CLIENT Medicaid

Anticonvulsant Drug Use Evaluation

Educational RetroDUR Mailing	☑Initial Study ❑Follow – up /Restudy

Executive Summary

Purpose:	To promote safe, cost-effective use of anticonvulsant medications.	
Why Issue was Selected:	Anticonvulsant medications are among the most commonly prescribed classes of medications. In addition to their primary use, controlling seizure activity, many anticonvulsants have a variety of other appropriate indications.[1,2] Unfortunately, off-label use of anticonvulsants, that lacks scientific support, is also very common.[3] Regardless of indication, various anticonvulsants are also associated with risks for drug-drug and drug-disease interactions as well as other potential toxicities. All of these variables have an impact on the cost/benefit ratio of the use of these medications.	
Program Specific Information:	Performance Indicators	Candidates
	• Anticonvulsant Drug-Drug Interactions	80
	• Increased risk of adverse event: anticonvulsants and contraindications	896
	• Use of anticonvulsants for unproven, off-label indications	4,124
	• Use of chemically and/or pharmacologically related anticonvulsants simultaneously	9
	• Monitoring for potential anticonvulsant toxicities	1,926
Setting & Population:	All patients with a drug claim for an anticonvulsant in the past 45 days	
Types of Intervention:	Cover letter with individual patient profiles.	
Main Outcome Measures:	The results of this intervention will be measured six months post-intervention. Targeted patient cases will be re-examined to determine whether changes in therapy have been made. The baseline number of patients identified with problematic therapy will be compared to the rates at six months post-intervention.	
Anticipated Results:	Physician reexamination of off-label use of anticonvulsants and cases where anticonvulsant use may result in adverse drug events may decrease drug therapy expenditures and reduce adverse events. Additionally, increased awareness of appropriate monitoring for potential anticonvulsant toxicities may reduce the risk for negative outcomes.	

Performance Indicator #1: Potential Drug-Drug Interactions Involving Anticonvulsants

Why has this indicator been selected?	Significant drug interactions can result when some anticonvulsants are used with other agents. Some of these interactions are potentially so severe that the combination of medications is considered to be contraindicated.
How will the patients be selected ?	
Candidates (denominator):	Patients receiving an anticonvulsant drug listed (see Appendix A) during the most recent 45-day period of claims.
Exception criteria (numerator):	Candidates concomitantly receiving an interacting drug (see Appendix A) for at least 7 of the 45 days.

Performance Indicator #2: Potential Increased Risk of Adverse Drug Events

Why has this indicator been selected?	Several anticonvulsants are associated with black box warnings and/or contraindications relating to their use in patients with certain concomitant illnesses. Patients taking an anticonvulsant in the presence of a contraindication are at increased risk for adverse events.
How will the patients be selected ?	
Candidates (denominator):	All patients receiving an anticonvulsant drug as listed (see Appendix B) during the most recent 45-day period of claims
Exception criteria (numerator):	Candidates who have a history of a contraindicated medical condition (see Appendix B)

Performance Indicator #3: Use of Anticonvulsant Therapy for Unproven Off-Label

Why has this indicator been selected?	Off-label use of anticonvulsants represents a significant percentage of anticonvulsant prescribing.[1,2] In some instance such off-label use is not supported by the scientific literature and potential benefits are questionable. Patients may benefit from use of more proven therapy for their condition.
How will the patients be selected ?	
Candidates (denominator):	All patients receiving an anticonvulsant drug during the most recent 45-day period of claims.
Exception criteria (numerator):	Candidates with no diagnosis for an established use of the identified anticonvulsant in the past 2 years. See Appendix C for a list of stablished

	uses for various anticonvulsants.

Performance Indicator #4: Concomitant Use of Chemically and/or Pharmacologically Related Anticonvulsants

Why has this indicator been selected?	Selected anticonvulsants are closely related chemically and/or pharmacologically. Co-prescription of anticonvulsants sharing the same primary mechanism of action appears to be associated with increased risk of neurotoxic effects.[4]
How will the patients be selected ?	
Candidates (denominator):	All patients receiving a selected anticonvulsant drug (see Appendix D) during the most recent 45-day period of claims.
Exception criteria (numerator):	Candidates concomitantly receiving a closely related drug (see Appendix D) for at least 7 of the 45 days.

Performance Indicator #5: Monitoring for Potential Anticonvulsant Toxicity

Why has this indicator been selected?	Selected anticonvulsants are associated with black box warnings relating to potential complications associated with their use. Official prescribing information for these agents suggests monitoring that should be employed to minimize the risk for complications.
How will the patients be selected ?	
Candidates (denominator):	All patients receiving a selected anticonvulsant drug (see Appendix E) during the most recent 45-day period of claims.
Exception criteria (numerator):	Candidates who do not have the recommended monitoring documented in the past 365 days (see Appendix E).

References

1. Ettinger AB, Argoff CE. Use of antiepileptic drugs for nonepileptic conditions: psychiatric disorders and chronic pain. Neurotherapeutics. 2007; 4:75-83.

2. Golden AS, Haut SR, Moshe SL. Nonepileptic uses of antiepileptic drugs in children and adolescents. Pediatr Neurol. 2006; 34:421-32.

