

New Medications for Epilepsy

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Epilepsy is a syndrome characterized by the tendency to have recurrent, unprovoked seizures. It affects 0.7% of the general population. Although advances in neuroimaging, genetics, and epidemiology contribute to our understanding of epilepsy, 30% or more of patients continue to have seizures despite therapy with traditional anticonvulsant medications.¹ Many patients are unable to tolerate effective dosages of individual anticonvulsant medications because of the side effects. When anticonvulsants are used in combination, the cumulative side effects are often greater than the added efficacy in reducing seizures. Combination therapy is further complicated by drug-drug interactions, which may affect the protein binding, liver metabolism, or renal clearance of the drugs.

Since 1993, nine new medications have been approved by the United States Food and Drug Administration (FDA) for the treatment of patients with seizures (**Table 1**). Four of these medications are variations of previously available medications, and the other five medications are unique compounds. These new medications dramatically increase the treatment options for patients with epilepsy. This article reviews these medications and describes their role in the management of patients with seizures.

NEW DRUGS FOR THE TREATMENT OF EPILEPSY

Tiagabine (Gabitril)

In 1997, the FDA approved tiagabine as adjunctive therapy for partial seizures in adults and children 12 years and older. Tiagabine is only indicated for partial onset seizures. It may exacerbate primary generalized seizures.

Clinical pharmacology. Tiagabine blocks the reuptake of gamma-aminobutyric acid (GABA) by glial cells, increasing the concentration of this inhibitory neurotransmitter at the neuronal synapse. The drug is readily absorbed through the gastrointestinal (GI) tract and has a half-life of 5 to 8 hours. Tiagabine is extensively metabolized by the liver and excreted into the feces and urine. The elimination half-life is 7 to 9 hours, and the average time to steady-state levels is 1 to 2 days.

The plasma concentration of tiagabine is decreased by carbamazepine, phenytoin, primidone, and phenobarbital. The free fraction of tiagabine in plasma is increased by valproate. Tiagabine does not induce or inhibit liver metabolic processes.²

Initiating therapy and maintenance dosing. Tiagabine is available in 4-, 12-, 16-, and 20-mg tablets. The typical starting dose is 4 mg at bedtime for the first week. The dose is increased weekly by 4 to 8 mg/day in 2 or 3 divided doses. The typical effective maintenance dose ranges from 36 to 64 mg/day. A therapeutic plasma concentration range has yet to be established. The maintenance dosage of tiagabine may need to be reduced in patients with liver disease.

Adverse effects. The most common adverse effects of tiagabine are nausea and vomiting. These adverse effects are often improved by taking the medicine with food and changing the dosing interval from twice daily to 3 times daily. Other relatively common adverse effects are dose related and include dizziness, tremor, irritability, and impaired concentration.^{3,4} No serious idiosyncratic side effects or abnormalities of laboratory studies have been reported.

Topiramate (Topamax)

In 1997, topiramate was approved by the FDA as adjunctive therapy for partial onset seizures in adults and children. The drug also appears to have benefit for patients with primary generalized tonic-clonic seizures and those with Lennox-Gastaut syndrome, a childhood disorder characterized by atypical absence, atonic, and myoclonic seizures, and mental retardation.

Clinical pharmacology. Topiramate is a sulfamate-substituted monosaccharide with multiple mechanisms of action, including state-dependent sodium channel blockade, potentiation of GABA effect, and inhibition

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Table 1. Medications Approved by FDA Since 1993 for Treatment of Patients with Seizures

