DSH PSYCHOTROPIC MEDICATION Operational Procedures

LAMOTRIGINE PROTOCOL:

I. Indications:

A. At least 1 of the following clinical indications is present and documented in the chart prior to treatment:

1. Seizure disorder, including monotherapy in partial seizures and adjunctive therapy for partial seizures and generalized seizures, including those due to Lennox-Gastaut syndrome.

2. DSM diagnosis of bipolar or schizoaffective disorder, including maintenance therapy (if used beyond 18 months, long-term usefulness is reevaluated) and use as second step during the depressive phase (effectiveness of lamotrigine for acute treatment of mood episodes has not been established but a recognized expert guideline recommends lamotrigine as a possible second step during the depressive phase, following the initiation or optimization of other mood stabilizers). Effectiveness in treating hypomania or mania appears absent.

3. Severe persistent self-injurious behavior, with evidence that:

a) A behavioral treatment, as part of a formal treatment program, was adequately implemented and found to be ineffective, and;

b) Less toxic pharmacological interventions including other anticonvulsants and antipsychotics have been considered, and;

c) Risk of onset of new aggressive behavior has been considered.

II. Contraindications:

A. Hypersensitivity to lamotrigine or any component of the preparation.

B. History of serious rash with systemic symptoms associated with prior lamotrigine treatment or history of hemophagocytic lymphohistiocytosis during lamotrigine treatment.

III. Precautions (risk/benefit analysis supports use):

A. Pregnancy or breast feeding.

B. Hepatic impairment (dose reduction may be needed)

C. Renal function impairment (use with caution and consider lower doses).

IV. The following initial workup and follow-up evaluations should be completed:

A. There is informed consent or alternate legal authorization.

B. Skin examination to rule out rash and documentation of baseline laboratory tests that might change in the event of a rash due to lamotrigine toxicity (CBC with differential, basic metabolic panel and liver function tests). Baseline labs should be obtained within 30 days. Individual should be educated about rash risk.

C. There is an order for nursing to check by inquiry and/or inspection the individual for skin rash at least weekly until 3 months after treatment has been stable (titration completed with no more than routine dose adjustments occurring).

V. Dose initiation, titration, and discontinuation:

A. SEIZURE TREATMENT WITH CONCURRENT VALPROIC ACID PRESENT: Typical initial dose for adjunct antiepileptic treatment in adults older than 18 years taking valproic acid is 25 mg every other day for week 1 and 2 and 25 mg every day for weeks 3 and 4. After that, dose may be increased by 25 – 50 mg/day every 1 to 2 weeks to reach maintenance level. In non-urgent clinical circumstances, a titration rate of 25 – 50 mg per week may reduce adverse risk of significant rash. Usual maintenance doses range between 100 – 400 mg/day (that can be divided in 2 doses).

B. SEIZURE TREATMENT WITH CONCURRENT ENZYME-INDUCING ANTIEPILEPTICS: Typical initial dose for adjunct antiepileptic treatment in adults older than 18 years taking enzyme-inducing antiepileptic drugs (carbamazepine, phenytoin, phenobarbital and primidone) and NOT taking valproic acid is 50 mg every day for weeks 1 and 2; and 100 mg/day in divided doses for weeks 3 and 4. After that, dose may be increased by 100 mg/day every 1 to 2 weeks to reach maintenance level. Usual maintenance doses range between 300 to 500 mg/day in 2 divided doses. In nonurgent clinical circumstances, a dose titration of 25 – 50 mg per week may be better tolerated.

C. PSYCHIATRIC TREATMENT WITH CONCURRENT VALPROIC ACID: Typical initial dose for bipolar or schizoaffective treatment in adults older than 18 years taking valproic acid is 25 mg every other day for weeks 1 and 2; 25 mg daily for weeks 3 and 4; 50 mg daily for week 5; and 100 mg daily for weeks 6 and 7. In non-urgent clinical circumstances, a titration of 25 – 50 mg per week may reduce the risk of serious rash. The target dose is approximately 100 – 200 mg BID Divided dosing is important in treating seizure disorders but is less relevant to treatment of mood and psychotic disorders.

D. PSYCHIATRIC TREATMENT WITH CONCURRENT ENZYME-INDUCING ANTIEPILEPTICS: Typical initial dose for bipolar or schizoaffective treatment in adults older than 18 years taking enzyme-inducing drug and NOT taking valproic acid is 50 mg daily for weeks 1 and 2; 100 mg daily in divided doses for weeks 3 and 4; 200 mg daily in divided doses for week 5; 300 mg daily in divided doses for week 6; and 400 mg daily in divided doses for week 7. As before, a titration rate of 25 – 50 mg per week may reduce the risk of serious rash. The target dose is approximately 400 mg/day. Divided doses are less relevant to psychiatric indications.

