GABAPENTIN

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Topic Overview

Gabapentin has been shown to be effective for a variety of conditions, including the treatment of partial seizures, painful neuropathies, spasticity in multiple sclerosis, tremor, and restless legs syndrome, and it may have potential effectiveness in reducing hot flashes in menopausal women or women with breast cancer. Important possible benefits of gabapentin include decreased sleep interference and fatigue, as well as increased quality of life, function, and work. A basic pharmacological overview of gabapentin, including off-label uses of the drug, as well as information on overdose and withdrawal, are discussed below.

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Type of Activity: Knowledge

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Estimated time to complete activity: 1 hour, including Course Test and course evaluation

Release Date: August 24, 2022 **Expiration Date:** August 24, 2025

Target Audience: This educational activity is for pharmacists.

How to Earn Credit: From August 24, 2022, through August 24, 2025, participants must:

1) Read the "learning objectives" and "author and planning team disclosures;"
2) Study the section entitled "educational activity;" and
3) Complete the Post-test and Evaluation form. The Post-test will be graded automatically. Following successful completion of the Post-test with a score of 70% or higher, a statement of participation will be made available immediately. (No partial credit will be given.)

Learning Objectives: Upon completion of this educational activity, participants should be able to:

1. **Identify** the uses of gabapentin for the treatment of seizure disorders, pain management, and restless leg syndrome
2. **Describe** the basic pharmacological profile, use, and clinical outcomes of gabapentin treatment
3. **Describe** the potential contraindications and side effects
4. **Identify** drug overdose and the use of drug tapering to discontinue gabapentin

Disclosures

The following individuals were involved in the development of this activity: Susan DePasquale, MSN, PMHNP-BC, Amanda Mayer, PharmD, Jeff Goldberg, PharmD, BCPP, and Steve Malen, PharmD. There are no financial relationships relevant to this activity to report or disclose by any of the individuals involved in the development of this activity.

Introduction

Gabapentin was originally developed as an anticonvulsant medication and, over time, has been used to treat a variety of medical conditions, including seizures, diabetic neuropathy, restless legs syndrome, postherpetic neuralgia, and fibromyalgia. Gabapentin is often used to treat acute or chronic pain associated with many of these conditions, which can help improve a patient's quality of life. Gabapentin has also been used in the treatment of anxiety and mood disorders; however, there are no formal randomized controlled trials on this topic. Gabapentin use can produce side effects such as somnolence, dizziness, ataxia, drowsiness, and fatigue.

History of the Drug

Gabapentin received U.S. Food and Drug Administration (FDA) approval under the brand name Neurontin® in 1993 as an adjunctive therapy in epilepsy patients over 12 years of age to treat partial seizures (with or without secondary tonic/clonic features).[3,4] In 2000, the FDA approved gabapentin as adjunctive therapy for the treatment of partial seizures in pediatric patients 3 to 12 years of age.[4] In 2004, gabapentin was FDA-approved for the management of postherpetic neuralgia in adults.[4]

In the years that followed, gabapentin has been prescribed for a myriad of off-label uses, driven in part by its availability in generic formulations.[6] A study of data collected from more than 4 million Medicare beneficiaries from 2013 to 2018 found that prescriptions for the drug increased by more than 36.3% in that time period.[5] Mattson, *et al.* (2022) confirmed the rise in gabapentin prescriptions, stating that "in 2019, 69 million gabapentin prescriptions were dispensed in the United States, making it the seventh most commonly prescribed medication nationally."[7] Its growth in use coincided with the efforts to address the opioid crisis. Gabapentinoids (such as gabapentin and pregabalin) were viewed as alternative treatments to opioids, but the expanded use of these medications has led to concern for a growing rate of misuse.[3,5] Gabapentin's expanded use to treat pain has also led to its co-

ingestion with prescribed or illicit opioids, implicating it in opioid-related deaths.[7]

Clinical Pharmacology

Mechanism of Action

Gabapentin is classified as an anticonvulsant.[1] The exact mechanism of action of gabapentin is not clear, but it is structurally related to gamma-aminobutyric acid (GABA), a major inhibitory neurotransmitter. Gabapentin does not bind to GABA receptors or seem to influence GABA metabolism.[1] The sites where gabapentin binds in the brain are in proximity to specific voltage-gated calcium channels, and the binding of gabapentin to these ion channels may decrease the release of excitatory neurotransmitters.[1] Gabapentin does not seem to exhibit affinity for other common receptor sites, including sites for benzodiazepines, NDMA, histamine, serotonin, or alpha- and beta-adrenergic sites.[8]