3. Radley DC, Finkelstein SN, Stafford RS. Off-label prescribing among office-based physicians. Arch Intern Med. 2006; 166:1021-6.

4. Perucca E. Clinically relevant drug interactions with antiepileptic drugs. Br J Clin Pharmacol. 2006; 61:246-55.

5. Harden DL, Leppik I. Optimizing therapy of seizures in women who use oral contraceptives. Neurology. 2006; 67(Suppl4):S56-8.

6. Thorneycroft I, Klein P, Simon J. The impact of antiepileptic drug therapy on steroidal contraceptive efficacy. Epilepsy and Behavior. 2006; 9:31-9.

Appendixes

Appendix A: Anticonvulsant Drug-Drug Interactions[%,#]

ANTICONVULSANT	INTERACTING DRUG(S)
Carbamazepine, Felbamate, Lamotrigine, Oxcarbazepine, Phenytoin, Phenobarbital, Primidone, Topiramate	Oral Contraceptives: Biphasic, Oral contraceptives: Triphasic, Oral Contraceptives: Progestin Only Etonogestrel: Implant, Etonogestrel-Ethinyl Estradiol Vaginal Ring
Carbamazepine, Phenytoin, Phenobarbital, Primidone	Darunavir, Delavirdine, Etravirine
Carbamazepine, Phenobarbital, Primidone	Voriconazole
Clonazepam, Diazepam Rectal, Phenobarbital, Primidone	Sodium Oxybate
Carbamazepine	Antidepressant: MAOI, Antiparkinson: MAOI, Linezolid
Phenytoin	Disopyramide, Nefazodone

[%] Official Prescribing Information. Available at: http://www.fda.gov/cder/ [last accessed 3/15/08].
[#] Level 1 Drug-Drug Interactions. First Data Bank; Indianapolis, IN.

Appendix B: Increased Risk of Anticonvulsant Adverse Effects[%]

ANTICONVULSANT	MEDICAL CONTRAINDICATIONS
Lamotrigine	Erythema Multiforme
Carbamazepine, Felbamate	Aplastic Anemia or Agranulocytosis
Valproic Acid Analogs	Pancreatitis, Urea Cycle Disorders
Phenobarbital, Primidone	Porphyria, Sleep Apnea, Asthma (Chronic Airway Obstruction), Obstructive Bronchitis, Apnea, or Dyspnea
Clonazepam, Valproic Acid Analogs, Felbamate	Liver Impairment
Phenytoin, Carbamazepine	Cardiac Conduction Disorder
Carbamazepine, Clonazepam, Lamotrigine, Phenobarbital, Phenytoin, Primidone, Valproic Acid Analogs	Pregnancy

[%] Official Prescribing Information. Available at: http://www.fda.gov/cder/ [last accessed 3/15/08].

Appendix C: Anticonvulsant Established Indications[%,*]

ANTICONVULSANT	ESTABLISHED INDICATIONS
Felbamate, Levetiracetam, Tiagabine, Zonisamide, Ethosuximide, Methsuxamide, Ethotoin, Phenytoin, Primidone	Convulsions / Seizure Disorders
Carbamazepine, Oxcarbazepine	Convulsions / Seizure Disorders, Bipolar Disorder, Trigeminal Neuralgia, Neuropathic Pain, Aggressive/Disruptive Behaviors
Valproic Acid Analogs	Convulsions / Seizure Disorders, Bipolar Disorder, Migraine, Aggressive/Disruptive Behaviors
Gabapentin	Convulsions / Seizure Disorders, Neuropathic Pain, Migraine, Vasomotor Symptoms of Menopause
Pregabalin	Convulsions / Seizure Disorders, Neuropathic Pain, Fibromyalgia
Lamotrigine	Convulsions / Seizure Disorders, Bipolar Disorder
Topiramate	Convulsions / Seizure Disorders, Migraine
Phenobarbital	Convulsions / Seizure Disorders, Insomnia
Mephobarbital	Convulsions / Seizure Disorders, Generalized Anxiety

[%] Official Prescribing Information. Available at: http://www.fda.gov/cder/ [last accessed 3/15/08].
* American Society of Health System Pharmacists Drug Information 2007. Available at : http://www.medicinescomplete. com/mc/ahfs/current/ [last accessed 3/17/08]

Appendix D: Chemically and/or Pharmacologically Related Anticonvulsants[%,*]

ANTICONVULSANT	RELATED ANTICONVULSANT
Phenobarbital	Primidone
Carbamazepine	Oxcarbazepine
Gabapentin	Pregabalin

[%] Official Prescribing Information. Available at: http://www.fda.gov/cder/ [last accessed 3/15/08].
* American Society of Health System Pharmacists Drug Information 2007. Available at
: http://www.medicinescomplete. com/mc/ahfs/current/ [last accessed 3/17/08]

Appendix E: Anticonvulsant Monitoring[%,*]

ANTICONVULSANT	RECOMMENDED MONITORING
Carbamazepine	Hepatic Function
Valproic Acid Analogs	Hepatic Function and Platelet Count

[%] Official Prescribing Information. Available at: http://www.fda.gov/cder/ [last accessed 3/15/08].

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