Medication	Indications	Initial Dosage	Maintenance Dosage	Side Effects
Tiagabine (Gabitril)	Partial onset seizures in adults and children 12 years and older	4 mg at bedtime for the first week, increased weekly by 4–8 mg/day in 2 or 3 divided doses	36–64 mg/day	Nausea, vomiting, dizziness, tremor, irritability, impaired concentration
Topiramate (Topamax)	Partial onset and primary generalized seizures, Lennox-Gastaut syndrome	25–50 mg/day, increased weekly by 25–50 mg/day	400 mg/day given in 2 divided doses	Sedation, speech disorders, ataxia, paresthesias, weight loss, nephrolithiasis
Lamotrigine (Lamictal)	Partial onset and primary generalized seizures, Lennox-Gastaut syndrome	<i>Without valproic acid:</i> 50 mg/day for the first 2 weeks <i>With valproic acid:</i> 25 mg every other day	<i>Without valproic acid:</i> 300–500 mg/day in 2 divided doses <i>With valproic acid:</i> 100–400 mg/day in 2 divided doses	Sedation, headache, ataxia, diplopia, rash, Stevens-Johnson syndrome
Gabapentin (Neurontin)	Partial onset seizures in adults	300 mg on day 1, 300 mg twice daily on day 2, and 300 mg 3 times daily on day 3	Up to 4800 mg/day given in 3 or 4 divided doses	Sedation, ataxia, dizziness
Felbamate (Felbatol)	Partial onset seizures, Lennox-Gastaut syndrome	1200 mg/day in 3 or 4 divided doses	2400–3600 mg/day given in 3 or 4 divided doses	Anxiety, insomnia, headache, weight loss, nausea, vomiting, aplastic anemia, liver failure
Fosphenytoin injection (Cerebyx)	Generalized convulsive status epilepticus, short-term parenteral treatment	<i>Generalized status epilepticus:</i> 20 mg phenytoin equivalents/kg body weight intravenously, not to exceed 150 mg/min	300–500 mg phenytoin equivalents/day	Nystagmus, dizziness, ataxia, somnolence, pruritus, paresthesias, nausea
Valproate sodium injection (Depacon)	Patients on valproate temporarily unable to take oral medication	Same total daily dosage, individual divided dose, and dosing frequency as usual oral dose	Same total daily dosage, individual divided dose, and dosing frequency as usual oral dose	Headache, nausea, vomiting, injection site irritation, dizziness, taste disturbance
Carbamazepine extended release (Carbatrol, Tegretol-XR)	Partial onset and generalized tonic-clonic seizures, trigeminal neuralgia	200 mg twice daily, increased by 200 mg/day at weekly intervals	800–1200 mg/day	Sedation, dizziness, ataxia, nausea, hyponatremia, rash
Diazepam rectal gel (Diastat)	To abort potential seizure clusters	0.2–0.5 mg/kg body weight, depending on age	Not a maintenance medication	Ataxia, euphoria, diarrhea, dizziness, rash

FDA = United States Food and Drug Administration.

of the excitatory amino acid glutamate. The drug is well absorbed by the GI tract, with a mean elimination half-life of 21 hours in patients with normal renal function. The drug reaches steady state levels in 4 to 5 days, and 13% to 17% of the drug is protein bound. Liver metabolism of the drug is limited, and topiramate is primarily excreted in the urine.^{1,5} Therefore, there is

less opportunity for drug-drug interactions between topiramate and drugs that are hepatically metabolized.

Initiating therapy and maintenance dosing. Topiramate is available in 25-, 100-, and 200-mg tablets, and in 15- and 25-mg sprinkle capsules. The typical starting dose for topiramate is 25 to 50 mg/day for the first week. The dose is increased by 25 to 50 mg/day at weekly intervals,

with a target dose of 400 mg/day given in 2 divided doses. The maintenance dosage of topiramate may need to be reduced in patients with liver disease or renal failure.

