**Appendix Table D49. Randomized controlled clinical trials that examined off label antidepressants for migraine prevention in adults**

| **Examined Drug** | **Reference, Total Sample Size**  **Number of Analyzed % Women** | **Definition of Migraine % of Patients without Aura** | **Baseline Monthly Migraine Frequency** | **Eligible Age Mean Age of Subjects** | **Duration of Migraine Prior Treatment** |
| --- | --- | --- | --- | --- | --- |
| Amitriptyline | Couch, 1979103 Sample 116 Analyzed 100 % women 84 | Modified 1962 Ad Hoc National Institutes of Health Committee  NR | NR | 15-60 NR | NR NR |
| Amitriptyline | Gomersall, 1973104 Sample 26 Analyzed 20 % women 75 | Ad hoc committee NR | NR | NR 21-30 years old:1  31-40 years old:4  41-50 years old:11  51-60 years old:2  61-70 years old:2 | 1-10 yr:5  11-20 yr:5  21-30 yr:6  31-40:2  41-50:2 NR |
| Amitriptyline | Mathew, 1981105 Sample 715 Analyzed 554 % women 94.5 | NR NR | NR | NR (age ranged from 19-57) Mean: 38 | NR NR |
| Amitriptyline | Bank, 1994106 Sample 64 Analyzed 51 % women 73.4 | International Headache Society 81.25 | Headache Unit Index active group = 0.16, Headache Unit Index control group = 0.24 | NR 34 | At least 12 months NR |
| Amitriptyline | Oguzhanoglu, 1999107 Sample 17 Analyzed 15 % women 80 | International Headache Society NR | NR | NR 31 | NR NR |
| Amitriptyline | Krymchantowski, 2002108 Sample 39 Analyzed 27 % women 66.7 | NR NR | NR | NR 36.4 | NR 100% overusing symptomatic medications |
| Amitriptyline | Bulut, 2004109 Sample 76 Analyzed 52 % women 84.6 | International Headache Society 77 | Yes | 16-50 31.9 | NR NR |
| Amitriptyline | Lampl, 2009110 Sample 132 Analyzed 132 % women 73 | International Headache Society 76 | Yes | 18-60 32 | 16 years NR |
| Amitriptyline | Couch, 2011111 Sample 391 Analyzed 317 % women 81 | Modified 1962 Ad Hoc National Institutes of Health Committee NR | NR | 18-70 34.9 | NR NR |
| Amitriptyline | Couch, 1976112 Sample 114 Analyzed 73 % women 84.9 | Not specified  NR | NR | NR NR | NR NR |
| Amitriptyline | Rafieian-Kopaei, 200564 Sample 105 Analyzed 95 % women NR | International Headache Society NR | Mean attack frequency: 4.02 (per month) | Adolescent & Adults NR | >1 (from inclusion criteria) NR |
| Amitriptyline | Rafieian-Kopaei, 200564 Sample 105 Analyzed 95 % women NR | International Headache Society NR | 4.02 migraine attacks per month, 25.12 h average duration | 15-45 NR | At least 12 months NR |
| Femoxetine | Orholm, 1986113 Sample 65 Analyzed 53 % women 84.9 | Paroxysmal headache associated with discomfort, possibly with inability to work, and at least one of the following symptoms: nausea, vomiting, visual disturbances and paresthesia NR | Yes | NR ≥50 years old = 12  30-50 years old = 38  <30 years old = 3 | NR NR |
| Femoxetine | Zeeberg, 1981114 Sample 59 Analyzed 45 % women 86.7 | Paroxysmal headache associated with discomfort, possibly with inability to work, and at least one of the following symptoms: nausea, vomiting, visual disturbances and paresthesia NR | Yes | NR ≥50 years old = 9  30-50 years old = 29  <30 years old = 7 | NR NR |
| Femoxetine | Kangasniemi, 198377 Sample 29 Analyzed 24 % women 86.2 | NR NR | Yes | NR 37 | NR NR |
| Femoxetine | Orholm, 1985115 Sample 59 Analyzed 47 % women NR | NR NR | NR | NR NR | NR NR |
| Fluoxetine | Adly, 1992116 Sample 32 Analyzed 18 % women 83.3 | the Ad hoc Committee on Classification of headache NR | Headache score 33.5 | NR 37.5 | NR 2 amitriptyline or nadolol, 1 imipramine |
| Fluoxetine | Saper, 1994117 Sample 111 Analyzed 111 % women 87.4 | International Headache Society NR | NR | 18-60 36.6 | At least 24 months NR |
| Fluoxetine | Steiner, 1998118 Sample 53 Analyzed 49 % women 75.5 | NR 54.8 | Yes | 18-45 40.6 | NR NR |
| Fluoxetine | d’Amato, 1999119 Sample 52 Analyzed 52 % women 63.5 | International Headache Society 1988 criteria 100 | NR | 18-65 37.6 | At least 6 months NR |
| Mianserin | Monro, 1985120 Sample 38 Analyzed 34 % women NR | NR NR | NR | 18-65 NR | NR NR |
| Tonabersat\* | Goadsby, 2009121 Sample 124 Analyzed 124 % women 92.3 | International Headache Society NR | Yes | 18-55 36 | NR NR |
| Venlafaxine | Ozyalcin, 2005122 Sample 60 Analyzed 49 % women 90 | International Headache Society 100 | Yes | 18-70 placebo 38.16; V75 34.25; V150 37.19 | NR NR |
| Venlafaxine | Tarlaci, 2009123 Sample 105 Analyzed 93 % women 81.7 | International Headache Society 93.5 | Yes | NR 31.4 | NR NR |

NR = not reported; \*Cortical spreading depression inhibitor