

# **Neuropathic Pain in Pediatric Oncology: A Clinical Decision Algorithm**

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**Supplementary Material**

**Supplementary Material - Mechanism of Action for Neuropathic Pain Medication Classes and Analgesic Efficacy**

<b>Medication Class</b>	<b>Mechanism of Action</b>	<b>NNT [2]</b>	<b>NNH [2]</b>
<b><u>Gabapentinoids</u></b>	Binding to $\alpha 2\delta$ -1 subunit of voltage-gated $\text{Ca}^{2+}$ channels and internalization of $\text{Ca}^{2+}$ channel [1-6]	-	-
gabapentin		6.3	25.6
extended release/Enacarbil		8.3	31.9
pregabalin		7.7	13.9
<b><u>TCA</u>s</b> (amitriptyline*, desipramine, nortriptyline, imipramine)	Local anesthetic effect: voltage-gated sodium channels block Central sensitization: NMDA receptors block Activation of interneurons that release GABA [1-5]	3.6	13.4
<b><u>SNRIs</u></b> (duloxetine, venlafaxine)	Inhibition of reuptake of serotonin and noradrenaline [1-5]	6.4	11.8
<b><u>Tramadol &amp; tapentadol</u></b>	SNRI mechanism and weak mu-opioid agonist [1-5,7]	4.7	12.6
<b><u>Strong opioids</u></b> (morphine, oxycodone*, hydromorphone)	Agonist of mu-opioid receptors, results in blocking synaptic communication [1-5]	4.3	11.7
<b><u>Topical/subcutaneous</u></b>	[1-5]	-	-
5% lidocaine patch	Voltage-gated $\text{Na}^+$ channels block [8]	-	-
8% capsaicin patch	TRPV1 agonist, increases intracellular $\text{Ca}^{2+}$ resulting in cellular dysfunction [9]	10.6	-
botulinum toxin A	Binds SNARE complex and prevents release of acetylcholine into the neuromuscular junction [10]	1.9	-

\*Medication used to calculate the NNT and NNH for the medication class

Abbreviations: NNT, number needed to treat; NNH, number needed to harm; TCAs, tricyclic antidepressants; NMDA, N-methyl-D-aspartic acid; GABA, gamma-aminobutyric acid; SNRIs, serotonin norepinephrine reuptake inhibitors; TRPV1, transient receptor potential cation channel subfamily V member 1; SNARE, Soluble NSF(N-ethylmaleimide-sensitive factor) Attachment Protein Receptor

**Supplementary Material - Adult Dosing Regimens for Neuropathic Pain Medications**

<b>Medication Class/Type</b>	<b>Dose Regimen (Maximum Total Daily)*</b>	<b>Recommended Duration**</b>
<b><u>Gabapentinoids</u></b>		
gabapentin	1200 mg TID (3600 mg)	5-10 weeks
extended released/Enacarbil	1200 mg BID (2400 mg)	
pregabalin	200 mg TID or 300 mg BID (600 mg)	4 weeks
<b><u>TCA's</u></b>	25-150 mg QD (150 mg)	8-10 weeks
<b><u>SNRIs</u></b>		
duloxetine	30-60 mg BID (120 mg)	4 weeks
venlafaxine	75-225 mg QD (225 mg)	4-6 weeks
<b><u>Tramadol &amp; tapentadol</u></b>		
tramadol	50-100 mg QID (400 mg)	4 weeks
tapentadol	50-100 mg Q4-6hrs (600 mg) [11]	
<b><u>Topical/subcutaneous</u></b>		
5% lidocaine patch	1-3 patches for up to 12 hours QD	3 weeks
8% capsaicin	1-4 patches for 30-60 mins Q3months	
botulinum toxin A	50-200 units Q3months	

Modified from [1,2]

\*Titration regimens are recommended, starting with lower doses titrated up to the dose cited in the table

\*\*Duration of treatment based on reference [1]

Abbreviations: TCAs, tricyclic antidepressants; SNRIs, serotonin norepinephrine reuptake inhibitors

## References

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