E. PSYCHIATRIC TREATMENT WITHOUT CONCURRENT VALPROIC ACID: Typical initial dose for bipolar or schizoaffective treatment in adults older than 18 years NOT taking valproic acid or enzyme-inducing antiepileptic drugs is 25 mg daily for weeks 1 and 2; 50 mg daily for weeks 3 and 4; 100 mg daily for week 5; and 200 mg daily for weeks 6 and 7. As before, a titration rate of 25 – 50 mg per week may reduce the risk of serious rash. The target dose is approximately 100 to 200 mg BID. As before, divided dosing is important for treatment of seizure disorders, but is less relevant to treatment of mood and psychotic disorders.

F. COMPLEX CASES: Neurological consultation is obtained for more complex antiepileptic treatment (including conversion from single antiepileptic to monotherapy with lamotrigine).

G. DISCONTINUATION OF VALPROIC ACID: When discontinuing valproic acid in a patient stabilized on lamotrigine, the dose of lamotrigine may need to be increased (valproic acid inhibits lamotrigine metabolism and lamotrigine levels may decrease by approximately half.) For example, if the individual is taking lamotrigine 100 mg/day and valproic acid, after discontinuation of valproic acid, lamotrigine may need to be increased to 150 mg/day in the first week; and to 200 mg/day after that.

H. DISCONTINUATION OF ENZYME-INDUCING ANTIEPILEPTICS: When discontinuing an antiepileptic with enzymatic inducing properties, including carbamazepine, phenytoin, phenobarbital and primidone, in an individual stabilized on these antiepileptics, the dose of lamotrigine may need to be decreased (lamotrigine levels may increase in a period of a few weeks increasing the risk of toxicity). For example, if an individual is taking lamotrigine 400 mg/day and carbamazepine, after discontinuation of carbamazepine, lamotrigine is decreased to 300 mg/day in the second week; then decreased to 200 mg/day in the third week.

I. EFFECTS BY OTHER DRUGS: Lamotrigine dosage accounts for possible increase in lamotrigine metabolism when lamotrigine is added to oral contraceptives with estrogens (particularly ethinylestradiol), rifampin or oxcarbazepine. Lamotrigine dosage accounts for possible decrease in lamotrigine metabolism when these drugs (oral contraceptives with estrogens, rifampin or oxcarbazepine) are discontinued.

J. AUTO-INDUCTION: If an individual previously responding to lamotrigine loses his/her response, a blood level may be obtained to consider: a) lack of adherence, and b) the possibility of lamotrigine's induction of its own metabolism, particularly in individuals NOT taking enzyme-inducing antiepileptic drugs (e.g., after a few weeks up to 6 weeks of a stable dose, levels spontaneously decrease by one-third to one-fourth).

K. DISCONTINUATION DUE TO ADVERSE EVENT: Dose is discontinued at the first sign of rash (unless rash is clearly not drug related, with documentation). Medical consultation, CBC with differential and liver function tests are obtained.

L. TAPERED DISCONTINUATION: If discontinued due to reasons other than safety, dose is decreased by 50% per week over at least 2 weeks.

VI. Possible adverse reactions:

A. Skin rash that may evolve to Stevens-Johnson syndrome and toxic epidermal necrolysis and/or internal syndrome of hemophagocytic lymphohistiocytosis.

B. Headaches, including due to aseptic meningitis.

C. Dizziness.

D. Ataxia.

E. Somnolence.

F. Nausea.

G. Diplopia.

H. Blurred vision.

I. Rhinitis.

J. Suicidal ideation.

VII. Additional considerations for skin rash:

A. Initial work up includes skin exam to rule out any skin rash before starting lamotrigine, CBC with differential, BMP and LFTs. The laboratory tests can be used as a baseline to compare with tests drawn in the rare event of the development of a rash that is suggestive of lamotrigine toxicity. The treated individual should be educated regarding rash risk and instructed to immediately report any rash to a physician or nursing staff.

B. There is an order for nursing to check by inquiry and/or inspection the individual for skin rash at least weekly until three months after treatment has been stable.

C. Order to check for skin rash is restarted (even if lamotrigine dose has been stable) when:

1. Valproic acid dose is increased, or;

2. Enzyme-inducing drugs (carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine, rifampin and oral contraceptives with estrogens) are discontinued.

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