **Pharmacokinetics:** T½ = 75 h. **Common side effects (MDD, adjunctive):** Akathisia (25%), restlessness (12%), insomnia (8%), fatigue (8%), blurred vision (6%), constipation 5%). **Common side effects (Mania):** Akathisia (13%), sedation (8%), restlessness (6%), tremor (6%), extra-pyramidal symptoms (5%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents and young adults. **Contraindications**: **Warnings and Precautions:** Use in elderly patients with dementia-related psychosis, clinical worsening of depression and suicide risk, NMS, TD, metabolic changes including hyperglycemia and diabetes mellitus, dyslipidemia and weight gain, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, seizures/convulsions, potential for cognitive and motor impairment, body temperature dysregulation, dysphagia, QTc prolongation, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics**: Metabolized by 3A4 and 2D6. **Significant drug-drug interactions:** Caution with 3A4 inducers (e.g., carbamazepine)—Abilify dosage should be doubled when coadministered with carbamazepine. Caution when co-administered with strong 3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and strong 2D6 inhibitors (e.g., fluoxetine and paroxetine). In both cases the Abilify dosage should be cut in half. Potential to enhance the effect of certain antihypertensives due to its α1-adrenergic receptor antagonism; Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet, Soluble, Oral Dissolving Tablet. **Generic Available:** Yes, **Cost**: **$**. **FDA label information from Drugs @FDA for Abilify dated 2.23.2017**.

ASENAPINE (SAPHRIS)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild to moderate; TD Risk: Unknown; Sedation: Mild to moderate Metabolic Effects: Mild
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start**: 5 mg bid (the **Initial Target and Typical Dose**). OF NOTE: This is a sublingual medication and the patient should not eat or drink for 10 min after administration. **Max Dose**: 10 mg bid, although there is little compelling evidence in schizophrenia for additional efficacy of 10 mg bid. **Initiation for Bipolar Manic/Mixed Episode: Start**: 5-10 mg bid (the **Initial Target and Typical Dose**) depending on episode severity. **Typical Dosage Range:** 5-10 mg bid**. Max Dose**: 10 mg bid. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Acute schizophrenia; Acute bipolar mania or mixed (monotherapy or as adjunctive). **Off-Label Indications:** None. **Pharmacokinetics:** T½ = 24 hrs. **Common side effects (Schizophrenia):** Somnolence (13%), EPS excluding akathisia (10%), akathisia (6%), oral hypoesthesia (5%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, TD, hyperglycemia and diabetes mellitus, weight gain, hypersensitivity reactions, orthostatic hypotension and syncope, falls, increased risk of leukopenia, neutropenia and agranulocytosis, QT prolongation, sudden cardiac death, hyperprolactinemia, seizures, potential for cognitive and motor impairment, body temperature regulation, dysphagia. **Metabolism/Pharmacogenomics**: Cleared primarily by glucuronidation and metabolism by 1A2. **Significant drug-drug interactions:** Saphris is a weak 2D6 inhibitor. Use caution when coadministered with drugs metabolized by 2D6 (e.g., venlafaxine). Caution when coadministered with potent 1A2 inhibitors (e.g., fluvoxamine); Check all drug-drug interactions before prescribing. **Dosage Form:** Sublingual tablet. **Generic Available:** No. **Cost: $$$. FDA label information from Drugs @FDA for Saphris dated 3.21.13**.

HALOPERIDOL (HALDOL)

