MOOD STABILIZERS

A. FDA approved indications (see Table 1)
   1. Acute mania associated with Bipolar Disorder
   2. Bipolar Disorder maintenance
   3. Bipolar Depression

B. Non-FDA approved, commonly used indications
   1. Schizoaffective Disorders
   2. Treatment resistant psychosis
   3. Impulse Control Disorders
   4. Personality Disorders
   5. Major Depression (adjunct)
   6. Anxiety Disorders
   7. Substance Withdrawal Syndrome

*Use of gabapentin (Neurontin) in psychiatry remains as non-formulary requiring NFDR and Medical Director’s approval.

C. Minimal documentation
   1. All standard outpatient & inpatient requirements

D. Maximum Dosage - See Medication Summary for MDD
   1. Dosage must be individualized according to serum levels and clinical response (Lithium, Depakote, and Carbamazepine extended release)
   2. Lamotrigine (Lamictal): Dosing recommendations should be strictly followed to minimize the risk of serious rash (refer to Package Insert)
   3. Caution in patients with renal insufficiency (Lamictal, Lithium)
   4. Caution in patients with impaired hepatic function (Carbamazepine extended release, Lamictal, Depakote)

E. Duration
   1. For Outpatient: Document rationale when making any medication change.
2. For Inpatient: Document rational when making more than 3 changes in any 7-day period.

F. Polypharmacy

1. When considering addition of more than one agent within a class, it is recommended to first titrate the initial agent to maximum tolerated dose; then provide clear supportive rationale for the additional agent(s).
2. When changing medications, a process of cross-tapering is recommended and may require up to 90 days to accomplish. If polypharmacy is necessary beyond the maximum period of 90 days to complete cross-tapering, clear documentation of the rationale for continuation of the polypharmacy is necessary.
3. If using >1 mood stabilizers is necessary, provide clear supportive rationale for adding the second mood stabilizer. Refer to Antipsychotic (Atypical and Conventional) sections for concomitant use of 2 or more antipsychotics.

G. Drug Interactions
(Refer to Atypical Antipsychotic Section for SGA, See 2004 Guideline to Psychiatric Drug Interactions in Appendix)

1. Drugs affecting cytochrome P-450 enzymes which may increase or decrease levels of Antiepileptic drugs.
2. Oral Contraceptives (OC)
   - May decrease effectiveness (Carbamazepine, Depakote, Trileptal)
   - May decrease Lamictal concentration (may require Lamictal dosage adjustment, can potentially increase effect of Lamictal during week off of OC pills.)
3. Concomitant use of Depakote and Lamictal (follow standard dosing guidelines in the PI)
4. Concomitant use of Aspirin, Salicylates, and Coumadin with Depakote can increase risk of bleeding.
5. Concomitant use of Lithium and Clozaril may increase risk of EPS, CNS adverse effects, consider decrease in Lithium dose.
6. Drugs that can increase lithium levels and increase risk of Lithium toxicity:
   - Diuretics
   - NSAID’s
   - ACE inhibitors (Captopril, Enalapril)
   - Tetracyclines,
7. Drugs that can lower Lithium levels by enhancing Lithium excretion:
- Methylxanthine bronchodilators (Aminophylline, Theophylline)
- Caffeine,
- Acetazolamide (Diamox),
- Urinary alkalinizers (potassium citrate, sodium citrate)

8. Concomitant use of Methotrexate, Sulfasalazine, Triamterene, and Trimethoprim with Lamictal may increase risk of blood dyscrasias due to additive antifolate effect.

