Texas Vendor Drug Program

Drug Use Criteria: Gabapentin

Publication History

1. Developed: June 2006
2. Revised: **January 2022**, November 2019; November 2017; September 2015; December 2013; January 2012; December 2011; April 2010; August 2006.

Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage

1.1 Adults [1-15]

Gabapentin (Neurontin®, Gralise®) is FDA-approved for use in adults with postherpetic neuralgia pain and as adjunctive therapy for managing partial seizures with or without secondary generalization in epileptic patients.[1-6] Gabapentin enacarbil (Horizant®) has been FDA-approved for management of moderate-to-severe restless legs syndrome (RLS) in adults, and is also approved for pain reduction in postherpetic neuralgia (PHN).[1-4, 7] Gralise® and Horizant® are not interchangeable with Neurontin® and available generics due to differing chemical forms and pharmacokinetic properties.[1-7] Maximum recommended adult dosages are summarized in Table 1. The maximum time interval between gabapentin immediate-release doses should not exceed 12 hours. Patient profiles containing doses that exceed the maximum recommended dose will be reviewed.

Table 1. Maximum Recommended Adult Gabapentin Dosages [1-7]

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage
Partial seizures with/without secondary generalized tonic-clonic seizures	gabapentin (Neurontin®, generics)	100 mg, 300 mg, 400 mg immediate-release (IR) capsules 600 mg, 800 mg IR tablet 250 mg/5 mL, **300 mg/ 6 mL** oral solution	2400 mg/day (in three divided doses*)
Postherpetic neuralgia-associated neuropathic pain	gabapentin (Neurontin®, generics)	100 mg, 300 mg, 400 mg IR capsules 600 mg, 800 mg IR tablet 250 mg/5 mL, **300 mg/ 6 mL** oral solution	3600 mg daily in divided doses+
Postherpetic neuralgia-associated neuropathic pain	gabapentin (Gralise®)	300 mg, 600 mg extended-release (ER) tablets	1800 mg once daily
Postherpetic neuralgia-associated neuropathic pain	gabapentin enacarbil (Horizant®)	300 mg, 600 mg ER tablet	1200 mg daily in two divided doses

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage
Restless legs syndrome	gabapentin enacarbil (Horizant®)	300 mg, 600 mg ER tablet	600 mg daily at 5 pm^

**Doses of 3600 mg/day have also been well tolerated in small numbers of patients for abbreviated treatment durations.*
+Doses up to 3600 mg/day have been administered with therapeutic effect; however, additional benefit with doses greater than 1800 mg/day may not be observed.
^Gabapentin enacarbil doses up to 1200 mg daily have been used in clinical trials with no additional benefit and increased adverse reactions.

While not FDA-approved, gabapentin has also been evaluated in adult clinical trials for use in neuropathic pain, fibromyalgia, and vasomotor symptoms with favorable results.[1-3]

1.2 Pediatrics

Gabapentin is FDA-approved for use as adjunctive therapy for partial seizures with or without generalization in pediatric epileptic patients 12 years of age and older, as well as adjunctive therapy for partial seizures in pediatric patients 3 years to 12 years of age.[1-5] Gabapentin extended-release formulations are not approved for use in pediatric patients as safety and efficacy in this patient population have not been established.[1-4, 6, 7] Maximum recommended pediatric gabapentin dosages are summarized in Table 2. The maximum time interval between gabapentin doses should not exceed 12 hours. Patient profiles containing gabapentin doses greater than maximum recommendations will be reviewed.

Table 2. Maximum Recommended Pediatric Gabapentin Dosages [5]

Treatment Indication	Drug Name	Dosage Form/ Strength	Maximum Recommended Dosage
Partial seizures with/without secondary generalized tonic-clonic seizures	gabapentin (Neurontin®, generics)	100 mg, 300 mg, 400 mg immediate-release (IR) capsules 600 mg, 800 mg IR tablet 250 mg/5 mL, **300 mg/ 6 mL** oral solution	*12 years and older:* 2400 mg/day (in three divided doses*) *5-11 years of age:* 35 mg/kg/day (in 3 divided doses+) *3-4 years of age:* 40 mg/kg/day (in 3 divided doses+)

+Doses up to 50 mg/kg/day have been well tolerated in an extended clinical trial.
**Doses of 3600 mg/day have also been well tolerated in small numbers of patients for abbreviated treatment durations.*

1.3 Renal Impairment

Gabapentin dosing guidelines for adult with renal impairment are summarized in Table 3. Dosing guidelines for gabapentin immediate-release are also applicable for adolescents 12 years of age and older with renal impairment. Gabapentin use in pediatric patients younger than 12 years of age with impaired renal function has not been evaluated.[1-7]