ANTIPSYCHOTIC RISK PROFILE: EPS: High; TD Risk: High; Sedation: Mild; Metabolic Effects: Mild.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Start**: haloperidol 1 - 2 mg bid (0.5 mg bid in the elderly)*. Week 2: Increase haloperidol to an **Initial Target Dose** of 2 mg bid (1 mg bid in the elderly), if tolerated. Week 3 and beyond: Assess for side effects and consider further increases in 1 mg bid increments, if tolerated, until symptom remission or max dose is reached. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. **Typical Dosage Range:** 2-5mg po bid (1-3 mg bid in the elderly). **Max Dose:** 20 mg (10 mg in the elderly). *OF NOTE: It is frequently necessary to prescribe an anticholinergic medication with Haldol to treat Parkinsonian side effects (diphenhydramine 25 mg or benztropine 0.5-2 mg PRN or scheduled bid). **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
***ONGOING MONITORING*:** EKG at target dose (at least once to assess QTc). At 4 weeks: weight. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually ongoing: waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.
GENERAL INFORMATION: Typical antipsychotic. **FDA Indications:** "Management of manifestation of psychotic disorders." **Pharmacokinetics:** T½ = up to 3 weeks. **Common side effects (Psychosis):** Extra-pyramidal symptoms (Parkinsonism, akathisia), orthostatic hypotension, sedation/fatigue, weight gain, dry mouth, nausea, insomnia, dizziness, anxiety. **Black Box Warning:**

Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: Severe toxic central nervous system depression or comatose states. Parkinson's disease. **Warnings/Precautions:** Increased risks in elderly patients with dementia-related psychosis, cardiovascular effects (sudden death, QT-prolongation, and Torsades de Pointes), TD, NMS, usage in pregnancy, combined use with lithium, increased risk of bronchopneumonia, potential for cognitive and motor impairment, use with alcohol, increased risk of leukopenia, neutropenia and agranulocytosis, hypotension, caution in patient with severe cardiovascular disease, seizures, hyperprolactinemia, potential for severe neurotoxicity in patients with thyrotoxicosis, dysphagia, body temperature regulation. **Metabolism/Pharmacogenomics**: Metabolized by glucuronidation and 3A4 and 2D6. **Significant drug-drug interactions:** Caution with 3A4 inducers (e.g., carbamazepine and St. John's wort) and inhibitors of 3A4 (ketoconazole and protease inhibitors) and 2D6 (e.g., fluoxetine and paroxetine); Check all drug-drug interactions before prescribing. **Reproductive potential/pregnancy/lactation:** Would recommend checking blood levels in the infant/toddler to confirm minimal maternal transfer of this medication given the variability in excretion between mothers. **Dosage Form:** Tablet, Concentrate. **Generic Available:** Yes. **Cost**: ¢. **FDA label for Haldol from dailymed.nlm.nih.gov, Rev. dated 10.2011.**

ILOPERIDONE (FANAPT)

ANTIPSYCHOTIC RISK PROFILE: EPS: Very low; TD Risk: Mild; Sedation: Unknown, likely low; Metabolic Effects: Moderate
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. **Titration schedule:** *Day 1:* 1 mg bid. *Day 3:* 2 mg bid. *Day 8:* 4 mg bid. *Day 15:* 6 mg bid (the **Initial Target Dose).** Titration can be slowed for orthostatic hypotension due to alpha adrenergic blocking properties or other side effects. Week 3: Consider further titration to max dosing as needed and tolerated. **Typical Dosage Range**: 6-12 mg bid. **Max Dose**: 24 mg/day. **Restarting therapy after discontinuation**: if medication has been stopped for greater than 3 days, the initial titration schedule should be followed. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.
GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia. **Off-Label Indications:** None. **Pharmacokinetics:** T½ = 18 hrs, active metabolite = 26 hrs. **Common side effects:** Dizziness (10%), somnolence (9%), dry mouth 8%), nasal congestion (5%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: **Warnings and Precautions:** Increased risks in elderly patients with dementia-related psychosis, QTc prolongation, NMS, TD, metabolic changes

including hyperglycemia and diabetes, dyslipidemia and weight gain, seizures, orthostatic hypotension and syncope, increased risk of leukopenia, neutropenia and agranulocytosis, hyperprolactinemia, body temperature regulation, dysphasia, **priapism**, potential for cognitive and motor impairment, sudden cardiac death, cardiovascular accident. **Metabolism/Pharmacogenomics**: Metabolized by 3A4 and 2D6. Caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Caution when co-administered with strong 3A4 inhibitors (e.g., ketoconazole) and strong 2D6 inhibitors (e.g., fluoxetine and paroxetine). In both cases the Fanapt dosage should be cut in half. Caution with centrally acting antihypertensives (due to its α1-adrenergic receptor antagonism). Should not be used with any other drugs that prolong the QT interval; Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet**. Generic Available:** No. **Cost: $$$**. **FDA label information from Drugs @FDA for Fanapt dated 3.21.2017**.