Adverse effects. The adverse effects of topiramate include sedation, word-finding problems, ataxia, and paresthesias.¹ These adverse effects are dose related and are often associated with the speed of titration of the medication. Decreased appetite and weight loss are seen in some patients, and nephrolithiasis occurs in 1.5% of patients.⁶

Lamotrigine (Lamictal)

In 1995, lamotrigine was approved by the FDA as adjunctive therapy for partial onset seizures in adults.^{7,8} The drug also appears to have efficacy in primary generalized seizures, including absence seizures, and in Lennox-Gastaut syndrome.⁹

Clinical pharmacology. Lamotrigine is an antiepileptic of the phenyltriazine class. Its chemical structure is unrelated to other available antiepileptic medications. The mechanism of action of lamotrigine is uncertain, but it appears to include neuronal membrane stabilization and inhibition of excitatory amino acid release by way of voltage-gated sodium channel blockade.^{7,9}

The drug is well absorbed after oral administration, with little first-pass metabolism. Lamotrigine is metabolized and eliminated by the liver. Clearance is accelerated by hepatic enzyme-inducing drugs (eg, phenytoin, carbamazepine, phenobarbital, primidone) and markedly reduced by valproate. The half-life is 25 hours with monotherapy, approximately 12 hours when given with hepatic enzyme-inducing medications, and 70 hours when given with valproate. The time to steady state varies from 3 to 15 days, depending on concomitant medications. Lamotrigine does not have a significant effect on the metabolism of other medications.

Initiating therapy and maintenance dosing. Lamotrigine is available as 25-, 100-, 150-, and 200-mg tablets, and in 5- and 25-mg chewable/dispersible tablets. As an adjunctive therapy in adult patients on a hepatic enzyme-inducing antiepileptic drug who are *not taking valproic acid*, the usual starting dose is 50 mg/day for the first 2 weeks. This dose can be increased to 100 mg/day in 2 divided doses during weeks 3 and 4. Lamotrigine is then titrated by 100 mg/day every 1 to 2 weeks, with a typical maintenance dose of 300 to 500 mg/day in 2 divided doses.

As adjunctive therapy in adult patients who are *taking valproic acid*, the typical starting dose is 25 mg every other day for the first 2 weeks, increasing to 25 mg/day for weeks 3 and 4. Lamotrigine is then titrated by 25 to 50 mg/day every 1 to 2 weeks, with a usual mainte-

nance dose of 100 to 400 mg/day given twice daily. The dosage may require adjustment in patients with renal failure. Lamotrigine should be used with caution in patients with impaired liver function.

Adverse effects. Sedation, headache, ataxia, and diplopia are common dose-related side effects of lamotrigine. Rash is the most significant serious side effect, occurring in 10% of patients, and it can progress to the potentially fatal Stevens-Johnson syndrome. Severe rash occurs more commonly in patients receiving faster titration rates, especially when lamotrigine is given with valproic acid.

A prior allergic reaction to other arene oxide-producing anticonvulsants (eg, phenobarbital, carbamazepine, phenytoin) is a contraindication to initiating therapy with lamotrigine.¹⁰

Gabapentin (Neurontin)

In 1994, gabapentin was approved by the FDA as adjunctive therapy for adults with partial onset seizures, with or without secondary generalization.¹¹ This drug is not useful for primary generalized seizure disorders.

Clinical pharmacology. Gabapentin is a GABA analog that does not interact with GABA receptors or metabolism.¹² The antiepileptic mechanism of action of gabapentin is unknown, but it appears to be unique from phenytoin, carbamazepine, or the barbiturates. The drug is well absorbed orally, although absorption of the drug is reduced by antacids. The drug is mostly unbound in the plasma, has no appreciable metabolism in the body, and is excreted unchanged in the urine. Gabapentin elimination is directly related to creatinine clearance, with a half-life of 5 to 7 hours in adults with normal renal function. Gabapentin has no known interactions with the metabolism or protein binding of other antiepileptic drugs.¹³

Initiating therapy and maintenance dosing. Gabapentin is available as 100-, 300-, and 400-mg capsules. The typical starting dose is a single, 300-mg dose on day 1, 300 mg twice daily on day 2, and 300 mg 3 times daily on day 3. The dose is then titrated up to 1800 mg/day, given in 3 divided doses. Doses up to 4800 mg/day are usually well tolerated and may be more effective. The dose-limiting factor is often not adverse effects, but bioavailability. When doses greater than 3600 mg/day are used, a 4-times-daily dosing schedule is recommended. Because gabapentin is eliminated by the kidneys, the dosage may need to be adjusted in patients with reduced creatinine clearance.

