**Appendix Table D 135. Treatment discontinuation due to adverse effects with off label migraine preventive drugs vs. placebo, pooled with random effects model results from randomized controlled clinical trials**

| **Active Drug** | **Reference** | **Events/**  **Randomized with Drug** | **Events/**  **Randomized with Placebo** | **Relative Risk**  **(95% CI)** | **Relative Risk**  **Weight**  **(Inverse Variance)** | **Absolute Risk Difference**  **(95% CI)** | **Absolute Risk Difference**  **Weight**  **(Inverse Variance)** | **Arcsine Transformed Risk Difference**  **(95% CI)** | **Arcsine Transformed Risk Difference**  **Weight** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Amitriptyline | Couch, 2011111 | 23/194 | 13/197 | 1.8  (0.9 to 3.4) | 85.8 | 0.05  (-0.01 to 0.11) | 70.37 | 0.09  (-0.01 to 0.19) | 77.17 |
| Amitriptyline | Couch, 1979103 | 5/55 | 2/61 | 2.8  (0.6 to 13.7) | 14.2 | 0.06  (-0.03 to 0.15) | 29.63 | 0.12  (-0.06 to 0.31) | 22.83 |
| Amitriptyline | Pooled | 28/249 | 15/258 | 1.9  (1.0 to 3.5) | 100 | 0.05  (0.01 to 0.10) | 100 | 0.10  (0.01 to 0.19) | 100 |
| Clonidine | Boisen, 1978146 | 2/71 | 0/71 | 5.0  (0.2 to 102.3) | 38.41 | 0.03  (-0.02 to 0.08) | 36.3 | 0.17  (0.00 to 0.33) | 44.23 |
| Clonidine | Adam. 1978148 | 2/96 | 1/96 | 2.0  (0.2 to 21.7) | 61.59 | 0.01  (-0.03 to 0.05) | 63.7 | 0.04  (-0.10 to 0.18) | 55.77 |
| Clonidine | Pooled | 4/167 | 1/167 | 2.8  (0.4 to 18.5) | 100 | 0.02  (-0.01 to 0.05) | 100 | 0.10  (-0.02 to 0.22) | 100 |
| Femoxetine | Orholm, 1986113 | 4/31 | 2/34 | 2.2  (0.4 to 11.2) | 52.65 | 0.07  (-0.07 to 0.21) | 50.09 | 0.12  (-0.12 to 0.37) | 52.37 |
| Femoxetine | Orholm, 1985115 | 3/29 | 2/30 | 1.6  (0.3 to 8.6) | 47.35 | 0.04  (-0.11 to 0.18) | 49.91 | 0.07  (-0.19 to 0.32) | 47.63 |
| Femoxetine | Pooled | 7/60 | 4/64 | 1.9  (0.6 to 6.1) | 100 | 0.05  (-0.05 to 0.15) | 100 | 0.10  (-0.08 to 0.27) | 100 |
| Gabapentin | NCT00742209192 | 13/62 | 2/20 | 2.1  (0.5 to 8.5) | 31.39 | 0.11  (-0.06 to 0.28) | 21.89 | 0.18  (-0.07 to 0.43) | 26.43 |
| Gabapentin | Mathew, 200181 | 16/98 | 4/45 | 1.8  (0.7 to 5.2) | 57.25 | 0.07  (-0.04 to 0.19) | 49.16 | 0.11  (-0.06 to 0.29) | 53.91 |
| Gabapentin | Wessely, 198784 | 2/23 | 1/22 | 1.9  (0.2 to 19.6) | 11.36 | 0.04  (-0.10 to 0.19) | 28.95 | 0.08  (-0.21 to 0.38) | 19.66 |
| Gabapentin | Pooled | 31/183 | 7/87 | 1.9  (0.9 to 4.2) | 100 | 0.07  (-0.01 to 0.15) | 100 | 0.13  (0.00 to 0.26) | 100 |