LURASIDONE (LATUDA)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild to Moderate; TD Risk: Unknown; Sedation: Moderate; Metabolic Effects: Mild.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. OF NOTE: It is important to take Latuda with food (at least 350 calories) for optimal absorption (increased by up to three fold). Also, grapefruit juice should be avoided. **Initiation for Schizophrenia: Start**: 40 mg qday (the **Initial Target Dosage**). Week 2: Assess for side effects. **Typical Dosage Range**: 40-160 mg qday. **Max Dose**: 160 mg/day. **Initiation for Bipolar Depression: Start**: 20 mg qday (**the Initial Target Dose**). Week 2: Assess for side effects. **Typical Dosage Range**: 20-60 mg/day. **Max Dose:** 120 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.
GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia; Bipolar I, depression as monotherapy or adjunct to lithium or valproate. **Off-Label Indications:** No data yet. **Pharmacokinetics:** T½ = 18 hrs. **Common Side Effects (Schizophrenia):** Somnolence (17%), EPS (14%), akathisia (13%), nausea (10%). **Common Side Effects (Bipolar Depression):** Nausea (14%), somnolence (11%), akathisia (9%), EPS (7%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. (3) Monitor for worsening and emergence of suicidal thoughts and behaviors. **Contraindications:** Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole and protease inhibitors) and inducers (e.g., carbamazepine and St. John's wort). **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis,

suicidal thoughts and behaviors in adolescents and young adults, NMS, TD, metabolic changes including hyperglycemia and diabetes, hyperprolactinemia, increased risk of leukopenia, neutropenia and agranulocytosis, orthostatic hypotension and syncope, seizures, potential for cognitive and motor impairment, body temperature dysregulation, hypomanic/manic switch, dysphagia, neurological adverse reactions in patient with Parkinson's disease or dementia with Lewy Bodies. **Metabolism/Pharmacogenomics**: Metabolized by 3A4. **Significant drug-drug interactions: Do not use Latuda in combination with strong 3A4 inhibitors (e.g., ketoconazole or protease inhibitors) or inducers (e.g., carbamazepine or St. John's wort).** Latuda dosage should be cut in half with moderate 3A4 inhibitors (e.g., diltiazem). Dosage adjustment may be necessary with coadministered with moderate 3A4 inducers. Grapefruit juice should be avoided. Check all drug-drug interactions and ***CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION***. **Dosage Form:** Tablet. **Generic Available:** No. **Cost: $$$**. **FDA label information from Drugs @FDA for Latuda dated 2.17.2017**.

OLANZAPINE (ZYPREXA)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Moderate to high; Metabolic Effects: Severe.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start**: 5 mg qHS. Week 2: Increase dose to the **Initial Target Dose** of 10 mg qHS, if tolerated. Week 3 and beyond: If still symptomatic, consider further increases, if tolerated, to 15-20 mg qHS. **Typical Dosage Range**: 10-20 mg qHS. **Max Dose**: 20 mg qHS. **Initiation for Bipolar Manic/Mixed Episode: Start**: 10 mg qHS (the **Initial Target Dose**). Week 2 and beyond: Increase dose to 15 mg qHS as needed and tolerated. **Typical Dosage Range**: 10-20 mg qHS mg. OF NOTE: Maintenance dosage is usually lower than dose used in acute episodes. **Max Dose**: 20 mg qHS. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.
GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia, Bipolar I disorder (manic or mixed episodes) with and without lithium or valproate. **Off-Label Indications:** PTSD/OCD augmentation, Depression augmentation. **Pharmacokinetics:** T½ = 30 hr. **Common Side Effects:** Weight gain/increased appetite (~17% >11 lb. gain at six weeks; ~40% >11 lb. gain at 6 months), somnolence (29%), dizziness (11%), dry mouth (9%), constipation (9%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** **Warnings and Precautions:** Elderly patients with dementia-related psychosis,