Adverse effects. Common adverse effects are usually dose related and include sedation, ataxia, and dizziness.¹³ No serious idiosyncratic side effects have been reported to date.

Felbamate (Felbatol)

In 1993, felbamate was introduced in the United States as either monotherapy or adjunctive therapy for partial onset seizures, with or without secondary generalization.¹⁴ It is also used as adjunctive therapy for partial and generalized seizures in children with Lennox-Gastaut syndrome. Clinical experience suggests that felbamate may be effective in absence seizures, infantile spasms, and juvenile myoclonic epilepsy.

Clinical pharmacology. The mechanism of action for felbamate is unknown. Felbamate is well absorbed after oral administration with a bioavailability of greater than 90%. Half of the drug is excreted unchanged in the urine, and half is metabolized by the liver. The half-life of felbamate is 20 to 24 hours in adults with normal hepatic and renal function. The usual time to steady-state plasma levels is 5 to 6 days. Felbamate increases serum levels of phenytoin and valproic acid through its effect on the hepatic cytochrome P₄₅₀ enzyme system. Although felbamate decreases serum levels of carbamazepine, it increases the level of an epoxide metabolite that is responsible for many of the adverse effects seen with carbamazepine. This can present a confusing clinical picture of increasing carbamazepine toxicity with declining serum levels.

Initiating therapy and maintenance dosing. Felbamate should not be used by a patient without a discussion with the prescribing physician about the potential risks of therapy. The manufacturer recommends that written informed consent be obtained prior to initiating treatment. Felbamate is contraindicated in patients with liver disease or blood dyscrasias. Because of potential drug interactions, felbamate is usually used as monotherapy.

Felbamate is available as 400- and 600-mg tablets and a 600 mg/5 ml oral suspension.

For adults receiving monotherapy, the usual initial dose is 1200 mg/day in 3 or 4 divided doses. The dose can be increased by 600 mg/day at 2-week intervals to reach a total daily dose of 2400 to 3600 mg/day, given in 3 or 4 divided doses.

For adults taking other antiepileptic medications, the usual initial dose is 1200 mg/day, given in 3 or 4 divided doses; the patient's daily dose of concomitant antiepileptic medications should be reduced by 20%. Felbamate can be increased by 1200 mg/day increments at weekly intervals. Further reductions in the dose of other anticonvulsant medications may be necessary.

Adverse effects. Idiosyncratic drug reactions, including aplastic anemia and liver failure, are the most serious adverse events associated with felbamate. Aplastic anemia occurs in patients treated with felbamate with an estimated frequency as high as 1 of every

5000 patients.¹⁵ Unfortunately, serial blood counts are unreliable for the early identification of patients developing aplastic anemia. Patients should be vigilant for signs of infection, bleeding, anemia, and easy bruising. They should report these symptoms and signs promptly to their physician.

Acute hepatic failure has been reported in patients receiving felbamate. The risk of death from felbamate-associated hepatic failure has been estimated at 1 in 26,000 to 34,000 exposures.¹⁵ As with the risk of aplastic anemia, the risk of hepatic failure may decrease over time with continued therapy.¹⁵ The manufacturer recommends that liver function studies (aspartate transaminase, alanine transaminase, bilirubin) should be performed before starting therapy with felbamate and at frequent intervals for the duration of therapy.

The most common adverse effects of felbamate include anxiety, insomnia, headache, loss of appetite, weight loss, nausea, and vomiting. Because of felbamate's effect on the metabolism of other antiepileptic medications, side effects of those medications may appear during initiation of or increases in the dose of felbamate. In contrast to most antiepileptic medications, felbamate is rarely sedating.

