PRESCRIBING DIRECTIONS FOR MOOD STABILIZERS

This brief information is provided to facilitate the use of these medications and is NOT intended to replace the information provided in the FDA labeling information. For any questions, please consult with your pharmacist or review FDA labeling information available at Drugs@FDA.

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**CARBAMAZEPINE EXTENDED RELEASE (TEGRETOL XR; EQUETRO)**

**DOSING INFORMATION:** Initiation: Check baseline labs (urine pregnancy, platelets, reticulocytes, serum iron, CMP—see below for guidelines regarding Asian patients). Week 1: Start 200 mg BID. Week 2-8: Check trough carbamazepine plasma level before the morning dose. If level is sub therapeutic, increase dosage by 200 mg/day. This process is repeated weekly over 8 weeks due to autoinduction of metabolism. **Target plasma level:** Therapeutic levels: 4-12 mcg/mL (600-1200 mg/day; usual max dosage: 1600 mg/day). **Toxic concentration:** >15 mcg/mL.

**ONGOING MONITORING:** Baseline labs: urine pregnancy, platelets, reticulocytes, serum iron, 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 including platelets): Qweekly X 8 weeks, Q2months X 2, and then q6-12months.

**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:** T ½ variable due to autoinduction; Initial: 35-40 hours Steady state: 12-17 hours. **Side effects:** Common: Dizziness (44%), somnolence (32%), nausea (29%), vomiting (18%), ataxia (15%), pruritis (8%), dry mouth (8%), blurred vision (6%), speech disorder (6%). **Warnings and Precautions:** Increased SI; Caution in patients with liver disease and hematologic dysfunction. **Contraindications:** Hypersensitivity to carbamazepine, tricyclic antidepressants, or any component of the formulation; bone marrow depression; with or within 14 days of MAO inhibitor use; concurrent use of nefazodone. **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. Asian patients and other high-risk patients should be screened for the presence of HLA-B*1502 prior to starting Tegretol. (2) Aplastic anemia and agranulocytosis. **Pregnancy:** Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk) and should be avoided in pregnancy.

**Breastfeeding:** The manufacturer does not recommend use while breast-feeding. However, AAP rates this medication "compatible" in breast-feeding. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing as Tegretol has multiple drug interactions including but not limited to decreasing warfarin and hormone contraceptives. **Generic Available:** Yes.

**DIVALPROEX SODIUM (DEPAKOTE ER, STAVZOR (IR))**

**DOSING INFORMATION:** Initiation: Check baseline labs (urine pregnancy, platelet counts, coagulation tests, and liver function tests). Week 1: Start Depakote ER (extended-release) 750 mg QHS. Week 2: Check trough Depakote ER plasma level before, but as close to the dosing time as possible. If level is sub therapeutic, add 250-500 mg to QHS dose. Repeat weekly as need to reach therapeutic dosage. **Target plasma level:** 85 to 125 mcg/mL. **Usual max dosage:** 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.

**ONGOING MONITORING:** Platelet counts, 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:** T ½ = 9-16 hrs. **Side effects:** Common: Headache (31%), somnolence (27%), fatigue (27%),...
tremor (25%), dizziness (25%), dyspepsia (23%), nausea (19%), diplopia (16%), vomiting (13%), diarrhea (12%), anorexia (12%), abdominal pain (10%), ataxia (8%), nystagmus (8%), weight gain (8%), alopecia (6%), cognitive impairment (6%), amnesia (5%). **Warnings and Precautions:** Hepatotoxicity, teratogenic effects, pancreatitis, suicidal behavior or ideation, thrombocytopenia, hyperammonemia and hyperammonemic encephalopathy, hypothermia, somnolence in the elderly, multi-organ hypersensitivity, Stevens-Johnson syndrome (1:5000).

**Contraindications:** Known hypersensitivity reaction to the product. Urea cycle disorders, hepatic disease or significant dysfunction. **Black Box Warnings:** (1) Hepatotoxicity, (2) pancreatitis and (3) teratogenicity.

**Pregnancy:** Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk) and should be avoided in pregnancy. May cause teratogenic effects such as neural tube defects (e.g., spina bifida) and lower cognitive test scores in children with fetal valproate exposure.

