Table G-12. Withdrawals and discontinuations in studies comparing older versus newer antiepileptic drugs

| Study, Year | Group | N | Withdrawal for any Reason (n) | Withdrawal Due to Ineffective Treatment (n) | Time to Withdrawal Due to Ineffective Treatment | Withdrawal Due to Adverse Drug Events (n) | Adverse Drug Events Contributing to Withdrawals  n (%) |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Reinikainen, 1987 | Carbamazepine | 18 | 6\* | - | - | - | Increased seizures: 2 (6%)  Poor compliance: 2 (6%) |
| Oxcarbazepine | 16 |  | - | - | - |  |
| Danner, 1988 | Carbamazepine | 13 | - | - | - | 3 | Allergic Rash: 3 (23%) |
| Oxcarbazepine | 12 | - | - | - | 1 | Allergic Rash: 1(8.33%) |
| Dam, 1989 | Carbamazepine | 98 | - | 2 | - | 25 | Allergy: 16 (16%)  Visual Disturbances: 1 (1%)  Headache: 1 (1%)  Tiredness/fatigue: 3 (3%)  Nausea: 1 (1%)  Diarrhoea: 2 (2%)  Loss of hair: 2 (2%)  Leukopenia: 1 (1%)  Liver parameters increased: 1 (1%) |
| Oxcarbazepine | 92 | - | 2 | - | 13 | Allergy: 9 (10%)  Dizziness/vertigo: 2 (2%)  Tiredness/fatigue: 1 (1%)  Physical lability: 1 (1%) |
| Sachdeo, 1992 | Valproic Acid | 22 | 1 | - | - | - | - |
| Felbamate | 22 | 1 | - | - | - | - |

| Table G-12. Withdrawals and discontinuations in studies comparing older versus newer antiepileptic drugs (continued) | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study, Year | Group | N | Withdrawal for any Reason (n) | Withdrawal Due to Ineffective Treatment (n) | Time to Withdrawal Due to Ineffective Treatment | Withdrawal Due to Adverse Drug Events (n) | Adverse Drug Events Contributing to Withdrawals  n (%) |
| Brodie, 1995 | Carbamazepine | 129 | 63 | 3 | - | 27 | Rash: 22 (17% )  Headache: 3 (2%)  Asthenia: 6 (5%)  Dizziness: 3 (2%)  Vomiting: 1 (1% )  Malaise: 5 (4%)  Nausea: 3 (2%)  Ataxia: 5 (4%)  Sleepiness: 5 (4%) |
| Lamotrigine | 131 | 46 | 3 | - | 15 | Rash: 15 (12%)  Headache: 5 (4%)  Asthenia: 5 (4%)  Dizziness: 3 (2%)  Vomiting: 3 (2% )  Malaise: 1 (1%)  Nausea: 1 (1%)  Ataxia: 0  Sleepiness: 0 |
| Kalviainen, 1995 | Carbamazepine | 50 | 20 | 3 | - | 12 | Rash: 7 (14%)  Hepatotoxicity: 3 (6%)  Elevation of blood glucose: 1 (2%)  Confusion and personality change: 1 (2%) |
| Vigabatrin | 50 | 20 | 13 | - | 0 | Rash: 0  Hepatotoxicity: 0  Elevation of blood glucose: 0  Confusion and personality change: 0 |
| Reunanen, 1996 | Carbamazepine | 117 | 29 | 0 | - | 12 | - |
| Lamotrigine 100 mg | 115 | 23 | 1 | - | 5 | - |
| Lamotrigine 200 mg | 111 | 10 | 0 | - | 5 | - |
| Tanganelli, 1996 | Carbamazepine | 25 | - | - | - | 1 | - |