Document G. Serious adverse effects
For BLACK BOX Warnings see Table 3
(Refer to Atypical Antipsychotic Section for SGA)

1. Marked sedation, confusion, or lethargy
2. Hepatic dysfunction (Depakote, Carbamazepine)
3. Bone marrow suppression: signs include fever, sore throat, mouth ulcers, easy bruising, and petechiae (Carbamazepine, Lamictal)
4. Severe dermatologic reactions: toxic epidermal necrolysis and Steven-Johnson syndrome (Lamictal, Carbamazepine, Trileptal)
5. Treatment with Carbamazepine in individuals with ancestry across broad areas of Asia, including South Asian Indians, should be screened for a particular human leukocyte antigen (HLA) allele, HLA-B*1502. Dangerous or even fatal skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis), that can be caused by Carbamazepine therapy, are significantly more common in patients with HLA-B*1502. Patient who test positive should not be started on Carbamazepine unless the expected benefit clearly outweighs the increased risk of serious skin reactions. Patients who have been taking Carbamazepine for more than a few months without developing skin reactions are at low risk of these events ever developing from Carbamazepine.
6. Coagulopathy and platelet dysfunction: signs include prolonged bleeding, easy bruising, petechiae (Depakote)
7. Pancreatitis (Depakote)
8. Osteoporosis/Osteopenia (Depakote, Lamictal, Carbamazepine)
9. Polycystic ovarian syndrome (Depakote, Carbamazepine)
10. Polyuria and polydipsia (Lithium)
11. Renal and thyroid dysfunction (Lithium)
12. Tremor
13. Hypersensitivity reactions: signs include fever, lymphadenopathy
14. Acute multi-organ failure (Lamictal)
15. Toxicity in melanin containing tissues and eyes with extended use (Lamictal)
16. Hyponatremia: signs include nausea, malaise, headache, lethargy, confusion (Carbamazepine)
17. Concomitant use of Lamictal with Depakote may increase risk of Stevens-Johnson, or other potentially life-threatening rashes
18. Intentional overdose
19. Any significant laboratory abnormalities during treatment
20. AV heart block, including second and third degree block, have been reported following Tegretol treatment. This occurred generally, but not solely, in patients with underlying EKG abnormalities or risk factors for conduction disturbances

**Documentation Required**

**H. Standard laboratory and examination requirements (see Table 2)**

* Refer to Atypical Antipsychotic Medications Sections for laboratory monitoring guidelines for SGA.

1. For inpatient: Basic laboratory studies on admission
2. For outpatient*: Baseline and ongoing lab studies are required with VPA, CBZ and Lithium (refer to table 2 for details).
3. For required lab studies with atypical antipsychotics, refer to Section I: Atypical Antipsychotics for details.
4. HLA-B*1502 allele screening is required before starting treatment with carbamazepine, patients with ancestry across broad areas of Asia, including South Asian Indians. The patient can be sent to lab for this screening.
   - If the patient test positive, Carbamazepine should not be started unless the expected benefit clearly outweighs the increased risk of serious skin reactions.
   - If testing is not available to the patient, carbamazepine products should ordinarily not be used.

**Documentation Required**

**I. Relative contraindications (requires documentation of justification)**

1. History of hypersensitivity to this class of drugs
2. Pregnancy or breast-feeding (See Table 4)
3. Additional relative contraindications for specific agents:
• **Carbamazepine (Equetro, Tegretol, Carbatrol)**
  - Hypersensitivity to Carbamazepine or tricyclic compounds
  - Concomitant use of MAOIs, or use within 14 days of discontinuing MAOIs
  - Bone marrow suppression or history of previous bone marrow depression

• **Lithium (Lithium extended release, Lithobid)**
  - Impaired renal function
  - Severe debilitation, dehydration, or sodium depletion
  - Impaired cardiovascular disease
  - Lactation
  - Age less than 12 years
  - Low sodium diet
  - Baseline ECG for patients over the age of 40 years old

• **Olanzapine/Fluoxetine (Symbyax)**
  - History of allergy to Zyprexa or Prozac
  - Concomitant use or use within a minimum of 5 weeks after discontinuation of the following: MAOIs, thioridazine, and pimozide (**Due to long half life of fluoxetine**).
  - Use of Symbyax within a minimum of 14 days of MAOI discontinuation

• **Divalproex sodium (Depakote)**
  - Hepatic disease or significant hepatic dysfunction
  - Hypersensitivity to Depakote or any of its compounds
  - Urea cycle disorders