Pharmacokinetics

Gabapentin is not appreciably metabolized in humans, and its bioavailability is not dose-proportional, with bioavailability declining with higher doses. Typically, gabapentin immediate-release (Neurontin®) is dosed three times a day with food having little effect on the absorption of immediate-release gabapentin. Gabapentin is eliminated renally as an unchanged drug In patients with normal renal function. The elimination half-life of immediate-release gabapentin ranges from 5 to 7 hours.[8]

Gabapentin extended-release (marketed under the trade name Gralise®) is a once-daily dose formulation. Gralise should be taken with food and the time to reach maximum plasma concentration is 8 hours, approximately 4-6 hours longer when compared to immediate release gabapentin. Taking this formulation with food increases the rate and extent of absorption of the medication.[9]

Gabapentin enacarbil (Horizant®) is a prodrug that is supplied as an extended-release preparation. After ingestion, gabapentin enacarbil is absorbed in the small intestine and converted to gabapentin.[10-12] This process of absorption and conversion results in higher bioavailability and an extended time to maximum concentration, more so than standard gabapentin preparations. Gabapentin enacarbil should be taken with food, as food increases the mean bioavailability (possibly by as much as 75%). Steady-state of this formulation is reached in two days with daily administration.[13] Gabapentin enacarbil's pharmacokinetic characteristics are a likely explanation for why gabapentin enacarbil is effective and well-tolerated as a treatment for restless legs syndrome, but other forms of gabapentin typically are not.[10-12]

The immediate-release and extended-release formulations of gabapentin are not interchangeable due to the same daily dose of the medication resulting in different plasma concentrations.[13]

Other Drugs Commonly Used to Treat Similar Pain

Gabapentin is widely used for various pain disorders and is currently not as commonly used for the treatment of seizures. Similar drugs used for the same pain disorders are as follows: pregabalin (Lyrica®) used to treat neuropathic pain and fibromyalgia; duloxetine (Cymbalta®) used to treat fibromyalgia, neuropathic pain, and musculoskeletal pain; amitriptyline (Elavil®) used to treat neuropathic pain, fibromyalgia, and postherpetic neuralgia; and lidocaine patch (Lidoderm®) used to treat postherpetic neuralgia.[14]

Labeled and Off-label Uses for Gabapentin

Labeled Uses

The labeled uses of gabapentin depend on the exact formulation/brand.[15]

a) Neurontin® immediate-release capsule/tablet: Postherpetic neuralgia in adults, adjunctive therapy for partial onset seizures in patients over the age of 3
b) Gralise® extended-release tablet: Postherpetic neuralgia
c) Horizant® extended-release tablet: Restless legs syndrome and postherpetic neuralgia in adults

Off-Label Uses

The off-label uses of gabapentin cover a variety of different symptoms and conditions and are listed as:[15]

- Alcohol use disorder
- Alcohol withdrawal
- Benzodiazepine withdrawal
- Brachioradial pruritus
- Diabetic neuropathy
- Fibromyalgia
- Hiccups
- Hot flashes
- Neuropathic pain
- Adjunctive treatment of postoperative pain
- Social anxiety disorder
- Uremic pruritus

Off-label use of gabapentin is common, ranking as one of the medications having the highest rates of off-label use.[16] Fukada, *et al.* (2012) described gabapentin as a "catch-all" medication that has attained widespread use because of its uncertain mechanism of action and effectiveness in a variety of different conditions.[4] In addition to the above list of off-label uses, Fukada, *et al.*, reports gabapentin is commonly used off-label for bipolar disorder, complex regional pain syndrome, attention deficit disorder, trigeminal neuralgia, periodic limb movement disorder of sleep, and migraine.[4] As mentioned above, gabapentin's use has been propelled in part by its availability in generic formulations and by efforts to address the opioid

crisis.[5,6] This practice has raised important concerns, especially in light of the rise in gabapentin's misuse.[4]

Administration and Dosage

Gabapentin is available in various forms. Its uses, administration, and dosing differ between the brand names Neurontin®, Gralise®, and Horizant®.[8,9,13,15]