NMS, hyperglycemia, hyperlipidemia, weight gain, TD, orthostatic hypotension, leukopenia, neutropenia, and agranulocytosis, dysphagia, seizures, potential for cognitive and motor impairment, body temperature dysregulation, hyperprolactinemia, QT prolongation, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics**: Primarily metabolized by direct glucuronidation and 1A2. **Significant drug-drug interactions:** Caution when coadministered with 1A2 inducers (e.g., carbamazepine) and potent 1A2 inhibitors (e.g., fluvoxamine—consider dosage adjustment); OF NOTE: tobacco induces the metabolism of olanzapine—consider dosage adjustment when starting or stopping tobacco; Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet, Tablet Dispersible**. Generic Available:** Yes. Cost: ¢. **FDA label information from Drugs @FDA for Zyprexa dated 3.30.2017**.

OLANZAPINE AND FLUOXETINE (SYMBYAX):

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild TD Risk: Mild Sedation: Moderate to high Metabolic Effects: Severe

DOSING INFORMATION: **Initiation for Bipolar Depression and Treatment Resistant Depression:** Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, EKG (to assess QTc) and AIMS test. Consider BMP for baseline sodium in older adults. **Start**: olanzapine 6 mg /fluoxetine 25 mg qHS (the **Initial Target Dose**). In patients with risk for orthostasis, start olanzapine 3mg /fluoxetine 25 mg qHS. Week 4 and beyond: Consider increase in dose if needed and tolerated. **Typical Dosage Range**: olanzapine 6 mg /fluoxetine 25 mg-olanzapine 12 mg/fluoxetine 50 mg qHS. **Max Dose**: olanzapine 12 mg /fluoxetine 50 mg qHS. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC. Consider posttreatment BMP to rule out hyponatremia in older adults.

GENERAL INFORMATION: Atypical antipsychotic combined with SSRI. **FDA Indications:** Depressive Episodes Associated with Bipolar I disorder and Treatment Resistant Depression. **Off-Label Indications:** None. **Pharmacokinetics:** T½ (olanzapine) = 30 hr; T½ (fluoxetine) = 4-6 days. **Common Side Effects:** Somnolence (27%), Weight gain (25%), increased appetite (20%), dry mouth (15%), edema (15%), fatigue (12%), tremor (9%), vision blurred (5%), disturbance in attention (5%). **Black Box Warnings:** (1) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants, (2) Monitor for worsening and emergence of suicidal thoughts and behaviors, (3) Increased mortality in elderly patients with dementia related psychosis.

Contraindications: Known hypersensitivity reaction to either fluoxetine or olanzapine. Use of a MAOI within 5 weeks of stopping Symbyax, concurrent use of a MAOI including drugs with significant MAOI activity (e.g., linezolid), or use of Symbyax within 5 weeks of stopping a MAOI. Do not use pimozide or thioridazine with Symbyax because of QT prolongation risk. **Warnings and Precautions:** Clinical worsening and suicide risk, elderly patients with dementia-related psychosis, NMS, hyperglycemia, hyperlipidemia, weight gain, serotonin syndrome, allergic reactions and rash, hypomanic/manic switch, TD, orthostatic hypotension, leukopenia, neutropenia, and agranulocytosis, dysphagia, seizures, abnormal bleeding, hyponatremia, potential for cognitive and motor impairment, body temperature dysregulation, QT prolongation, hyperprolactinemia, long elimination half-life of fluoxetine, discontinuation reactions, sudden cardiac death, cerebrovascular accident. **Metabolism/ Pharmacogenomics:** Fluoxetine: primarily metabolized by 2D6**.** Use caution with 2D6 poor metabolizers. Olanzapine: primarily metabolized by direct glucuronidation and 1A2. **Significant drug-drug interactions:** Fluoxetine: potent 2D6 inhibitor; Use significant caution when coadministered with drugs metabolized by 2D6 (e.g., TCAs). Olanzapine: caution when coadministered with 1A2 inducers (e.g., carbamazepine) and potent 1A2 inhibitors (e.g., fluvoxamine—consider dosage adjustment). OF NOTE: tobacco induces the metabolism of olanzapine—consider dosage adjustment when starting or stopping tobacco. Check all drug-drug interactions before prescribing. **Dosage Form:** Capsule. **Significant drug-drug interactions:** Check all drug-drug interactions. **Generic Available:** Yes. **Cost: $$ (if components purchased separately, $)**. **FDA label information from Drugs @FDA for Symbyax dated 1.25.2018**.