NEW FORMULATIONS OF PREVIOUSLY AVAILABLE EPILEPSY MEDICATIONS

Fosphenytoin Sodium Injection (Cerebyx)

Fosphenytoin was introduced in the United States in 1995. It is approved for use in patients with generalized convulsive status epilepticus and for short-term parenteral treatment of patients taking phenytoin who are unable to take oral medications.

Clinical pharmacology. Fosphenytoin is a disodium phosphate ester of phenytoin that is a prodrug metabolized to phenytoin after parenteral administration. The conversion half-life of fosphenytoin to phenytoin is approximately 15 minutes. With intravenous (IV) administration, maximum serum levels of fosphenytoin are achieved by the end of the infusion. Fosphenytoin is completely absorbed with intramuscular (IM) administration, and maximum levels of the prodrug are reached in approximately 30 minutes. Phenytoin is insoluble in water and requires a solvent of ethylene glycol with a pH of 12. In contrast, fosphenytoin is water soluble. Because it is water soluble, the prodrug formulation avoids the hypotension, tissue necrosis with extravasation, and cardiac arrhythmias associated with IV phenytoin. This difference permits faster IV administration of fosphenytoin.¹⁶ The 100% bioavailability with IM administration allows parenteral administration of fosphenytoin when IV access is not readily available.¹⁷

The active drug is the phenytoin metabolite. Phenytoin exerts its antiseizure effect by blocking voltage-controlled and use-dependent sodium channels.

Initiating therapy and maintenance dosing. Fosphenytoin is available as an injectable solution of 50 mg phenytoin equivalent units (PE)/mL in a 10-mL vial (500 mg PE) and a 2-mL vial (100 mg PE); 1.5 mg of fosphenytoin is equivalent to 1 mg of phenytoin.

Calculating the appropriate dose of fosphenytoin is made much simpler by the manufacturer's labeling the product in PEs. This allows all dosage calculations to use standard phenytoin dosing without the need to translate to fosphenytoin.

For short-term parenteral use in patients already on phenytoin, the daily dose of fosphenytoin is roughly the same as the daily oral dose. (Because oral phenytoin has a bioavailability of 90% and fosphenytoin has a bioavailability of 100%, some patients may experience a small increase in serum phenytoin levels when changed to the same dose of the parenteral prodrug.) Fosphenytoin should not be given faster than 150 mg PE/min.

For patients with generalized status epilepticus, the loading dose is 20 mg PE/kg body weight, not to exceed a rate 150 mg PE/min given the IV route. The IM route is not recommended for patients in status epilepticus because of the potential for slower absorption and longer time to reach peak levels.

For nonemergent loading, the typical dose is 10 to 20 mg PE/kg body weight, not to exceed a rate 150 mg PE/min. The usual daily maintenance dose of fosphenytoin is 300 to 400 mg PE/day. Both the loading and maintenance dose can be given either IV or IM.

Adverse effects. Common adverse effects include nystagmus, dizziness, ataxia, somnolence, pruritus, and nausea. Nearly 30% of patients receiving fosphenytoin will experience paresthesias in the groin, abdomen, back, head, or neck. The mechanism of the sensation is unknown, and the symptom resolves spontaneously.¹⁶ A small decrease in systolic blood pressure can occur with IV administration.

Valproate Sodium Injection (Depacon)

Valproic acid was approved by the FDA in 1978 and is indicated for the treatment of primary and secondary generalized, partial onset, absence, myoclonic, and atonic seizures. Until recently, there has not been a parenteral form of the medication.