**J. Precautions**

1. Abrupt discontinuation
2. **Additional precautions for specific agents:**
   - **Carbamazepine**
     - Cardiac conduction disturbance or history of, increased risk of atrioventricular heart block;
     - Cardiac damage,
     - Increased intraocular pressure
     - History of atypical absence seizures
     - History of adverse hematological reaction to any drug
     - History of increase risk of bone marrow suppression
- Kidney or liver damage
- Hepatic porphyria
- Elderly patients may cause confusion or agitation
- Mental illness, history; risk of latent psychosis activation
- Do not administer Tegretol suspension with other liquid preparations due to formation of an insoluble precipitate

**Lithium**
- Pregnancy
- Protracted diarrhea, sweating, or infection with increased temperatures may decrease tolerance to lithium
- Significant cardiac disease
- Organic brain damage,
- Sodium depletion, restricted dietary salt intake, or diuretic requirement may increase the possibility of lithium intoxication.
- Do not increase lithium & antipsychotic dose at same time due to risk of neurotoxicity
- Debilitated or elderly patients
- Discontinue lithium at least one week before initiating electroconvulsive therapy (ECT) and withhold lithium for several days after completing ECT
- Ensure adequate fluid intake (2500 to 3000 mL) and maintain normal diet and salt intake at least during the stabilization period

**Olanzapine/Fluoxetine**
- Bipolar disorder, increase risk of mixed or manic episode
- Suicidal ideation and behavior or worsening depression; increased risk particularly in children, adolescents, and young adults in the first few months of therapy or following changes in dosage.
- Concomitant use of drugs that affect coagulation
- Elderly with dementia-related psychosis; increased risk of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) including death
- Cardiovascular or cerebrovascular disease or conditions that may predispose patients to hypotension
- Allergic reaction, systemic: may cause rash, vasculitis
- May cause neuroleptic malignant syndrome
- May cause tardive dyskinesias
- May increase risk of hyperglycemia, hyperlipidemia, and weight gain.
- Breast cancer or prolactin-dependent tumors; reports of elevated prolactin levels
- Concomitant use of NSAIDs, aspirin, or other drugs that affect coagulation; abnormal bleeding, particularly the gastrointestinal tract, may occur
- Concomitant serotonergic drug use (serotonin precursors (tryptophan), SSRIs, serotonin-norepinephrine reuptake inhibitors); risk of serotonin syndrome, use is not recommended

- **Divalproex**
  - Concomitant use of multiple anticonvulsants increases risk of hepatotoxicity
  - Concomitant use of CNS depressants
  - Concomitant use with other agents that affect platelet function
  - Pancreatitis
  - Diabetic patients may have false-positive ketone results; Hepatic disease, history of, increased risk of hepatotoxicity
  - Pregnancy; increased risk of birth defects
  - Ataxia, cyclical vomiting, lethargy, irritability, mental retardation; possible undiagnosed urea cycle disorder, which is a contraindication
  - Elderly; increased incidence of adverse effects (i.e. somnolence, dehydration)
  - Higher doses (i.e. approximately 50 mg/kg/day); increased risk for dose-related thrombocytopenia and elevated liver enzymes
  - Concomitant use with Topiramate can increase risk of hyperammonemia, with or without encephalopathy

### Documentation Required

**M. Other agents used Off Label for the Treatment of Bipolar Disorder**

Prescribing any of the agents below requires supportive documentation in the Progress Notes:

1. Gabapentin (Neurontin)
2. Topiramate (Topamax)
3. Oxcarbazepine (Trileptal)
4. Tiagabine (Gabitril)
5. Zonisamide (Zonegran)
6. Levetiracetam (Keppra)
Recent Findings (6/2013) related to Oxcarbamazepine (Trileptal):

Oxcarbamazepine is structurally very similar to carbamazepine with the exception of having an additional oxygen molecule. This small structural change is believed to account for its more favorable safety profile compared to carbamazepine. However, it seems to be less efficacious than other traditional agents and does not have a place among the “first-line” treatments for bipolar disorder. For details please refer to the full article published in Psycheduction in 6/2013 and the full prescribing package insert for each agent.