| Lamotrigine | Steiner, 199787 | 7/18 | 3/40 | 5.2  (1.5 to 17.8) | 54.39 | 0.31  (0.07 to 0.55) | 43.22 | 0.40  (0.12 to 0.67) | 46.23 |
| Lamotrigine | Gupta, 200744 | 3/60 | 3/60 | 1.0  (0.2 to 4.8) | 45.61 | 0.00  (-0.08 to 0.08) | 56.78 | 0.00  (-0.18 to 0.18) | 53.77 |
| Lamotrigine | Pooled | 10/78 | 6/100 | 2.4  (0.5 to 12.2) | 100 | 0.14  (-0.17 to 0.44) | 100 | 0.18  (-0.20 to 0.57) | 100 |
| Magnesium | Pfaffenrath, 1996194 | 3/35 | 1/34 | 2.9  (0.3 to 26.7) | 63.69 | 0.06  (-0.05 to 0.17) | 39.24 | 0.13  (-0.11 to 0.36) | 46.09 |
| Magnesium | Peikert, 1996195 | 3/43 | 0/38 | 6.2  (0.3 to 116.4) | 36.31 | 0.07  (-0.02 to 0.16) | 60.76 | 0.27  (0.05 to 0.49) | 53.91 |
| Magnesium | Pooled | 6/78 | 1/72 | 3.8  (0.7 to 22.4) | 100 | 0.06  (0.00 to 0.13) | 100 | 0.20  (0.04 to 0.36) | 100 |
| Naproxen sodium | Welch, 1985237, 238 | 2/46 | 1/46 | 2.0  (0.2 to 21.3) | 64.25 | 0.02  (-0.05 to 0.09) | 45.78 | 0.06  (-0.14 to 0.27) | 53.49 |
| Naproxen sodium | Ziegler, 1985239 | 1/40 | 0/40 | 3.  0(0.1 to 71.5) | 35.75 | 0.03  (-0.04 to 0.09) | 54.22 | 0.16  (-0.06 to 0.38) | 46.51 |
| Naproxen sodium | Pooled | 3/86 | 1/86 | 2.3  (0.3 to 15.4) | 100 | 0.02  (-0.03 to 0.07) | 100 | 0.11  (-0.04 to 0.26) | 100 |
| Nimodipine | Havanka-Kanniainen, 1985132 | 0/33 | 1/33 | 0.3  (0.0 to 7.9) | 17.11 | -0.03  (-0.11 to 0.05) | 66 | -0.18  (-0.42 to 0.07) | 42.61 |
| Nimodipine | MINES, 1989133 | 3/43 | 4/46 | 0.8  (0.2 to 3.4) | 82.89 | -0.02  (-0.13 to 0.09) | 34 | -0.03  (-0.24 to 0.18) | 57.39 |
| Nimodipine | Pooled | 3/76 | 5/79 | 0.7  (0.2 to 2.6) | 100 | -0.03  (-0.09 to 0.04) | 100 | -0.09  (-0.25 to 0.07) | 100 |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Active Drug** | **Degree of Freedom** | **P Value**  **Relative Risk** | **I Squared**  **Relative Risk** | **P Value**  **Absolute Risk**  **Difference** | **I Squared**  **Absolute Risk Difference** | **P Value, Arcsine Transformed Risk Difference** | **I Squared, Arcsine Transformed Risk Difference** |
| Amitriptyline | 1 | 0.62 | 0.00% | 0.01 | 60.30% | 0.02 | 58.40% |
| Clonidine | 1 | 0.64 | 0.00% | 0.22 | 32.30% | 0.24 | 26.90% |
| Femoxetine | 1 | 0.77 | 0.00% | 0.31 | 4.60% | 0.31 | 2.90% |
| Gabapentin | 2 | 0.99 | 0.00% | 0.86 | 0.00% | 0.67 | 0.00% |
| Lamotrigine | 1 | 0.11 | 62.00% | 0.92 | 0.00% | 0.76 | 0.00% |
| Magnesium | 1 | 0.69 | 0.00% | 0.55 | 0.00% | 0.26 | 22.90% |
| Naproxen | 1 | 0.84 | 0.00% | 0.75 | 0.00% | 0.76 | 0.00% |
| Nimodipine | 1 | 0.62 | 0.00% | 0.83 | 0.00% | 0.87 | 0.00% |