In 1998, valproate sodium injection was approved by the FDA. The IV form of the drug is used in the same types of epilepsy as the oral form. It is intended for patients who temporarily cannot take oral medication. There are no prospective clinical trials of IV val-

proate in the treatment of status epilepticus. Although it may prove to have a role in the future, it is not currently recommended for this use.¹⁸

Clinical pharmacology. The exact mechanism of valproic acid's anticonvulsant effect is unknown. Valproic acid inhibits voltage-gated and use-dependent sodium channels and likely has other effects.¹⁹ Valproic acid is metabolized almost completely by the liver. Plasma protein binding of valproic acid increases as the serum concentration of the drug increases. This produces a free fraction that ranges from 10% to 18% across usual therapeutic serum concentrations.

Initiating therapy and maintenance dosing. Depacon is produced as a solution for injection equivalent to 100 mg of valproic acid per mL, in 5-mL (500-mg) vials. When converting a patient from oral valproic acid preparations to the IV drug, the same total daily dosage, individual divided dose, and dosing frequency should be used. Depacon should be administered as an IV infusion over 60 minutes but at a rate no faster than 20 mg/min. The patient should be converted to an oral preparation of valproic acid as soon as it is clinically feasible.

Adverse effects. The most common adverse effects include headache, nausea, vomiting, and irritation at the injection site. Dizziness, injection site pain, and taste disturbance are infrequent adverse effects associated with the rate of the infusion.²⁰ Potential adverse effects with Depacon include all those associated with oral preparations of the drug. The manufacturer recommends that valproate sodium injection should not be given to patients with liver disease.

Carbamazepine Extended Release Tablets (Carbatrol, Tegretol-XR)

These drugs are reformulations of carbamazepine that permit twice-daily dosing. Carbamazepine is approved for the treatment of complex partial seizures, generalized tonic-clonic seizures, and mixed seizure patterns, including other partial or generalized seizures. Carbamazepine is also indicated for the treatment of trigeminal neuralgia. It does not appear to be effective for absence (petit mal) seizures.

Approved by the FDA in 1996, Tegretol-XR uses a unique sequential delivery system with a tablet that is not absorbed.²¹ Carbatrol is a multicomponent capsule that contains 3 types of beads—immediate release, extended release, and enteric release.²² The ratio of the beads is calculated to allow twice-daily dosing.

Clinical pharmacology. The 2 formulations are new delivery mechanisms for carbamazepine. The anti-epileptic effect of carbamazepine is thought to be due

Table 2. Suggested Dose of Diazepam Rectal Gel Based on Patient's Age

Age (Years)	Recommended Dose (mg/kg body weight)
2-5	0.5
6-11	0.3
12 and older	0.2

to inhibition of repetitive firing of action potentials in depolarized neurons through blockade of voltage-controlled and use-dependent sodium channels.¹⁹

The shell of the Tegretol-XR tablet is not absorbed and passes through the GI tract intact. The sequential release of carbamazepine from Tegretol-XR given twice daily provides serum levels approximately the same as standard formulations of carbamazepine give on a 4-times-daily schedule. Tegretol-XR tablets must be swallowed whole. The tablet should not be used if it is chipped or cracked.

Carbatrol can be swallowed whole or opened and sprinkled over food. The capsule should not be chewed or crushed. When taken every 12 hours, Carbatrol delivers steady state plasma levels similar to standard release carbamazepine preparations taken every 6 hours. With chronic administration, the time to peak levels averaged 6 hours, and the average half-life ranged from 12 to 17 hours.

Carbamazepine is primarily metabolized by the hepatic cytochrome P-450 system. Because carbamazepine induces its own metabolism, the half-life may vary. Carbamazepine is 70% to 80% bound to plasma proteins. By virtue of its effect on protein binding and liver enzyme induction, carbamazepine has extensive interactions with other medications.

Initiating therapy and maintenance dosing. Tegretol-XR is available as 100-, 200-, and 400-mg tablets. Carbatrol is available as 200- or 300-mg, hard gelatin capsules. For adults, the initial dose of both sustained-release products is 200-mg twice daily. The dose can be increased by 200 mg/day at weekly intervals. The usual therapeutic dose in adults is 800 to 1200 mg/day. When adults taking an immediate-release preparation are being converted to either of the sustained release drugs, the same total daily dose is given divided in 2 divided doses.