Neurontin® (immediate-release gabapentin) is approved for the treatment of partial seizures and postherpetic neuralgia.[15] For postherpetic neuralgia, dosing starts at 300 mg once daily on day 1, and it may be titrated up to 1800 mg/day in three divided doses. For partial onset seizures, Neurontin® dosing depends on age. In adults and children greater than 12 years old, the initial dose is 300 mg by mouth three times daily, and it may be titrated to 600 mg three times daily if needed. Doses as high as 2400-3600 mg/day have been used. In children 3 to 11 years old, the initial dose is 10-15 mg/kg/day, and it is generally dosed three times daily. In children 5 to 11 years old, the goal maintenance dose is 25-35 mg/kg/day. The goal maintenance dose in children 3 to 4 years old is 40 mg/kg/day. Dose titration generally occurs every three days.[15]

Gralise® is approved to treat postherpetic neuralgia in adults.[15] The initial dose is 300 mg by mouth once daily with the evening meal. The dose is gradually titrated over 15 days up to 1800 mg once daily. Since Gralise is an extended-release formulation, tablets must not be crushed, split, or chewed. If discontinuing Gralise®, it must be slowly tapered over one week or longer.[15]

Horizant® is used to treat restless legs syndrome and postherpetic neuralgia in adults.[15] For the treatment of restless legs syndrome, the dose is 600 mg once daily at approximately 5 pm with food. Dose increases beyond 600 mg daily are not recommended by the manufacturer as higher doses were not associated with improved symptoms and adverse reactions were more prevalent. This formulation is not recommended for patients who are required to sleep during the day and remain awake at night.[15] For the treatment of

postherpetic neuralgia, dosing starts at 600 mg by mouth every morning for 3 days and then increases to 600 mg twice daily thereafter. Increasing the dose beyond 1200 mg/day is not recommended by the manufacturer due to no proven additional benefit and increased risk of adverse effects.[15]

Formulations and Strengths

Available forms of gabapentin:[8,9,13,15]

- Neurontin® and generic immediate release formulations
  - 100 mg, 300 mg, and 400 mg capsules
  - 600 mg and 800 mg tablets
  - 250 mg/5 mL solution
- Gralise®
  - 300 mg and 600 mg extended-release tablets
- Horizant®
  - 300 mg and 600 mg extended-release tablets

Significant Warnings/Precautions

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan Hypersensitivity: Potentially fatal or life-threatening, fever, rash, lymphadenopathy, hepatitis, nephritis, eosinophilia, and myocarditis resembling acute, viral infection.[15]

Driving and operating heavy machinery: Until the patient is tolerant to the medication and familiar with its effects, it should be assumed that it can affect coordination significantly.[15]

Seizure from withdrawal: Avoid discontinuing gabapentin abruptly as this may increase the risk of seizures.[15]

Suicidal behavior and ideation: During analysis of 199 placebo-controlled clinical studies, it was observed that patients on gabapentin had double the risk of suicidal thoughts or ideation compared to placebo.[15]

Adverse Reactions

Some common adverse effects of gabapentin include somnolence, dizziness, headache, diarrhea, ataxia, edema, and fatigue. Serious adverse effects are generally uncommon in patients taking gabapentin.[15]

Drug Interactions

Other CNS depressants may have additive effects with gabapentin and should be used with caution. Morphine increases gabapentin levels in the blood. Patients should be carefully observed for signs of CNS depression, and doses of either gabapentin or morphine should be reduced if needed.[2,15] Hydrocodone also increases gabapentin levels in the blood. Antacids with aluminum and magnesium hydroxide have been shown to reduce the bioavailability of immediate-release gabapentin by about 20% if taken at the same time and approximately 5% if taken 2 hours apart. The Gralise® package insert recommends taking the medication at least two hours post-antacid administration.[9]

Specific Populations

- Pregnancy - There are no adequate or well-controlled studies in pregnant women. It should only be used in pregnancy if the potential benefit justifies the potential risk to the fetus. Previously categorized as Pregnancy Category C.[8]
- Lactation - Gabapentin is secreted into human milk following administration. The effect on the nursing infant is unknown, and it should only be used if the benefits clearly outweigh the risks.[8]
- Pediatric Use - Safety and efficacy in patients under 3 years of age have not been established. It is currently indicated for use only as adjunctive therapy for partial onset seizures in patients older than 3 years of age.[8]
- Geriatric Use - If used in elderly patients, gabapentin should be dosed cautiously, starting at the low end of the dosing range and titrated slowly.[8]