Attachments:  Table 1: FDA-Approved Indications  
                    Table 2: Laboratory Requirements  
                    Table 3: Black Box Warnings  
                    Table 4: Pregnancy & Breastfeeding Categories  
                    Table 5: Available Strength and Dosage Forms

References:
1. Prescribing Information (PI)  
2. Micromedex  
3. APA’s Practice Guidelines for the Treatment of Patients with Bipolar Disorder revision 2004  

Refer to Appendices:
1. APA’s Practice Guidelines for the Treatment of Patients with Bipolar Disorder revision 2004  
2. 2004 Guide to Psychiatric Drug Interaction  
Table 1: FDA-approved Indications

<table>
<thead>
<tr>
<th>Agent</th>
<th>Brand</th>
<th>Bipolar Manic</th>
<th>Bipolar Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine extended release</td>
<td>Equeiro*</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Lamictal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproate/Divalproex</td>
<td>Depakene, Depakote</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>Abilify</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Zyprexa</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Risperidone</td>
<td>Risperdal</td>
<td>X (kids &gt;10yo)</td>
<td></td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Seroquel</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>Geodon</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>Lithobid*</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Olanzapine/fluoxetine*</td>
<td>Symbyax*</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Asenapine</td>
<td>Saphris</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lurasidone</td>
<td>Latuda</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

* Currently Not on SCVH&HS formulary. NFDR and Medical Director's approval are required before initiation of medication.

References: Prescribing Information (PI), Micromedex

1 Carbamazepine (Tegretol) is not FDA approved for Bipolar Disorder. Carbamazepine extended release is available as Tegretol XR, Carbatrol and Equeiro. Only Equeiro has FDA approval for Bipolar Disorder.

2 For patients taking Lamictal and Depakote, the MDD for Lamictal is 100mg. For patients take Carbamazepine, Phenytoin, Phenobarbital, Primidone, or Rifampin, but not taking Depakote, and Lamictal, the MDD for Lamictal is 400mg.

3 Lithium is available as lithium carbonate, lithium carbonate ER (generic or as Lithobid 300). The brand Eskalith and Eskalith ER has been discontinued from the US.

4 Divalproex sodium is available as Depakote and Depakote ER. When switching from Depakote to Depakote ER, the Depakote ER should be administered once-daily using a dose 8% to 20% higher than the total daily dose of Depakote (Please See Table 5 in the Mood Stabilizer section for Conversion chart.).
## Table 2: Laboratory Requirements A1

<table>
<thead>
<tr>
<th>Agents</th>
<th>Weight</th>
<th>Bun/Creatinine</th>
<th>CBC / Platelets</th>
<th>Drug Serum Level B2</th>
<th>Electrolytes</th>
<th>LFT</th>
<th>Pregnancy Test</th>
<th>TSH/T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine C3</td>
<td>b</td>
<td>b, qmx2, then q6m</td>
<td>qmx2, then q6m</td>
<td>b, q12m</td>
<td>b, qmx2, then q6m</td>
<td>b, prn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lithium C4</td>
<td>b, q3m</td>
<td>b, 3m, 6m, then q12m</td>
<td>Inpt: 2x in 1st 10 days, then q2wk Outpt: qmx2, then q6m</td>
<td>b, 3m, 6m, then q12m</td>
<td>b, prn</td>
<td>b, 6m, then q12m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproate/Divalproex</td>
<td>b, q3m</td>
<td>Plt: b, qmx2, then q6m</td>
<td>qmx2, then q6m</td>
<td>b, qmx2, then q6m</td>
<td>b, prn</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**

A1 More frequent lab monitoring may be warranted based on clinical status.

B2 More frequent drug serum level monitoring may be warranted if side effects are suspected due to supra therapeutic levels i.e. worsening tremor, diarrhea, vomiting, drowsiness, muscular weakness, lack of coordination may be due to Lithium toxicity. Assessment of serum levels and subsequent dosage changes (if necessary) should be carefully documented to reflect risk vs. benefit analysis of continuing the regime with no changes.