Table 3. Gabapentin Dosage Guidelines in Adults, Adolescents 12 Years of Age and Older with Renal Impairment [1-7]

	Creatinine Clearance (CrCl)	Recommended Dosage Adjustments
Gabapentin immediate-release		
	60 ml/min or greater	900 mg to 3600 mg daily, in three divided doses
	30-59 ml/min	400 mg to 1400 mg daily, in two divided doses
	15-29 ml/min	200 mg to 700 mg once daily
	15 ml/min	100 mg to 300 mg once daily

	Creatinine Clearance (CrCl)	Recommended Dosage Adjustments
	< 15 ml/min	daily dose decreased in proportion to CrCl (e.g., CrCl = 7.5 ml/min – administer 50% of dose for CrCl of 15 ml/min)
	anephric patients	maintenance doses based on CrCl estimates, with supplemental doses of 125 mg to 350 mg administered after every 4-hour hemodialysis session
Gabapentin extended-release		
Gralise®		
	60 ml/min or greater	no dosage adjustment needed – 1800 mg once daily with evening meal
	30 – 59 ml/min	600 mg to 1800 mg once daily with evening meal
	< 30 ml/min	avoid administering Gralise®
	hemodialysis patients	avoid administering Gralise®
Horizant®		
Restless legs syndrome	60 ml/min or greater	no dosage adjustment needed
	30 – 59 ml/min	start with 300 mg daily with evening meal (~ 5 pm), increasing to 600 mg daily with evening meal as needed
	15-29 ml/min	300 mg daily with evening meal (~ 5 pm)
	< 15 ml/min	300 mg every other day with evening meal (~ 5 pm)
	< 15 ml/min on hemodialysis	Horizant® not recommended for use
Postherpetic neuralgia	60 ml/min or greater	no dosage adjustment needed
	30 – 59 ml/min	*Titration:* 300 mg in morning for 3 days *Maintenance:* 300 mg twice daily; increase to 600 mg twice daily if needed *Taper:* reduce current maintenance dose to once daily in morning for 1 week before drug discontinuation

	Creatinine Clearance (CrCl)	Recommended Dosage Adjustments
	15-29 ml/min	*Titration:* 300 mg in morning on day 1 and day 3 *Maintenance:* 300 mg in morning; increase to 300 mg twice daily if needed *Taper:* if taking 300 mg twice daily, decrease to 300 mg once daily in morning for 1 week; if taking 300 mg once daily in morning, no taper needed
	< 15 ml/min	*Titration:* none *Maintenance:* 300 mg every other day in morning; increase to 300 mg once daily in morning if needed *Taper:* none
	< 15 ml/min on hemodialysis	*Titration:* none *Maintenance:* 300 mg following every dialysis; increase to 600 mg after every dialysis if needed *Taper:* none

2 Duration of Therapy [8]

There is no basis for limiting the duration of gabapentin therapy since patients may suffer from epilepsy or RLS on a chronic basis, and postherpetic neuralgia management may require weeks to months of therapy.

3 Duplicative Therapy

Gabapentin dosage formulations are not interchangeable due to variations in chemical forms and pharmacokinetic properties. Concurrent administration of two or more gabapentin formulations is not recommended due to lack of additional therapeutic benefit and increased risk of adverse effects. Patient profiles containing concomitant prescriptions for two or more gabapentin dosage formulations for more than two months will be reviewed.

4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens, which may result in clinically significant drug-drug interactions. Drug-drug interactions considered clinically relevant for gabapentin are summarized in Table 4. Only those drug-drug interactions identified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed:

Table 4. Gabapentin Drug-Drug Interactions [1-7]

Interacting Drug	Interaction	Recommendation	Clinical Significance Level[#]
antacids	decreased gabapentin oral availability by approximately 20%	administer gabapentin at least two hours after antacids to avoid bioavailability problems	moderate (DrugReax) 3-moderate (CP)
hydrocodone	potential for decreased hydrocodone peak concentrations and AUC with concomitant gabapentin-hydrocodone administration in dose-dependent fashion; minor increases in gabapentin AUC	observe patients for decreased hydrocodone efficacy or additive drowsiness	3-moderate (CP)
morphine	concurrent administration may result in increased gabapentin serum levels (gabapentin AUC increased by 44% when morphine 60 mg controlled- release given 2 hours prior to gabapentin 600 mg)	monitor patients for increased CNS depression; adjust gabapentin and/or morphine doses as necessary	moderate (DrugReax) 3-moderate (CP)

[#]CP = Clinical Pharmacology

5 References

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