**Breastfeeding:** Probably safe. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing because they are common with this medication. Example drugs that increase Depakote level (erythromycin, fluoxetine, aspirin, ibuprofen); Example drugs that decrease Depakote level (rifampin, carbamazepine). **Generic Available:** ER, DR; Moderately expensive.

**LAMOTRIGINE (LAMICTAL)**

**DOsing INFORMATION:** **Initiation:** Week 1 and 2: 25 mg Qday. Week 3 and 4: 50 mg Qday. Week 5: 100 mg QDay. Week 6: 200 mg QDay. Dosage will need to be adjusted for patients taking carbamazepine, phenytoin, phenobarbital, primidone, or valproate (see FDA guidelines). Estrogen containing oral contraceptives increase metabolism of Lamictal such that target dose may need to be increased. **Target Dosage:** 200 mg Qday; No evidence of increased mood stabilization benefit at higher doses.

**ONGOING MONITORING:** Typically do not measure drug levels. **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.

**GENERAL INFORMATION:** **Mechanism of action:** Antiepileptic drug with mood stabilizer efficacy. **FDA Indications:** Bipolar Disorder, maintenance. **Off-Label Indications:** Bipolar, depression. **Pharmacokinetics:** T½ = 25-37hrs. **Side effects:** **Common:** Dizziness (31%), headache (29%), double vision (24%), nausea (18%), somnolence (14%), blurred vision (11%), unsteadiness/ataxia (10%). **Warnings and Precautions:** Suicidal ideation, blood dyscrasias, multi-organ failure, aseptic meningitis, withdrawal seizures. **Contraindications:** Known hypersensitivity reaction to the product. **Black Box Warning:** (1) For serious, life-threatening rashes requiring hospitalization and discontinuation of treatment (Stevens Johnson syndrome @ approx. 1:1000 to 2000). 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. Nearly all cases of life-threatening rashes associated with lamotrigine have occurred within 2 to 8 weeks of treatment initiation. Lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug related. **Pregnancy:** Category C; North American Antiepileptic Drug Pregnancy Registry (NAAED) suggest an increased incidence of cleft lip and/or cleft palate following first trimester exposure. **Breastfeeding:** Enters breast milk/not recommended. American Academy of Pediatrics Committee on Drugs considers the use of lamotrigine "of concern" in breastfeeding. **Significant drug-drug interactions:** Check all drug-drug interactions before prescribing. Notable interactions include: estrogen containing oral contraceptive increase metabolism, carbamazepine, phenytoin, phenobarbital, primidone, or valproate. **Generic Available:** Yes, Moderately expensive.

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

**DOsing INFORMATION:** **Initiation:** Check baseline labs (urine pregnancy, basic metabolic panel (baseline BUN and Cr), CBC (for baseline WBC) TSH, EKG (for patients over 40 y/o). **Week 1:** Start 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:** Check lithium level weekly and as indicated increase dose in 300 mg/day increments to target plasma level of 0.8-1.0meq/L. **Typical Target:** Plasma level 0.8-1.0meq/L and less than 1.2meq/L which usually equates with daily dose of 1200mg to 1800mg. **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.
ONGOING MONITORING: Lithium: 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 X 2 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: T ½ = ~24hrs. Side effects: Common: 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).

Warnings and Precautions: The two most important long-term adverse effects of lithium involve the kidneys and thyroid gland. Cardiac rhythm disturbances have been described (these almost always occur in patients with preexisting cardiac disease). Contraindications: Known hypersensitivity reaction to the product. Significant renal impairment, significant cardiovascular disease, psoriasis, sodium depletion, dehydration, debilitation. Black Box Warning: (1) 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. Pregnancy: Category D; associated w/ increased risk of teratogenesis (need to inform women of childbearing age of this risk). Cardiac malformations, including Epstein’s anomaly (background rate of this defect is 1/20,000 births compared to the 1/1000 rate among infants exposed to lithium in utero), are the primary risk of using lithium during the first trimester. Breastfeeding: American Academy of Pediatrics Committee on Drugs has classified lithium as "incompatible" with breastfeeding, due to documented accumulations in both maternal breast milk and infant serum. Significant drug-drug interactions: Check all drug-drug interactions before prescribing. Examples include thiazide diuretics, NSAIDS (except aspirin), ACE-inhibitors, tetracyclines, metronidazole, potassium-sparing diuretics, theophylline, loop diuretics, and calcium channel blockers. Generic Available: Yes, inexpensive.