



## **Supplementary Material**

**Article Title:** Preventive Effects of Lamotrigine in Bipolar II Versus Bipolar I Disorder

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### **Disclaimer**

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**Supplementary eTable 1: Mean daily dose of lamotrigine, and concomitant drug for Bipolar Disorder**

| Patient background factor/category | Bipolar I<br>(n=191) | Bipolar II<br>(n=399) |
|------------------------------------|----------------------|-----------------------|
| ≤50                                | 31 (16.2)            | 51 (12.8)             |
| >50 to ≤100                        | 48 (25.1)            | 84 (21.1)             |
| >100 to ≤150                       | 15 (7.9)             | 49 (12.3)             |
| >150 to ≤200                       | 46 (24.1)            | 109 (27.3)            |
| >200 to ≤250                       | 8 (4.2)              | 18 (4.5)              |
| >250 to ≤300                       | 9 (4.7)              | 12 (3.0)              |
| >300 to ≤350                       | 1 (0.5)              | 3 (0.8)               |
| >350 to ≤400                       | 4 (2.1)              | 8 (2.0)               |
| Unknown                            | 29 (15.2)            | 65 (16.3)             |
| Min-max                            | 25.0-400.0           | 21.0-400.0            |
| Mean±SD                            | 137.6±82.1           | 142.7±78.2            |
| Median                             | 106.8                | 136.2                 |
| Mode                               | 100.0                | 200.0                 |
| Concomitant medications            |                      |                       |
| Mood stabilizers                   | 122 (63.9)           | 171 (42.9)            |
| Lithium                            | 91 (47.6)            | 105 (26.3)            |
| Valproate sodium                   | 48 (25.1)            | 66 (16.5)             |
| Carbamazepine                      | 8 (4.2)              | 12 (3.0)              |
| Typical antipsychotics             | 26 (13.6)            | 42 (10.5)             |
| Sulpiride                          | 3 (1.6)              | 22 (5.5)              |
| Levomepromazine maleate            | 9 (4.7)              | 14 (3.5)              |
| Atypical antipsychotics            | 98 (51.3)            | 126 (31.6)            |
| Olanzapine                         | 37 (19.4)            | 41 (10.3)             |
| Aripiprazole                       | 33 (17.3)            | 50 (12.5)             |
| Quetiapine                         | 29 (15.2)            | 38 (9.5)              |
| Risperidone                        | 13 (6.8)             | 4 (1.0)               |
| Antidepressants                    | 55 (28.8)            | 195 (48.9)            |
| Duloxetine hydrochloride           | 2 (1.0)              | 53 (13.3)             |
| Mirtazapine                        | 8 (4.2)              | 48 (12.0)             |
| Paroxetine hydrochloride hydrate   | 11 (5.8)             | 44 (11.0)             |
| Fluvoxamine maleate                | 8 (4.2)              | 28 (7.0)              |
| Sertraline hydrochloride           | 5 (2.6)              | 28 (7.0)              |
| Milnacipran hydrochloride          | 7 (3.7)              | 11 (2.8)              |
| Escitalopram oxalate               | 3 (1.6)              | 7 (1.8)               |
| Amoxapine                          | 6 (3.1)              | 6 (1.5)               |

<sup>a</sup>Values expressed as n (%) unless otherwise noted.

**Supplementary eTable 2: Frequency of ADRs ( $\geq 3\%$  by SOC) (Safety Analysis Set)**

|                                 | <b>Bipolar I</b><br>(n=191) | <b>Bipolar II</b><br>(n=399) |
|---------------------------------|-----------------------------|------------------------------|
| No. of patients with ADRs       | 42                          | 87                           |
| No. of ADRs                     | 54                          | 132                          |
| Incidence rate of ADRs (%)      | 22.0                        | 21.8                         |
| Type of ADRs                    | No. of patients with ADRs   |                              |
| <b>Psychiatric disorders</b>    | <b>10 (5.2)</b>             | <b>13 (3.3)</b>              |
| Aggression                      | 1 (0.5)                     | 0 (0.0)                      |
| Anger                           | 1 (0.5)                     | 3 (0.8)                      |
| Anxiety                         | 1 (0.5)                     | 1 (0.3)                      |
| Depression                      | 0 (0.0)                     | 1 (0.3)                      |
| Dissociative disorder           | 0 (0.0)                     | 1 (0.3)                      |
| Hypomania                       | 1 (0.5)                     | 1 (0.3)                      |
| Insomnia                        | 1 (0.5)                     | 2 (0.5)                      |
| Intentional self-injury         | 0 (0.0)                     | 1 (0.3)                      |
| Irritability                    | 4 (2.1)                     | 1 (0.3)                      |
| Mania                           | 0 (0.0)                     | 2 (0.5)                      |
| Panic attack                    | 0 (0.0)                     | 1 (0.3)                      |
| Suicidal ideation               | 2 (1.1)                     | 1 (0.3)                      |
| Depressive symptom              | 0 (0.0)                     | 1 (0.3)                      |
| Somatic hallucination           | 0 (0.0)                     | 1 (0.3)                      |
| <b>Nervous system disorders</b> | <b>4 (2.1)</b>              | <b>17 (4.3)</b>              |
| Akathisia                       | 1 (0.5)                     | 0 (0.0)                      |
| Dizziness                       | 0 (0.0)                     | 5 (1.3)                      |
| Dizziness postural              | 0 (0.0)                     | 1 (0.3)                      |
| Headache                        | 1 (0.5)                     | 3 (0.8)                      |
| Hypersomnia                     | 0 (0.0)                     | 2 (0.5)                      |
| Hypoaesthesia                   | 0 (0.0)                     | 1 (0.3)                      |
| Migraine                        | 0 (0.0)                     | 1 (0.3)                      |
| Neuralgia                       | 0 (0.0)                     | 1 (0.3)                      |
| Paraesthesia                    | 0 (0.0)                     | 1 (0.3)                      |
| Sedation                        | 0 (0.0)                     | 1 (0.3)                      |
| Somnolence                      | 1 (0.5)                     | 5 (1.3)                      |
| Tremor                          | 1 (0.5)                     | 2 (0.5)                      |

<sup>a</sup>Values expressed as n (%) unless otherwise noted.

| Skin and subcutaneous tissue disorders                   | 22 (11.5) | 46 (11.5) |
|--|-----------|-----------|
| Chloasma   | 0 (0.0)   | 1 (0.3)   |
| Cold sweat   | 0 (0.0)   | 1 (0.3)   |
| Drug eruption  | 2 (1.1)   | 3 (0.8)   |
| Eczema   | 0 (0.0)   | 1 (0.3)   |
| Erythema   | 1 (0.5)   | 1 (0.3)   |
| Erythema multiforme                                      | 0 (0.0)   | 1 (0.3)   |
| Pruritus   | 3 (1.6)   | 4 (1.0)   |
| Purpura  | 1 (0.5)   | 0 (0.0)   |
| Rash   | 17 (8.9)  | 34 (8.5)  |
| Skin erosion   | 0 (0.0)   | 1 (0.3)   |
| Skin exfoliation   | 0 (0.0)   | 1 (0.3)   |
| Stevens-Johnson Syndrome                                 | 0 (0.0)   | 1 (0.3)   |
| Swelling face  | 0 (0.0)   | 1 (0.3)   |
| Drug reaction with eosinophilia<br>and systemic symptoms | 0 (0.0)   | 1 (0.3)   |

<sup>a</sup>Values expressed as n (%) unless otherwise noted.

(MedDRA/J version 18.1)

MedDRA=Medical Dictionary for Regulatory Activities. SOC=System Organ Class.