C3 HLA-B*1502 allele screening is required before starting treatment with carbamazepine, patients with ancestry across broad areas of Asia, including South Asian Indians. If testing is not available to the patient, carbamazepine products should ordinarily not be used.

C4 Baseline ECG for patients > 40 y.o. with Lithium

**Definitions:**
- b: Baseline (before initiating treatment)
- q: every
- m: month
- prn: as needed

**References:**
1. Prescribing Information (PI)
2. Micromedex
3. APA’s Practice Guideline for the Treatment of Patients with Bipolar Disorder revision 2004
### Table 3: Black Box Warnings

<table>
<thead>
<tr>
<th>Medication</th>
<th>Black Box Warnings</th>
</tr>
</thead>
</table>
| **Carbamazepine-Extended Release** | - Aplastic anemia and agranulocytosis have been reported in association with the use of Carbamazepine.  
- Although reports of transient or persistent decreased platelet or white blood cell counts are not uncommon in association with the use of Carbamazepine, data are not available to estimate accurately their incidence or outcome.  
- Because of the very low incidence of agranulocytosis and aplastic anemia, the vast majority of minor hematologic changes observed in monitoring of patients on Carbamazepine are unlikely to signal the occurrence of either abnormality. Nonetheless, complete pretreatment hematological testing should be obtained as a baseline.  
- Patients with ancestry in genetically at-risk populations should be screened for the presence of hla-b*1502 prior to initiating treatment with tegretol. Patients testing positive for the allele should not be treated with tegretol unless the benefit clearly outweighs the risk. |
| **Lamotrigine (Lamictal)** | - Serious rashes requiring hospitalization and discontinuation of treatment have been reported in association with the use of Lamotrigine.  
- Other than age, there are as yet no factors identified that are known to predict the risk of occurrence or the severity of rash associated with Lamotrigine.  
- Nearly all cases of life-threatening rashes associated with Lamotrigine have occurred within 2 to 8 weeks of treatment initiation. However, isolated cases have been reported after prolonged treatment (e.g., 6 months).  
- Although benign rashes also occur with Lamotrigine, it is not possible to predict reliably which rashes will prove to be serious or life threatening. Accordingly, Lamotrigine should ordinarily be discontinued at the first sign of rash, unless the rash is clearly not drug related. |
| **Lithium, Lithium ER** | - Lithium toxicity is closely related to serum lithium levels, and can occur at doses close to therapeutic levels. Facilities for prompt and accurate serum lithium determinations should be available before initiating therapy. |
| **Divalproex Sodium (Depakote)** | - HEPATOTOXICITY Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid and its derivatives. These incidents usually have occurred during the first six months of treatment. Serious or fatal hepatotoxicity may be preceded by non-specific symptoms such as malaise, weakness, lethargy, facial edema, anorexia, and vomiting.  
- TERATOGENICITY Valproate can produce teratogenic effects such as neural tube defects (e.g., spina bifida). Accordingly, the use of Divalproex sodium tablets in women of childbearing potential requires that the benefits of its use be weighed against the risk of injury to the fetus. An information sheet describing the teratogenic potential of Valproate is available for patients.  
- PANCREATITIS Cases of life-threatening pancreatitis have been reported in both children and adults receiving Valproate. Cases have been reported shortly after initial use as well as after several years of use. Patients and guardians should be warned that abdominal pain, nausea, vomiting, and/or anorexia can be symptoms of pancreatitis that require prompt medical evaluation. |

**Bolded agents reflect non-formulary status at SCVH&HS.**

References: Prescribing Information (PI), Micromedx
Table 4: Pregnancy and Breastfeeding Categories