Adverse effects. The most common dose-related side effects of carbamazepine are sedation, dizziness, ataxia, and nausea. These adverse effects are related to peak serum levels and may be less severe with the

smoother serum levels provided by the sustained release medications.

Carbamazepine is associated with a variety of idiosyncratic reactions. The most frequent is a morbilliform rash that occurs in 10% of patients. Less frequently, erythema multiforme and the Stevens-Johnson syndrome occur. At higher plasma levels, carbamazepine can cause hyponatremia through an antidiuretic-like effect. Other idiosyncratic reactions, including cardiac arrhythmias, blood dyscrasias, and hepatotoxicity, are rare.¹⁹

Diazepam Rectal Gel (Diastat)

Diastat is diazepam gel in a prefilled plastic syringe with a molded, flexible tip for rectal administration. It is intended for the intermittent treatment of bouts of increased seizure activity in patients with refractory epilepsy who are already on a regular anticonvulsant regimen.²³

Clinical pharmacology. Diazepam appears to reduce seizure activity by its effect on receptors for the inhibitory neurotransmitter GABA. It is believed that diazepam increases GABA effect by improving the binding of GABA to its receptor. Diazepam is well absorbed when administered rectally. The bioavailability of Diastat is 90% of the bioavailability of intravenous diazepam. Peak serum levels are achieved at 90 minutes. It is extensively metabolized in the liver to 1 major active metabolite, desmethyldiazepam, and to 2 minor active metabolites. The mean half-life of elimination of diazepam is 46 hours, and 71 hours for the major active metabolite.

Therapy with diazepam rectal gel. Diastat is available as gel-filled syringes with a 4.4-cm tip for pediatric use. Syringes contain 2.5-, 5-, or 10-mg of the diazepam gel. Syringes with a 6-cm tip for adult use are available containing 10-, 15-, and 20-mg of diazepam gel. The suggested dose of diazepam rectal gel changes with age (Table 2).

A second dose may be given 4 to 12 hours after the initial dose, if required. The manufacturer recommends that the diazepam rectal gel should be used to treat no more than 5 episodes per month and no more than 1 episode every 5 days.

Adverse effects. The most serious potential adverse effect with diazepam rectal gel is respiratory depression. The most common adverse effect is sedation.²⁴ Other side effects include ataxia, euphoria, diarrhea, dizziness, and rash. Diazepam is a schedule IV controlled substance and can produce drug dependence. Diastat is contraindicated in patients with a known hypersensitivity to diazepam and in patients with acute narrow angle glaucoma.

CONCLUSION

There are several new medications for epilepsy and more on the horizon. The current standard of care is to start with the traditional medications, such as carbamazepine, phenytoin, and valproate. However, if the patient has inadequate seizure control or adverse drug effects, the newer medications give the physician and patient an alternative.

Because these new medications are, in general, unique with respect to each other as well as to the traditional medications, they have some potential advantages over the traditional agents. The new medications may have different mechanisms of anticonvulsant activity and tend to have fewer drug-drug interactions. As ongoing trials of these medicines are completed and clinical experience is accumulated, the newer agents may replace the traditional medicines in certain situations.

Finally, there are new formulations of traditional medicines, which appear to be significant improvements. Fosphenytoin is a phosphorylated form of phenytoin with significantly fewer side effects than the parent compound. This allows faster administration of the drug in emergency situations, including status epilepticus. The new diazepam rectal gel is a useful preparation for patients with a history of seizure clusters. The use of this product may reduce the number of emergency department visits.

A significant number of patients with epilepsy have difficult-to-control seizures, adverse effects caused by their medication, or both. These new anticonvulsant medications offer alternatives for the treating physician and hope for the patient. HP

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