- Renal Impairment - Reduction of dose may be required in patients with compromised renal function.[8]

Lookalike/Soundalike Concerns

The Institute for Safe Medication Practices (ISMP) lists gemfibrozil as a drug that may be confused with gabapentin.[17]

Storage and Handling

All formulations of gabapentin, except for the oral solution, should be stored at room temperature. Gabapentin oral solution should be refrigerated.[8,9,13,18]

Postmarketing Clinical Studies

Postherpetic Neuralgia

Gabapentin has been proven in controlled, randomized trials to be an effective and safe treatment for postherpetic neuralgia pain.[19,20] Postherpetic neuralgia is the most common complication of herpes zoster infection.[21]

Restless Legs Syndrome

In 2020, a meta-analysis of twelve randomized controlled trials (RCTs) comprising 498 patients showed results that gabapentin is the most effective treatment for restless legs syndrome in patients with end-stage renal disease.[22] In 2017, another meta-analysis of 24 RCTs and 5137 patients showed results that gabapentin was equivalent to pregabalin and rotigotine and gabapentin was more effective than ropinirole for treating restless legs syndrome.[23]

Diabetic Neuropathy

Gabapentin has been successfully used to treat painful peripheral diabetic neuropathy, but its effectiveness and its place in the therapy of this disease have not been completely determined.[24] Controlled trials have shown that gabapentin can provide effective relief from pain caused by diabetic peripheral neuropathy, and it is considered by some to be a first-line choice for the condition.[24,25]

Fibromyalgia

Marske, *et al.* (2018) performed a small pilot study with 29 subjects divided into three groups; 1) patients receiving gabapentin only, 900 mg per day, 2) patients receiving gabapentin and osteopathic manipulative medicine treatments, and 3) patients receiving osteopathic manipulative medicine treatments only.[26] The subjects were treated for 8 weeks. The gabapentin-only group had no significant relief from pain or in their functional status (*i.e.*, energy level, mood, work performance). The gabapentin plus the osteopathic treatments and the osteopathic treatment only groups had significant relief from pain but no improvement in functional status.[26]

Mood Disorders/Depression/Anxiety

Gabapentin may be useful as an adjunctive treatment in patients with bipolar disorder with poor response to other mood stabilizers. It has also been prescribed for depression and anxiety.[27] It should be noted that anxiety is also listed as an adverse effect in post-marketing trials and reports, so patients should be monitored when gabapentin is written for these indications.

Dystonias in Children

Although it is not a labeled use, gabapentin has been used to treat dystonias in the pediatric population. Fehlings, *et al.* (2018) reviewed published literature on the management of dystonias in people who have cerebral palsy. The authors wrote that gabapentin has increasingly been used

in pediatric patients.[28] A search of the literature located one article that discussed the topic of gabapentin for treating dystonias in children. Liow, *et al.* (2016), in a retrospective study of 69 children who suffered from severe dystonia, reported that after administration of gabapentin, there was a significant improvement.[29] Treatment outcomes were based on the Dystonia Severity Assessment Plan (DSAP) levels. A majority of the patients had their DSAP level decrease from grade 3 (the child cannot sit, cannot tolerate lying, and is unable to fall asleep or stay asleep) to grade 1 (the child can sit comfortably, and sleep is regular and uninterrupted).[29]

Gabapentin Misuse

Gabapentin's misuse has grown significantly.[7,30,31] Gabapentin is increasingly used with illicit opioids by users looking for increased euphoria.[7,30] Patients with an opioid use disorder may take gabapentin to "control pain, substitute for opioids, mitigate opioid withdrawal, reduce opioid craving, and control mood and anxiety."[31] Patients who are at the highest risk for misusing gabapentin are patients with an opioid use disorder, mental illness, or a history of misusing prescription medications.[32,33]

Gabapentin has been misused so significantly that some states have categorized it as a Schedule V controlled substance, and some states require that prescriptions of the drug be monitored through the state's prescription monitoring program.[32] In spite of its misuse, gabapentin has not been listed as a controlled substance under the federal Controlled Substances Act.[32] Because of the variations in state laws governing gabapentin's prescribing rules, pharmacists and pharmacy technicians must be up to date on the laws of the state in which they are licensed to determine gabapentin's status.