<table>
<thead>
<tr>
<th>Drug</th>
<th>Use During Pregnancy</th>
<th>Breastfeeding Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine- Extended Release</td>
<td>Increased risk of congenital malformations, including spina bifida.</td>
<td>• AAP Lactation Rating: Maternal medication usually compatible with breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• WHO Lactation Rating: Compatible with breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thomson Lactation Rating: Infant risk cannot be ruled out.</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>There are no adequate and well-controlled studies in pregnant women. Lamictal should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.</td>
<td>• Preliminary data indicate that lamotrigine passes into human milk. Because the effects on the infant exposed to LAMICTAL by this route are unknown. Breastfeeding while taking LAMICTAL is not recommended.</td>
</tr>
<tr>
<td>Lithium</td>
<td>In humans, lithium may cause fetal harm when administered to a pregnant woman. Data from lithium birth registries suggest an increase in cardiac and other anomalies, especially Ebstein's anomaly</td>
<td>• AAP Lactation Rating: Drugs that have been associated with significant effects on some nursing infants and should be given to nursing mothers with caution.</td>
</tr>
<tr>
<td>Lithium ER</td>
<td></td>
<td>• WHO Lactation Rating: Avoid breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thomson Lactation Rating: Infant risk cannot be ruled out.</td>
</tr>
<tr>
<td>Divalproex Sodium (Depakote)</td>
<td>Increased risk of congenital malformations i.e. neural tube defects</td>
<td>• AAP Lactation Rating: Maternal medication usually compatible with breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• WHO Lactation Rating: Compatible with breastfeeding. Monitor infant for side effects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Thomson Lactation Rating: Infant risk cannot be ruled out.</td>
</tr>
</tbody>
</table>

References: Prescribing Information (PI), Micromedex
Refer to Pregnancy and Drug Dilemma in Appendix for definition of Pregnancy Category
Refer to Table 5, Section I for Pregnancy and Breastfeeding Categories on atypicals
### Table 5: Available Strength and Dosage Forms

<table>
<thead>
<tr>
<th>Medication</th>
<th>Strengths &amp; Dosage Forms</th>
</tr>
</thead>
</table>
| Carbamazepine- Extended Release (Equetro) | - **Carbatrol**: Oral Capsule, Extended Release: 100 MG  
- **Equetro**: Oral Capsule, Extended Release: 100 MG, 200 MG, 300 MG  
- **Tegretol-XR**: Oral Tablet, Extended Release: 100 MG, 200 MG, 400 MG |
| Lamotrigine (Lamictal) | - **Generic**: Oral Tablet, Chewable: 5 MG, 25 MG  
- **Lamictal CD**: Oral Tablet, Chewable: 2 MG, 5 MG, 25 MG  
- **Lamictal**: Oral Tablet: 25 MG, 100 MG, 150 MG, 200 MG |
| Lithium Lithium ER (Lithobid) | - **Generic**:  
  - Oral Capsule: 150 MG, 300 MG, 600 MG  
  - Oral Tablet: 300 MG  
  - Oral Tablet, Extended Release: 300 MG, 450 MG  
  - Oral Solution: 8 MEQ/5 ML  
- **Lithobid**: Oral Tablet, Extended Release: 300 MG |
| Divalproex Sodium (Depakote) | - **Depakote ER**: Oral Tablet, Extended Release: 250 MG, 500 MG  
- **Depakote**: Oral Tablet, Enteric Coated: 125 MG, 250 MG, 500 MG  
- **Depakote Sprinkle**: Oral Capsule, Delayed Release: 125 MG |

Bolded agents reflect non-formulary status at SCVH&HS.

**Conversion from DEPAKOTE to DEPAKOTE ER**:

<table>
<thead>
<tr>
<th>DEPAKOTE Total Daily Dose (mg)</th>
<th>DEPAKOTE ER Total Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500*</td>
<td>750</td>
</tr>
<tr>
<td>1000*</td>
<td>1250</td>
</tr>
<tr>
<td>1500</td>
<td>1750</td>
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<tr>
<td>2000</td>
<td>2250</td>
</tr>
<tr>
<td>2500</td>
<td>3000</td>
</tr>
<tr>
<td>3000</td>
<td>3500</td>
</tr>
</tbody>
</table>

References: Prescribing Information (PI), Micromedex