PALIPERIDONE (INVEGA)–ORAL FORMULATION

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Moderate; Sedation: Moderate; Metabolic Effects: Moderate.
DOSING INFORMATION: **Initiation for Schizophrenia and Schizoaffective Disorder:** Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, and EKG (to assess QTc) and AIMS test. **Start**: 3 mg qAM. Week 2: Increase to an **Initial Target Dose** of 6 mg qAM, if tolerated. Week 3 and beyond: Consider further increases in 3 mg increments up to a maximum of 12 mg/day, if tolerated. **Typical Dosage Range**: 3-12 mg qday. **Max Dose**: 12 mg/day. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, AIMS test. Repeat CBC in patients with previous low WBC.
GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia; Schizoaffective disorder (monotherapy or as adjunctive). **Off-Label Indications:** Bipolar, mixed or manic. **Pharmacokinetics:** T½ =23 hrs. **Common Side Effects (Schizophrenia):**

Somnolence (20%), extra-pyramidal symptoms (18%), akathisia (11%), tachycardia (9%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, QT prolongation, sudden cardiac death, cerebrovascular accidents, TD, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, hyperprolactinemia, potential for gastrointestinal obstruction, orthostatic hypotension and syncope, increased risk of leukopenia, neutropenia and agranulocytosis, potential for cognitive and motor impairment, seizures, dysphagia, **priapism**, potential increased risk for thrombotic thrombocytopenic purpura, body temperature dysregulation, antiemetic effect. **Metabolism/Pharmacogenomics**: Majority of absorbed dose is renally excreted unchanged. Multiple minor hepatic metabolic pathways. **Significant drug-drug interactions:** Caution with use of other drug that can cause orthostatic hypotension; Carbamazepine increases the renal clearance of Invega by ~40% whereas valproate increases the effective dosage of Invega by ~50%. Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet, Suspension. **Generic Available:** No. **Cost:** **$$$**. **FDA label information from Drugs @FDA for INVEGA dated 1.17.2018**.

PERPHENAZINE (TRILAFON)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: High; Sedation: Moderate; Metabolic Effects: Mild.
DOSING INFORMATION: Week 1: Assess baseline Weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC) and EKG (to assess QTc) and AIMS test. **Start**: 4 mg bid. Week 2: Increase to an **Initial Target Dose** of 8 mg bid, if tolerated. Week 3 and beyond: Assess for side effects and consider further increases to 12 mg bid if still symptomatic. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. **Typical Dosage Range**: 8-24 mg/day. **Max Dose**: 24 mg/day in an outpatient setting. OF NOTE: Consider lower overall dosing in the elderly. **Discontinuation:** Taper slowly to minimize withdrawal symptoms
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile and AIMS test.
GENERAL INFORMATION: Typical antipsychotic. **FDA Indications:** Schizophrenia. **Pharmacokinetics:** T½ = 9-12 hrs. **Common Side Effects:** Extra-pyramidal symptoms (seen at higher doses; Parkinsonism, akathisia), orthostatic hypotension, sedation/fatigue and anticholinergic side effects (blurred vision, urinary retention, xerostomia, constipation). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications:** Use in comatose or greatly obtunded patients and in patients receiving large doses of CNS depressants, in patients with suspected or established subcortical brain damage, with or without

