Table I-1. Evaluation of applicability for individual studies for innovator versus generic antiepileptic drug evaluation

| Study, Year | Effectiveness Study Designation  and Composite Score | Effectiveness Study Criteria Met | Applicability Limitation Category | Specific Factors Limiting Applicability |
| --- | --- | --- | --- | --- |
| Zachry, 2009  N=1664 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration with clinically relevant treatments  Adequate sample size | Population, Outcomes | In this study, patients were switched from one version of the medication to another “A” rated version. This could be from innovator to generic, generic to generic, or generic to innovator. As such it is not a true comparison of innovator to generic switching.  ADRs not reported |
| Rascati, 2009  N=3964 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration with clinically relevant treatments  Adequate sample size | Population, Outcomes | In this study, patients were switched from one version of the medication to another “A” rated version. This could be from innovator to generic, generic to generic, or generic to innovator. As such it is not a true comparison of innovator to generic switching.  ADRs not reported |
| Devine, 2010  N=11796 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration with clinically relevant treatments  Adequate sample size | Population, Outcomes | In this study, patients were switched from one version of the medication to another “A” rated version. This could be from innovator to generic, generic to generic, or generic to innovator. As such it is not a true comparison of innovator to generic switching.  ADRs not reported |
| Labiner, 2010a  N=18125 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration with clinically relevant treatments  Adequate sample size | Outcomes | ADRs not reported |
| Labiner 2010b  N=15500 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration with clinically relevant treatments  Adequate sample size | Outcomes | ADRs not reported |
| Kauko, 1974  N=20 | Study Designation:  Efficacy study  Composite Score:  1 of 7 | Intention to treat analysis | Population, Intervention, Comparator, Outcomes, Setting | Only in mentally retarded patients  No final health outcomes reported  Short duration of followup (30 days)  Small sample size (only 20 patients enrolled)  ADRs not reported  Institutionalized facility for mentally retarded  Conducted in Europe  Study conducted before 1990 |

| Table I-1. Evaluation of applicability for individual studies for innovator versus generic antiepileptic drug evaluation (continued) | | | | |
| --- | --- | --- | --- | --- |
| Study, Year | Effectiveness Study Designation  and Composite Score | Effectiveness Study Criteria Met | Applicability Limitation Category | Specific Factors Limiting Applicability |
| Glende, 1983  N=5 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator, Outcomes, Setting | Short duration of followup (4 weeks total, 2 weeks per group)  Small sample size (only 5 patients enrolled)  Conducted in Europe  Study conducted before 1990 |
| Jumao-as, 1989  N=10 | Study Designation:  Effectiveness study  Composite Score:  5 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator, Setting | Short duration of followup (10 weeks total, 5 weeks per group)  Small sample size (only 10 patients enrolled)  Study conducted before 1990 |
| Hartley, 1990  N=23 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Assessed final health outcomes  Assessed adverse outcomes  Enrolled primary care population | Population, Intervention, Comparator, Outcomes, Setting | Patients all young (6–15 years)  No final health outcomes reported  Short study duration (12 weeks total, 6 weeks per group)  Small sample size (only 23 patients enrolled)  Patients withdrawn were taken out of the final analysis  Conducted in Europe |
| Hartley, 1991  N=12 | Study Designation:  Efficacy study  Composite Score:  2 of 7 | Intention to treat analysis  Enrolled primary care population | Population, Intervention, Comparator, Outcomes, Setting | Patients all young (6.5–15 years)  No final health outcomes reported  No ADRs reported  Small sample size (only 12 patients enrolled)  Short duration of followup (12 weeks total, 6 weeks per group)  Conducted in Europe |
| Oles, 1992a  N=20 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Assessed final health outcomes  Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Population, Intervention, Comparator | Patients had to be 13 years or older  Patients had to be seizure free for extended time (5 months to 2 years)  Had to have been receiving carbamazepine for at least 6 months  Small sample size (only 20 patients enrolled)  Short duration of followup (3 months in each group) |
| Oles 1992b  N=20 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Assessed final health outcomes  Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Population, Intervention, Comparator | Patients had to be 13 years or older  Patients had to have refractory seizures (at least 2 per month in previous 3 months)  Had to have been receiving CBZ for at least 6 months  Small sample size (only 20 patients enrolled)  Short duration of followup (3 months in each group) |
| Reunanen, 1992  N=21 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Enrolled primary care population | Intervention, Comparator, Setting | Small sample size (only 21 patients enrolled)  Short duration of followup (3 months in each group)  Conducted in Europe |
