**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 AgeMean Age of Subjects** | **Duration of MigrainePrior Treatment** |
| --- | --- | --- | --- | --- | --- |
| Amitriptyline | Couch, 1979103Sample 116Analyzed 100% women 84 | Modified 1962 Ad Hoc National Institutes of Health Committee NR | NR | 15-60NR | NRNR |
| Amitriptyline | Gomersall, 1973104Sample 26Analyzed 20% women 75 | Ad hoc committeeNR | NR | NR21-30 years old:131-40 years old:441-50 years old:1151-60 years old:261-70 years old:2 | 1-10 yr:511-20 yr:521-30 yr:631-40:241-50:2NR |
| Amitriptyline | Mathew, 1981105Sample 715Analyzed 554% women 94.5 | NRNR | NR | NR (age ranged from 19-57)Mean: 38 | NRNR |
| Amitriptyline | Bank, 1994106Sample 64Analyzed 51% women 73.4 | International Headache Society81.25 | Headache Unit Index active group = 0.16, Headache Unit Index control group = 0.24 | NR34 | At least 12 monthsNR |
| Amitriptyline | Oguzhanoglu, 1999107Sample 17Analyzed 15% women 80 | International Headache SocietyNR | NR | NR31 | NRNR |
| Amitriptyline | Krymchantowski, 2002108Sample 39Analyzed 27% women 66.7 | NRNR | NR | NR36.4 | NR100% overusing symptomatic medications |
| Amitriptyline | Bulut, 2004109Sample 76Analyzed 52% women 84.6 | International Headache Society77 | Yes | 16-5031.9 | NRNR |
| Amitriptyline | Lampl, 2009110Sample 132Analyzed 132% women 73 | International Headache Society76 | Yes | 18-6032 | 16 yearsNR |
| Amitriptyline | Couch, 2011111Sample 391Analyzed 317% women 81 | Modified 1962 Ad Hoc National Institutes of Health Committee NR | NR | 18-7034.9 | NRNR |
| Amitriptyline | Couch, 1976112Sample 114Analyzed 73% women 84.9 | Not specifiedNR | NR | NRNR | NRNR |
| Amitriptyline | Rafieian-Kopaei, 200564Sample 105Analyzed 95% women NR | International Headache SocietyNR | Mean attack frequency: 4.02 (per month) | Adolescent & AdultsNR | >1 (from inclusion criteria)NR |
| Amitriptyline | Rafieian-Kopaei, 200564Sample 105Analyzed 95% women NR | International Headache SocietyNR | 4.02 migraine attacks per month, 25.12 h average duration | 15-45NR | At least 12 monthsNR |
| Femoxetine | Orholm, 1986113Sample 65Analyzed 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 paresthesiaNR | Yes | NR≥50 years old = 12 30-50 years old = 38<30 years old = 3 | NRNR |
| Femoxetine | Zeeberg, 1981114Sample 59Analyzed 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 paresthesiaNR | Yes | NR≥50 years old = 930-50 years old = 29<30 years old = 7 | NRNR |
| Femoxetine | Kangasniemi, 198377Sample 29Analyzed 24% women 86.2 | NRNR | Yes | NR37 | NRNR |
| Femoxetine | Orholm, 1985115Sample 59Analyzed 47% women NR | NRNR | NR | NRNR | NRNR |
| Fluoxetine | Adly, 1992116Sample 32Analyzed 18% women 83.3 | the Ad hoc Committee on Classification of headacheNR | Headache score 33.5 | NR37.5 | NR2 amitriptyline or nadolol, 1 imipramine |
| Fluoxetine | Saper, 1994117Sample 111Analyzed 111% women 87.4 | International Headache SocietyNR | NR | 18-6036.6 | At least 24 monthsNR |
| Fluoxetine | Steiner, 1998118Sample 53Analyzed 49% women 75.5 | NR54.8 | Yes | 18-4540.6 | NRNR |
| Fluoxetine | d’Amato, 1999119Sample 52Analyzed 52% women 63.5 | International Headache Society 1988 criteria100 | NR | 18-6537.6 | At least 6 monthsNR |
| Mianserin | Monro, 1985120Sample 38Analyzed 34% women NR | NRNR | NR | 18-65NR | NRNR |
| Tonabersat\* | Goadsby, 2009121Sample 124Analyzed 124% women 92.3 | International Headache SocietyNR | Yes | 18-5536 | NRNR |
| Venlafaxine | Ozyalcin, 2005122Sample 60Analyzed 49% women 90 | International Headache Society100 | Yes | 18-70placebo 38.16; V75 34.25; V150 37.19 | NRNR |
| Venlafaxine | Tarlaci, 2009123Sample 105Analyzed 93% women 81.7 | International Headache Society93.5 | Yes | NR31.4 | NRNR |

NR = not reported; \*Cortical spreading depression inhibitor