hypothalamic damage, in the presence of existing blood dyscrasias, bone marrow depression, or liver damage. **Warnings/Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, tardive dyskinesia, NMS, suicidality, seizures, caution in patient with depression, potential for cognitive and motor impairment, orthostatic hypotension, QTc prolongation, hyperprolactinemia, sudden cardiac death, cerebrovascular accident, body temperature dysregulation, increased risk of leukopenia, neutropenia and agranulocytosis long term use associated with potential liver damage, corneal and lenticular deposits. **Metabolism/Pharmacogenomics**: Metabolized by 2D6. Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** Use caution with potent 2D6 inhibitors (e.g., fluoxetine and paroxetine). Check all drug-drug interactions before prescribing. **Dosage Form:** Tablet. **Generic Available:** Yes. **Cost:** **$**. **FDA label information from Drugs @FDA for Trilafon dated 5.2.2002**. **FDA label for perphenazine from dailymed.nlm.nih.gov, Rev. dated 12.2013.**

QUETIAPINE (SEROQUEL (IR), SEROQUEL XR)

ANTIPSYCHOTIC RISK PROFILE: EPS: Mild; TD Risk: Mild; Sedation: Moderate; Metabolic Effects: Moderate to severe.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia or Bipolar Manic/Mixed Episode**: **Start Seroquel-IR**: Day 1, 25 mg bid; Day 2, 50 mg bid; Day 3, 100 mg bid; Day 4, 150 mg bid and Day 5, 200 mg bid (**Initial Target Dose IR**). This titration schedule can be slowed down because of side effects. At higher daily dosages consider scheduling a greater proportion of dose qHS to limit daytime sedation. **Start Seroquel-XR:** Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 200 mg qHS; Day 4, 300 mg qHS and Day 5, 400 mg qHS (**Initial Target Dose XR**). This titration schedule can be slowed down because of side effects. Week 2: Can consider further increases in 100 mg increments, if tolerated, up to **Max Dose (IR/XR)** of 800 mg/day. **Typical Dosage Range (IR/XR):** 400-800 mg/day. **Initiation for Bipolar Depression: Start Seroquel IR/XR:** Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 200 mg qHS; and Day 4, 300 mg qHS (**Initial Target Dose IR/XR**). **Typical Dosage Range (IR/XR):** 300-600 mg/day. **Max Dose (IR/XR)**: 600 mg/day. **Initiation for Adjunctive Treatment for Major Depression: Start Seroquel XR**: Day 1, 50 mg qHS; Day 2, 100 mg qHS; Day 3, 150 mg qHS (**Initial Target Dosage XR**). **Typical Dosage Range (XR):** 150-300 mg qHS. **Maximum Dose (XR)**: 300 mg qHS. OF NOTE: for the elderly consider a slower rate of dose titration and a lower target dose for all indications. **Discontinuation:** Stopping medication abruptly may cause discontinuation syndrome (insomnia, nausea, headache, diarrhea, vomiting, irritability).
***ONGOING MONITORING*:** EKG at target dose (at least once to assess QTc). At 4 weeks: Weight, Fasting lipid profile. At 8 weeks: weight. At 12 weeks: weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: weight. Annually /ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile and AIMS test. Consider checking for cataracts.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Schizophrenia (IR, XR), Bipolar I – manic (IR, XR), Bipolar I – mixed (XR), Bipolar disorder – depressive episode (IR, XR), Bipolar maintenance as adjunctive to lithium or divalproex (IR, XR), Adjunctive treatment of MDD (XR). **Off-Label Indications:** Anxiety disorders augmentation. **Pharmacokinetics:** T½ = 6 hr (IR); 7 hrs (XR). **Common Side Effects (Schizophrenia and Bipolar Mania—Seroquel IR):** Headache (21%), somnolence (18%), dizziness (11%), dry mouth (9%), constipation (8%), weight gain (5%), dyspepsia (5%), ALT increased (5%). **Common Side Effects (Bipolar Depression—Seroquel XR):** Somnolence (52%), dry mouth (37%), Increased appetite (12%), dyspepsia (7%), weight gain (7%), fatigue (6%). **Black Box Warnings:** (1) Increased mortality in elderly patients with dementia related psychosis. (2) Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants. (3) Monitor for worsening and emergence of suicidal thoughts and behaviors. **Contraindications**: **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, suicidal thoughts and behaviors in adolescents and young adults, NMS, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, TD, hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, cataracts, QT prolongation, seizures, hypothyroidism, hyperprolactinemia, potential for cognitive and motor impairment, body temperature dysregulation, dysphagia, discontinuation syndrome, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics**: Metabolized by 3A4. **Significant drug-drug interactions:** Dosage adjustment is required when quetiapine is coadministered with strong 3A4 inhibitors (e.g., reduce the dosage to one sixth with ketoconazole and ritonavir) or with chronic treatment (>7-14 days) with potent 3A4 inducers (e.g., increase the dosage by 5 fold with phenytoin, rifampin, St. John's wort). Caution with medications that cause QTc prolongation. Check all drug-drug interactions and ***CONSIDER CONSULTATION WITH A PHARMACIST BEFORE PRESCRIBING THIS MEDICATION***. **Dosage Form:** Tablet, Tablet-24-hour. **Generic Available:** IR: yes; XR: No. **Cost:** IR: ¢, XR: $. **FDA label information from Drugs @FDA for Seroquel IR dated 10.29.14. FDA label information from Drugs @FDA for Seroquel XR dated 4.30.2013**.