Gabapentin Overdose

Few cases of gabapentin overdose have been reported in the medical literature.[30,34] Gabapentin overdoses usually involve co-ingestion of an opioid, alcohol, or other drugs.[7,30,35] This has led to uncertainty regarding gabapentin's cause or contribution to overdose deaths.[35] Gabapentin use is

common, and the medication is often obtained illegally without a prescription.[31]

Wills, *et al.* (2014) used poison control center data to perform a retrospective study on anticonvulsant overdose.[36] With respect to gabapentin specifically, they found 116 overdoses.[36] The median ingested dose was 6000 mg (daily maximum dose for gabapentin is 1800 mg - 3600 mg, given in divided doses). The results showed that 39 patients (33.6%) had no effect, 57 patients (49%) had a minor effect (*i.e.*, drowsiness), 17 patients (14.6%) had a moderate effect *(i.e.*, hypotension), 3 patients (2.6%) had a major effect (*i.e.*, seizures), and there were no deaths.[36] The authors identified two limitations of their study. They could not identify a relationship between the ingested dose and clinical effects, and the amount ingested was often reported by the patient and could not be confirmed.[36]

Symptoms of Gabapentin Overdose

In many cases, the effects of a gabapentin overdose lead to relatively minor or moderate adverse effects that may be resolved in an outpatient setting;[36] however, it can also have serious consequences and may even lead to death.[30,34,37] Symptoms from gabapentin toxicity are reportedly less severe than other anticonvulsants, such as the effects associated with carbamazepine and valproic acid toxicity.[38]

Special attention should be given to patients with decreased renal function.[35] Patients with decreased renal function or those on dialysis are more likely to present with gabapentin toxicity due to decreased clearance.[38]

The primary symptom associated with a gabapentin overdose is drowsiness.[38] Seizures may occur on rare occasions, but they are usually self-limiting, short, single episodes lasting less than 24 hours.[38] More severe clinical presentations "include coma, bradycardia, hypotension, and respiratory failure…."[38]

Qiu, *et al.* (2019) reported on a case where a 39-year-old male patient was hospitalized with symptoms of an "altered mental status and acute kidney injury secondary to rhabdomyolysis."[37] They determined the symptoms were "most likely due to gabapentin overdose."[37] This patient required kidney replacement surgery.[37]

A gabapentin overdose may lead to death, but this appears to be rare.[30,35] In most cases in which gabapentinoids were implicated in the death of a patient, opioids, alcohol, and/or other drugs were present.[7,30] Gabapentin overdose may cause or exacerbate respiratory depression, especially when used in a setting of concomitant opioid use.[39] Kriikku, *et al.* (2021) reported on only one death from a gabapentin overdose in which gabapentin was considered the only contributing substance.[30] This led the authors to conclude that when gabapentinoids are used alone, they have relatively low toxicity.[30]

Risks Associated with Prescribing Gabapentin with Opioids

Gomes, *et al.* (2017) found that patients prescribed gabapentin and opioids had a "higher risk of opioid-related death."[34] This risk was greater at higher prescription doses of gabapentin.[34] Clinicians co-prescribing opioids and gabapentin should proceed with caution. Clinicians should determine if combining these drugs is necessary, and if necessary, the patient should be monitored closely, and doses adjusted accordingly.[34]

Overdose Treatment

There is no specific treatment for gabapentin overdose, and there is no antidote for gabapentin poisoning.[38,40] Patients should be treated with standard, supportive care, and discontinuation of gabapentin until stable.[38] Treatments are directed at the clinical effects of a gabapentin overdose as described above.[38,40] As mentioned above, special attention is required for patients with decreased renal function.[38]

Withdrawal from Gabapentin

Abrupt discontinuation of gabapentin should be avoided if possible. Gabapentin should generally be tapered over a minimum of one week.[8,12] The most frequent symptoms reported with gabapentin withdrawal are anxiety, insomnia, nausea, pain, and sweating.[8] Other symptoms may include agitation, confusion, tremulousness, gastrointestinal distress, tachycardia, and hypertension.[41] A patient may experience generalized seizures and status epilepticus from gabapentin withdrawal, but this is uncommon.[42] Withdrawal symptoms typically occur within 12 hours to 7 days following discontinuation of gabapentin.[43]