| Vigabratin | 26 | - | - | - | 0 | - |
| Bill, 1997 | Phenytoin | 144 | 61 | 1 | - | 16 | Rash: 10 (7%)  Hirsutism/Gum Hyperplasia: 5 (3.5%)  Other: 1 (0.7%) |
| Oxcarbazepine | 143 | 56 | 1 | - | 5 | Rash: 1 (0.7%)  Hirsutimsm/Gum Hyperplasia: 0  Other: 4 (2.8%)  (1 patient in the other group withdrew due to suicidal ideation) |
| Christie, 1997 | Sodium Valproate | 121 | 41 | 6 | - | 10 | Allergic Reaction: 0  Hair loss: 4 (3.31%)  Pregnancy: 2 (1.65%)  Nausea: 2 (1.65%)  Drowsiness: 0  Other: 2 (1.65%) |
| Oxcarbazepine | 128 | 52 | 6 | - | 15 | Allergic Reaction with skin symptoms: 6 (4.69%)  Hair Loss: 0  Pregnancy: 1 (0.8%)  Drowsiness: 2 (1.56%)  Other: 2 (1.56%) |
| Guerreiro, 1997 | Pheyntion | 96 | 34 | 3 | - | 14 | Hypertrichosis and/or gingival hyperplasia: 10 (10%) (1 patient also had ataxia)  Rash: 4 (4%) (1 patient also had fever, ataxia, dizziness and vomiting) |
| Oxcarbazepine | 97 | 24 | 4 | - | 2 | Rash: 2 (2%) |
| Chadwick, 1998 | Carbamazepine | 74 | 47 | - | - | 18 | - |
| Gabapentin  300 mg | 72 | 54 | - | - | 0 | - |
| Gabapentin  900 mg | 72 | 44 | - | - | 3 | - |
| Gabapentin  1800 mg | 74 | 46 | - | - | 10 | - |
| Brodie, 1999a | Carbamazepine | 48 | 28 | 0 | - | 20 | Rash: 9 (19%)  Somnolence: 3 (6%)  Asthenia: 3 (6%)  Nausea: 1 (2%)  Incoordination: 1 (2%) |
| Lamotrigine | 102 | 30 | 0 | - | 18 | Rash: 3 (3%)  Somnolence: 2 (2%)  Asthenia: 1 (1%)  Nausea: 3 (3%)  Incooridination: 3 (3%) |
| Brodie, 1999b | Valproate | 107 | 32 | 19 | - | 12 | - |
| Vigabatrin | 108 | 22 | 11 | - | 12 | - |
| Chadwick, 1999† | Carbamazepine | 229 | 97 | 9 |  | 61 | - |
| Vigabatrin | 228 | 98 | 23 | No significant treatment differences between vigabatrin and carbamazepine groups  Hazard ratio: 0.83  95% CI: 0.57-1.20 | 43 | - |
| Gobbi, 1999 | Carbamazepine | 40 | 0 | 0 | - | 0 | 0 |
| Vigabatrin | 37 | 9 | 8 | - | 0 | 0 |
| Steiner, 1999 | Phenytoin | 95 | 50 | 2 | - | 18 | - |
| Lamotrigine | 86 | 45 | 1 | - | 13 | - |
| Aldenkamp,  2000 | Valproic Acid | 30 | 4 | 1 | - | - | - |
| Topiramate | 29 | 8 | 0 | - | - | - |
| Lamotirgine | 146 | 18 | - | - | 35 | - |
| Biton, 2001 | Valproate | 68 | 30 | - | - | 9 | - |
| Lamotrigine | 65 | 19 | - | - | 6 | - |
| Kwan, 2001 | Carbamazepine | 212 | 124 | 53 | - | 57 | - |
| Sodium Valproate | 101 | 43 | 26 | - | 13 | - |
| Lamotrigine | 78 | 30 | 20 | - | 8 | - |
| Nieto-Barrera, 2001 | Carbamazepine | 201 | 46 | - | - | 27 | - |
| Lamotrigine | 417 | 79 | - | - | 38 | - |
| Biton, 2003 | Valproate | 20 | 6 | - | - | 1 | Aspiration of fluids: 1(5%) |