RISPERIDONE (RISPERDAL)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Moderate; Sedation: Moderate; Metabolic Effects: Moderate.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start**: 1 mg qHS. Week 2: Increase risperidone to 1 mg bid, if tolerated. Week 3: Increase to an **Initial Target Dose** of 1 mg qAM and 2 mg qHS, if tolerated. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. Week 4 and beyond: Assess side effects and consider further increases in 1 mg increments, if tolerated until symptom remission or **Max Dose** of 8 mg reached. **Typical Dosage Range**: 3-4 mg/day. OF NOTE: dosages above 4 mg/day are much more likely to be associated with EPS and it may be necessary to prescribe an

anticholinergic medication to deal with Parkinsonian side effects (Benadryl 25 mg or Cogentin 1-2 mg PRN or scheduled). **Initiation for Bipolar Mania and Mixed Episodes: Start**: 1-2 mg/day (bid or qHS) depending on episode severity. Week 2: Increase to an **Initial Target Dose** of 2-3 mg/day (with more at HS), if tolerated and depending on episode severity. Week 3 and beyond: Assess for side effects and consider further increases in 1 mg increments until symptom remission or **Max Dose** of 6 mg reached. If qAM dosage is excessively sedating consider consolidating more of the dose to qHS. In severe cases of mania consider accelerating this titration schedule. **Typical Dosage Range**: 1-4 mg/day. OF NOTE: dosages above 4 mg/day are much more likely to be associated with EPS and it may be necessary to prescribe an anticholinergic medication to deal with Parkinsonian side effects (Benadryl 25 mg or Cogentin 1-2 mg PRN or scheduled). **Discontinuation:** Taper slowly to minimize withdrawal symptoms.
ONGOING MONITORING: EKG at target dose (at least once to assess QTc). At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.
GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Bipolar mania and mixed episode; Schizophrenia. **Off-Label Indications:** Depression augmentation, anxiety disorders augmentation. **Pharmacokinetics:** T½ = 3 hrs for risperidone and 21 hours the active metabolite. **Common side effects (mania):** Parkinsonism (25%), sedation (11%), akathisia (9%), tremor (6%), dystonia (5%), nausea (5%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: **Warnings and Precautions:** Increased mortality and risk of cerebrovascular adverse events including stroke in elderly patients with dementia-related psychosis, NMS, TD, metabolic changes including hyperglycemia and diabetes, dyslipidemia and weight gain, hyperprolactinemia, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, cataracts, potential for cognitive and motor impairment, seizures, dysphagia, **priapism**, body temperature dysregulation, patients with phenylketonuria, QTc prolongation, sudden cardiac death, cerebrovascular accident. **Metabolism/Pharmacogenomics**: Metabolized by 2D6 and 3A4 (minor). Use caution with 2D6 poor metabolizers. **Significant drug-drug interactions:** The dosage of Risperdal should be adjusted with 2D6 inhibitors (e.g., fluoxetine, and paroxetine) and enzyme 3A4 inducers (e.g., carbamazepine and St. John's wort). See the FDA label for specific recommendations. Check all drug-drug interactions before prescribing. **Dosage Form:** Solution, Tablet, Dispersible Tablet. **Generic available:** Yes. **Cost:** ¢. **FDA label information from Drugs @FDA for Risperdal 3.16.2017**.