Case Study: Gabapentin Withdrawal

Mah, *et al.* (2013) presented a case study involving a 75-year-old woman with a 20-year history of fibromyalgia and postherpetic neuralgia.[41] Her medication regimen included gabapentin 1800 mg/day as well as sertraline and lorazepam for recurrent depression. This patient was admitted for recurrent falls thought to be caused by her psychotropic agents. Gabapentin was discontinued by tapering over a 10-day period, with no complaints until day 11, when the patient had mild abdominal pain and a headache.[41] The following day, the patient reported chills, cold sweats, nausea, insomnia, and increased blood pressure. Initially, the symptoms were thought to be caused by the taper of lorazepam which started the day after the gabapentin taper was initiated. Symptoms failed to improve despite restarting lorazepam.[41]

Gabapentin withdrawal was suspected when symptoms did not improve with the reinitiation of lorazepam; therefore, gabapentin was reintroduced.[41] Upon reintroduction of gabapentin, the patient was no longer diaphoretic and had partial relief of anxiety and abdominal pain; however, insomnia continued. Gabapentin was increased to 1,400 mg/day due to renal impairment, and her symptoms completely resolved within three days.[41]

The authors discussed that gabapentin withdrawal was reported infrequently and may be due to underlying conditions that predispose a patient to withdrawal symptoms.[41] Case reports involving older individuals seemed to be more common, potentially due to age-related reduction of GABA-mediated cortical inhibition or alterations in the expression of glutamate receptors. All patients should be monitored for withdrawal symptoms upon discontinuation of gabapentin, especially those of advanced age or those who have been taking gabapentin for an extended period of time.[41]

Summary

Gabapentin is a GABA analog that is FDA approved for the treatment of partial onset seizures, postherpetic neuralgia, and restless legs syndrome. It is also commonly prescribed for peripheral diabetic neuropathy, as well as many other off-label uses.

Common adverse effects from gabapentin, such as drowsiness, dizziness, and headache, are usually mild. Additionally, population-based studies suggest that the risk for birth complications, fetal harm, or pregnancy complications is very low from gabapentin use, although more studies are needed to determine the safety of gabapentin use during pregnancy.

Gabapentin overdose appears to be relatively benign and well tolerated. There is no antidote for gabapentin overdose, and the treatment should consist of symptomatic and supportive care. Upon discontinuation of gabapentin, patients should be monitored for withdrawal symptoms.

Course Test

1. Gabapentin is classified as an

a. antidepressant.
b. opioid.
c. antiemetic.
d. anticonvulsant.

2. True or False: Gabapentin binds to GABA (gamma-aminobutyric acid) receptors, and it influences GABA metabolism.

a. True
b. False

3. Gabapentin has been used off-label to treat

a. dementia in Huntington's disease.
b. fibromyalgia.
c. dementia in Alzheimer's disease.
d. ataxia.

4. _____ is FDA-approved to treat restless legs syndrome in adults.

a. Horizant extended-release tablets
b. Gralise extended-release tablet
c. Neurontin immediate-release capsule
d. Gralise immediate-release tablet

5. Gabapentin is FDA-approved as an adjunctive therapy for the treatment of

a. grand mal seizures in patients of any age.
b. diabetic neuropathy in patients 12 years of age or older.
c. partial onset seizures in patients older than 3 years of age.
d. social anxiety disorder in adults.

6. During placebo-controlled clinical studies, it was observed that patients on gabapentin had _____ risk of suicidal thoughts compared to placebo.

a. a lower
b. the same
c. double the
d. one-tenth the

"Suicidal Behavior and Ideation: During analysis of 199 placebo-controlled clinical studies, it was observed that patients on gabapentin had double the risk of suicidal thoughts or ideation compared to placebo."

7. _____ is an extended-release prodrug that is absorbed in the small intestine.

a. Gabapentin enacarbil (Horizant)
b. Gralise liquid formula
c. Neurontin
d. Gralise

8. Which of the following is a more common side effect of gabapentin use?

a. Hypotension
b. Ataxia
c. Neuroleptic malignant syndrome
d. Bradycardia

9. Patients prescribed gabapentin and opioids are

a. less likely to have an adverse event.
b. more likely to have better outcomes.
c. at a lower risk of suicidal ideation.
d. at a higher risk of opioid-related death.

10. True or False: Patients with decreased renal function or who are on dialysis are more likely to present with gabapentin toxicity because of poor drug clearance.

a. True
b. False

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