| Silpakit, 1997  N=18 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Enrolled primary care population | Intervention, Comparator, Setting | Small sample size (only 18 patients enrolled)  Short duration of followup (12 weeks total, 3 weeks on each phase)  Conducted in Asia |
| Aldenkamp, 1998  N=12 | Study Designation:  Efficacy study  Composite Score:  5 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator, Setting | Small sample size (only 12 patients enrolled)  Short duration of followup (9 days total, 3 days per therapy)  Conducted in Europe |
| LeLorier, 2008a  N=671 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration  Adequate sample size | Outcomes, Setting | No ADRs reported  Conducted in Canada |
| LeLorier, 2008b  N=1060 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Adequate study duration  Adequate sample size | Outcomes, Setting | No final health outcomes reported  No ADRs reported  Conducted in Canada |
| LeLorier, 2008c  N=202 | Study Designation:  Efficacy study  Composite Score:  2 of 7 | Less stringent eligibility criteria  Adequate study duration | Outcomes, Setting | No final health outcomes reported  No ADRs reported  Conducted in Canada |
| LeLorier 2008d  N=851 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Adequate study duration  Adequate study sample | Outcomes, Setting | No final health outcomes reported  No ADRs reported  Conducted in Canada |
| Andermann, 2007a  N=1142 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Adequate study duration  Adequate sample size | Population, Outcomes, Setting | Population not well specified  No final health outcomes reported  No ADRs reported  Conducted in Canada |
| Andermann, 2007b  N=1600 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Adequate study duration  Adequate sample size | Population, Outcomes, Setting | Population not well specified  No final health outcomes reported  No ADRs reported  Conducted in Canada |
| Andermann, 2007c  N=2017 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Adequate study duration  Adequate sample size | Population, Outcomes, Setting | Population not well specified  No final health outcomes reported  No ADRs reported  Conducted in Canada |
| Nielsen, 2008a  N=9 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator, Outcomes, Setting | No final health outcomes reported  No ADRs reported  Short duration of followup (2 weeks on innovator and 7-15 days on generic)  Small sample size (only 9 patients enrolled)  Conducted in Europe |
| Lund, 1974    N=9 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Population, Setting | Patients treated with drug for at least one year admitted to hospital to exclude irregular drug intake  No final health outcomes reported  Short duration of followup (8 days on innovator and 11 days on generic)  Small sample size (only 9 patients enrolled)  Conducted in Europe  Conducted before 1990 |
| Chen, 1982  N=18 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Less stringent eligibility criteria  Assessed adverse outcomes  Enrolled primary care population | Intervention, Comparator, Outcomes, Setting | No final health outcomes reported  Short duration of followup (9 weeks total, 3 weeks per therapy)  Small sample size (only 20 patients enrolled)  Conducted in Europe  Conducted before 1990 |
| Hodges, 1986  N=30 | Study Designation:  Efficacy study  Composite Score:  3 of 7 | Assessed final health outcomes  Assessed adverse outcomes  Enrolled primary care population | Population, Intervention, Comparator, Setting | Only pediatric patients (3–15 years)  Short duration of followup (12 weeks total, 4 weeks on each therapy)  Small sample size (only 30 patients enrolled)  Conducted in Europe  Conducted before 1990 |
| Kishore, 1986  N=60 | Study Designation:  Effectiveness study  Composite Score:  5 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator, Setting | Short duration of followup (3 months)  Small sample size (only 60 patients enrolled)  Conducted in Asia  Conducted before 1990 |
| Mikati, 1992  N=10 | Study Designation:  Effectiveness study  Composite Score:  6 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Adequate study duration  Intention to treat analysis  Enrolled primary care population | Intervention, Comparator | Small sample size (only 10 pts enrolled) |
| Soryal, 1992  N=14 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Assessed adverse outcomes  Enrolled primary care population | Intervention, Comparator, Setting | Short duration of followup (4 weeks per therapy)  Small sample size (only 14 patients enrolled)  Conducted in Europe |
| Duh, 2009  N=948 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration  Adequate sample size | Outcomes, Setting | No ADRs reported  Conducted in Canada |
| Paradis, 2009a  N=1164 | Study Designation:  Efficacy study  Composite Score:  4 of 7 | Less stringent eligibility criteria  Assessed final health outcomes  Adequate study duration  Adequate sample size | Outcomes, Setting | No ADRs reported  Conducted in Canada |
| Vadney, 1997  N=64 | Study Designation:  Efficacy study  Composite Score:  2 of 7 | Assessed final health outcomes  Assessed adverse outcomes | Population, Intervention, Comparator | Limited to patients with mental retardation  Short duration of followup (8 weeks total, 4 weeks on each therapy)  Small sample size (only 64 patients enrolled) |