| Lamotrigine | 18 | 3 | - | - | 1 | Multiple side effects leading to withdrawal for 1 patient including mental confusion insomnia somnolence increased appetite dizziness ataxia nystagmus resting tremor and intention tremor  1 (5.55%) |
| Meador, 2003 | Valproate | 29 | 4 | - | - | 2 | - |
| Topiramate | 34 | 7 | - | - | 6 | - |
| Privitera, 2003 | Carbamazepine | 126 | 56 | 10 | - | 32 | - |
| Valproic Acid | 78 | 43 | 9 | - | 18 | - |
| Topiramate  100 mg | 210 | 91 | 23 | - | 40 | - |
| Topiramate 200 mg | 199 | 95 | 18 | - | 55 | - |
| Clemens, 2004 | Carbamazepine | 20 | - | - | - | - | - |
| Oxcarbazepine | 20 | - | - | - | 1 | Rash: 1 (5%) |
| Coppola, 2004 | Valproic Acid | 19 | 3 | 3 | - | 0 | 0 |
| Lamotrigine | 19 | 6 | 6 | - | 0 | 0 |
| Fakhoury, 2004 | Carbamazepine | 46 | 7 | - | - | 12 | - |
| Lamotrigine | 98 | 19 | - | - | 14 | - |
| Valproic Acid | 53 | 16 | - | - | 11 | - |
| Lamotrigine | 105 | 28 | - | - | 14 | - |
| Wheless, 2004 | Carbamazepine | 23 | 55‡ | 16§ | - | 1 | - |
| Valproic Acid | 19 |  |  | - | 6 | - |
| Topiramate 100 mg | 38 |  |  | - | 4 | - |
| Topiramate 200 mg | 39 |  |  | - | 7 | - |
| Rowan, 2005 | Carbamazepine | 197 | 127 | 5 | - | 61 | - |
| Gabapentin | 194 | 99 | 8 | - | 42 | - |
| Lamotrigine | 199 | 88 | 11 | - | 24 | - |
| Sobaniec, 2005 | Carbamazepine | 28 | 0 | - | - | - | - |
| Vigabratin | 26 | 4 | - | - | - | - |
| Steinhoff, 2005 | Carbamazepine | 88 | 29 | 0 | - | 17 | - |
| Lamotrigine | 88 | 24 | 1 | - | 7 | - |
| Valproate | 30 | 4 | 0 | - | 1 | - |
| Lamotrigine | 33 | 5 | 2 | - | 2 | - |
| Brodie, 2007 | Carbamazepine-Controlled Release | 291 | 97 | 13 | - | 56 | Vertigo: 2 (0.7%)  Nausea: 3 (1.0%)  Asthenia: 3 (1.0%)  Fatigue: 4 (1.4%)  Ataxia: 3 (1.0)  Dizziness: 3 (1.0%)  Somnolence: 2 (0.7%)  Aggression: 3 (1.0%)  Anxiety: 1 (0.3%)  Depression: 2 (0.7%)  Rash: 9 (3.1%) |
| Levetiracetam | 285 | 95 | 31 | - | 41 | Vertigo: 6 (2.1%)  Nausea: 0  Asthenia: 0  Fatigue: 5 (1.8%)  Ataxia: 0  Dizziness: 2 (0.7%)  Somnolence: 6 (2.1%)  Aggression: 0  Anxiety: 3 (1.1%)  Depression: 5 (1.8%)  Rash: 4 (1.4%) |
| Kang, 2007 | Carbamazepine | 54 | 11 | - | - | 5 | - |
| Topiramate | 58 | 13 | - | - | 6 | - |
| Kim, 2007 | Carbamazepine | 10 | 0 | 0 | - | 0 | - |
| Valproic Acid | 15 | 0 | 0 | - | 0 | - |
| Lamotrigine | 8 | 0 | 0 | - | 0 | - |
| Levisohn, 2007 | Valproic Acid | 9 | 5 | 0 | - | 1 | - |
| Topiramate | 19 | 7 | 2 | - | 2 | - |
| Marson 2007  SANAD Arm A | Carbamazepine | 378 | 227 | 43 | - | 102 | - |
| Gabapentin | 376 | 249 | 99 | - | 57 | - |
| Lamotrigine | 378 | 197 | 60 | - | 60 | - |
| Oxcarbazepine | 210 | 117 | 24 | - | 49 | - |
| Topirimate | 374 | 241 | 55 | - | 101 | - |
| Marson 2007  SANAD Arm B | Valproic Acid | 238 | 141 | 21 | - | 35 | - |
| Lamotrigine | 237 | 128 | 53 | - | 25 | - |
| Topirimate | 238 | 154 | 28 | - | 57 | - |
| Saetre, 2007 | Carbamazepine-Sustained Release | 91 | 30 | - | - | 23 | - |
| Lamotrigine | 93 | 25 | - | - | 13 | - |
| Stephen, 2007 | Valproate | 111 | 55 | 16 | - | 26 | - |
| Lamotrigine | 114 | 43 | 11 | - | 15 | - |
| Morrell, 2008 | Valproate | 225 | 55 | 1 | - | 9 | - |
| Lamotrigine | 222 | 52 | 2 | - | 9 | - |
| Perry, 2008 | Carbamazepine | 20 | 4 | - | - | 1 | Increased irritability: 1 (5%) |
| Levetiracetam | 66 | 22 | 2 | - | 8 | Behaviour changes : 5 (63%)  Irritability or mood change: 1 (12%) Increased seizure frequency  Rash: 1(12%)  Undetermined: 1(12%) |
| Kim, 2009 | Carbamazepine | 105 | 89 | 24 | - | 7 | - |
| Topiramate | 41 | 31 | 5 | - | 1 | - |
| Kwan, 2009 | Valproic Acid | 44 | 16 | 1 | - | 5 | - |
| Lamotrigine | 37 | 9 | 0 | - | 5 | - |
| Ma, 2009 | Carbamazepine | 120 | - | 21 | - | 20 | - |
| Valproic Acid | 234 | - | 40 | - | 10 | - |
| Topirimate | 143 | - | 25 | - | 17 | - |
| Glauser, 2010  Glauser, 2010 (continued) | Ethosuximide | 154 | 20 | - | - | 37 | Nervous system, behavioural or psychological effects: 12 (32%)  Digestive disorders: 9 (24%)  Rash: 6 (16%)  Fatigue: 3 (8%)  Headache: 3 (8%)  BMI increase that met exit criterion: 0  Laboratory abnormalities: 1 (3%)  Other: 4 (11%) |
| Valproic Acid | 146 | 15 | - | - | 25 | Nervous system, behavioural or psychological effects: 20 (57%)  Digestive disorders: 6 (17%)  Rash: 2 (6%)  Fatigue: 5 (14%)  Headache: 2 (6%)  BMI increase that met exit criterion: 4 (11%)  Laboratory abnormalities: 2 (6%)  Other: 5 (14%) |
| Lamotrigine | 146 | 18 | - | - | 35 | Nervous system, behavioural or psychological effects: 9 (36%)  Digestive disorders: 3 (12%)  Rash: 5 (20%)  Fatigue: 2 (8%)  Headache: 2 (8%)  BMI increase that met exit criterion: 1 (4%)  Laboratory abnormalities: 2 (8%)  Other: 4 (16%) |
| Ramsay, 2010 | Phenytoin |  | 17  N=128 | - | - | 17  N=127 | Cognitive adverse events: 2 (1.5%) |
| Topiramate |  | 27  N=133 | - | - | 9  N=132 | Skin Rash: 8 (6.3%) |

- = not reported; n = number of patients with event; N = sample size; SANAD Arm A = Standard and New Antiepileptic Drugs Trial Arm A; SANAD Arm B = Standard and New Antiepileptic Drugs Trial Arm B  
\*6 patients withdrew for any reason from the total population †Carbamazepine group is referent ‡55 patients withdrew for any reason from the total population  
§16 patients withdrew from the total population due to lack of efficacy