VALPROIC ACID (DEPAKENE®), DIVALPROEX SODIUM (DEPAKOTE®, DEPAKOTE® ER)

INDICATIONS

1) Bipolar disorder and other cyclic mood disorders
2) Aggressive behavior secondary to a psychiatric disorder
3) Impulse control disorders

PRECAUTIONS TO CONSIDER

Contraindications

Absolute:

1) History of anaphylactic reaction or similarly severe significant hypersensitivity to medication prescribed
2) Severe hepatic dysfunction
3) Known mitochondrial disorders caused by mutations in mitochondrial DNA polymerase gamma
4) Urea cycle disorders

Relative

1) Mild to moderate hepatic disease/impairment
2) Blood dyscrasias, clotting disorders or concomitant drugs that alter clotting function (aspirin, non-steroidal anti-inflammatory drugs, warfarin, heparin, low molecular weight heparins, clopidogrel etc.)
3) Pregnancy/nursing mothers
4) Hyperammonemia

Precautions

1) Hypoalbuminemia
2) Renal impairment
3) Pancreatitis
4) Concomitant topiramate use
5) Polycystic ovarian syndrome
6) Use of concomitant medications that can cause blood dyscrasias (e.g., carbamazepine, clozapine, etc.)
7) HIV or CMV infection
8) Brain atrophy (e.g. Cerebellar atrophy)

Pregnancy and Breast-Feeding

See relative contraindications. FDA Pregnancy Category D for Bipolar Disorder. FDA Category X for migraines. Lactation Risk L4.

Drug Interactions of Major Significance

1) Concomitant CNS depressants
2) Anticoagulants
3) Carbamazepine
4) Felbamate
5) Concomitant hepatotoxic medications
6) Mefloquine
7) Phenytoin
8) Lamotrigine
9) Non-steroidal anti-inflammatory drugs
10) Aspirin (for doses > 81 mg/day)
11) Phenobarbital, primidone
12) Diazepam
13) Amitriptyline, nortriptyline, desipramine, fluoxetine
14) Topiramate
15) Rifampin
16) Carbapenem antibiotics
17) Ethosuximide
18) Zidovudine

Age-specific Considerations

1) Age younger than 10 years old due to high risk of hepatic toxicity
2) Geriatric patients have increased amounts of free drug (use lower total plasma concentration or get free VPA plasma concentration)
3) Women of child-bearing age (e.g., teratogenicity, polycystic ovarian syndrome)

VALPROIC ACID (DEPAKENE®), DIVALPROEX SODIUM (DEPAKOTE®, DEPAKOTE® ER) - continued

PRECAUTIONS TO CONSIDER (continued)

Side Effects Which Require Medical Attention

1) Worsening confusion or disorientation
2) Nausea, vomiting, diarrhea, abdominal discomfort or anorexia, pancreatitis
3) Bruising or bleeding
4) Clinically significant weight gain
5) Tremors
6) Signs/symptoms of infection (e.g., fever, sore throat, malaise, etc.)
7) Ataxia, gait disturbances, dysarthria
8) Sedation
9) Alopecia
10) Peripheral edema
11) Rash
12) oligomenorrhea, signs/symptoms of hyperandrogenism
13) Suicide ideation

PATIENT MONITORING

Patient Monitoring Parameters

1) CBC - with differential and platelet count - baseline then one (1) to two (2) weeks after each dosage increase, every 3 months for the first year of treatment, then annually and as clinically indicated
2) Comprehensive Metabolic Panel (hepatic function, serum creatinine, BUN and electrolytes) – baseline, every 3 months for the first year of treatment, then annually and as clinically indicated.
3) Pregnancy Test – baseline as appropriate, and as clinically indicated
4) Valproic acid level – 1-2 weeks after initiation and dosage change, then as clinically indicated.
5) Weight – baseline, quarterly for the first year of treatment, then annually and as clinically indicated
6) Monitor for the emergence of suicidal ideation or behavior

- Usual therapeutic trough levels for bipolar disorder is 50-125 mcg/ml for valproic acid and divalproex delayed release (Depakote®).
- For divalproex extended release (Depakote® ER) it is 85 – 125 mcg/ml (trough) for the treatment of acute mania. A lower therapeutic trough level may be needed with divalproex extended release for maintenance treatment. For extended release products, a trough level is considered to be 18 to 24 hours after the last dose.
- Therapeutic ranges for the lab used should be listed on the report.

Dosing

1) Take with food to avoid stomach upset
2) See DSHS/DADS Formulary for dosage guidelines.
3) Exceptions to maximum dosage must be justified as per medication rule.