ZIPRASIDONE (GEODON)

ANTIPSYCHOTIC RISK PROFILE: EPS: Moderate; TD Risk: Mild; Sedation: Moderate; Metabolic Effects: Mild.
DOSING INFORMATION: Week 1: Assess baseline weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile, CBC (for baseline WBC), CMP for patients at risk of significant electrolyte disturbances should have baseline serum potassium

and magnesium measurements and EKG (to assess QTc) and AIMS test. **Initiation for Schizophrenia: Start**: 20 mg twice daily (with food). Week 2 and beyond: Consider increasing dose by 20 mg bid per week as needed and tolerated. **Typical Dosage Range**: 20-80 mg bid. **Initiation for Bipolar Mania and Mixed Episodes: Start**: 40 mg bid (with food). Week 2 and beyond: Increase dose in 20 mg bid per week increments as needed and tolerated. In severe cases of mania consider accelerating this titration schedule (can increase to 60-80 mg bid on day 2 of treatment if needed). **Typical Dosage Range:** 40-80 mg bid (Mean ~60 mg bid). **Max Dose**: 100 mg bid. **Discontinuation:** Taper slowly to minimize withdrawal symptoms.

ONGOING MONITORING: EKG at target dose (at least once to assess QTc). Ziprasidone should be discontinued in patients who are found to have persistent QTc measurements >500 msec. At 4 weeks: Weight. At 8 weeks: Weight. At 12 weeks: Weight, blood pressure, fasting plasma glucose, fasting lipid profile. Quarterly thereafter: Weight. Annually ongoing: Waist circumference, weight, blood pressure, fasting plasma glucose, fasting lipid profile, and AIMS test.

GENERAL INFORMATION: Atypical antipsychotic. **FDA Indications:** Treatment of schizophrenia. Acute treatment of a mixed or manic episode in bipolar I disorder. Bipolar I disorder maintenance therapy as an adjunct to lithium or valproate. **Off-Label Indications:** Schizoaffective disorder. **Pharmacokinetics:** T½ = 7 hrs. **Common Side Effects (Schizophrenia)**: Somnolence (14%), extrapyramidal symptoms (14%), nausea (10%), respiratory track infection (8%), dizziness (8%). **Black Box Warnings:** Increased mortality in elderly patients with dementia related psychosis. **Contraindications**: Do not use in patients with (1) a known history of QT prolongation, (2) a recent acute myocardial infarction, (3) with uncompensated heart failure. Do not use in combination with other drugs that have demonstrated QT prolongation. **Warnings and Precautions:** Increased mortality in elderly patient with dementia-related psychosis, QT prolongation and risk of sudden death, NMS, TD, metabolic changes including hyperglycemia and diabetes, rash, orthostatic hypotension, increased risk of leukopenia, neutropenia and agranulocytosis, seizures, dysphagia, hyperprolactinemia, potential for cognitive and motor impairment, **priapism**, body temperature dysregulation, cerebrovascular accident.

Metabolism/Pharmacogenomics: Primarily metabolized by aldehyde oxidase. Some metabolism via 3A4. **Significant drug-drug interactions: Methadone, and any medications that prolong the QT interval are contraindicated**. Potent 3A4 inhibitors (e.g., ketoconazole) and inducers (e.g., carbamazepine) increase and decrease Geodon levels by approximately 35-40% respectively. Check all drug-drug interactions before prescribing. **Dosage Form:** Capsule. **Generic available:** Yes. **Cost**: **$**. **FDA label information from Drugs @FDA for Geodon 6.29.2017**.

REFERENCES:

ONLINE RESOURCES:

Drugs@FDA: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/.
DailyMed: http://dailymed.nlm.nih.gov/dailymed/about.cfm
LactMed: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT