



Tramadol Dosage Forms

The analgesic activity of tramadol is due to both the parent drug tramadol, and the O-demethylated M1 metabolite. Tramadol is metabolized hepatically by CYP2D6 to the more pharmacologically active M1 metabolite.

At least two complementary processes appear responsible for the mechanism of action:

- binding of the parent moiety (low affinity) and the M1 metabolite (higher affinity than parent tramadol but less than other opioids) to μ -opioid receptors, causing inhibition of ascending pain pathways in the central nervous system
- weak inhibition of reuptake of norepinephrine and serotonin

Tramadol is indicated for moderate to moderately severe pain in adults. Long-acting dosage forms are indicated for adults who require continuous treatment for several days or more.¹

Due to differences in pharmacokinetic properties, the various tramadol dosage forms are not considered interchangeable.²

Single ingredient tramadol dosage forms currently (2017) available in Canada¹:

Immediate Release (IR)

Ultram, Apo-Tramadol

Extended Release (XL, ER)

Durela

Ralivia

Tridural, Taro-Tramadol ER

Zytram XL

Table 1 compares the characteristics of these products. Most information is provided by the manufacturers, which explains the differences in dose titrations, maximum daily recommended doses, administration recommendations, etc.

Table 1: Comparison of Tramadol Dosage Forms³⁻⁹

Name of Product	Dosage Form	Available Strengths	Pharmacokinetics	Drug-Food Interaction	Additional Comments
Ultram, Apo-Tramadol	IR Tablet	50mg	<ul style="list-style-type: none"> - Onset: within 1h - Peak effect: 2-3h - Half-life: tramadol ~6-7h M1 ~ 7-9h - C_{ss}: within 2 days with QID dosing 	<ul style="list-style-type: none"> - Administered without regard to food - Rate and extent of absorption not significantly affected by food 	<ul style="list-style-type: none"> - Maximum daily dose not to exceed 400mg - For chronic pain, start at 25mg daily and titrate up with divided doses every 3 days to 50mg - 100mg QID
Durela	ER Capsules –contains an IR tablet and ER beads	100mg (25mg IR + 75mg ER) 200mg (50mg IR + 150mg ER) 300mg (50mg IR + 250mgER)	<ul style="list-style-type: none"> - Onset: within 1h followed by a consistent release over ~ 24h - C_{ss}: 5 days with once daily dosing 	<ul style="list-style-type: none"> - Administered without regard to food - Rate and extent of absorption not significantly affected by food - Capsules to be swallowed whole 	<ul style="list-style-type: none"> - Maximum daily dose 300mg - Once daily dosing starting with 100mg and titrating with ≥ 5 days between dose adjustments
Ralivia	ER Tablets –polymer diffusion-based film and semi-permeable coating	100mg, 200mg, 300mg	<ul style="list-style-type: none"> - Lag-time to onset with peak plasma levels at 12-15h - C_{ss}: 4 days with once daily dosing. 	<ul style="list-style-type: none"> - T_{max} delayed by ~3 h when administered with food - Can be administered without regard to food as long as administration is consistent - Tablets should be swallowed whole 	<ul style="list-style-type: none"> - Maximum daily dose 300mg - Once daily dosing starting with 100mg and titrating with ≥ 5 days between dose adjustments
Tridural	ER Tablets Tridural –outer IR matrix and an inner ER core	100mg, 200mg, 300mg (25% IR, 75% ER)	<ul style="list-style-type: none"> - Onset: within 1h followed by SR phase providing a smooth plasma concentration/ time profile. - C_{ss}: 48h with once daily dosing. 	<ul style="list-style-type: none"> - Rate and extent of absorption not significantly affected by food - Consistent once daily dosing at breakfast is recommended 	<ul style="list-style-type: none"> - Maximum daily dose 300mg - Once daily dosing starting with 100mg and titrating in 100mg increments every 2 days - For maximum dose of 300mg/day, titration should take at least 4 days

Taro-Tramadol ER	Taro-Tramadol ER -based on osmotic drug delivery - ingredients contained within a non-absorbable shell which slowly releases drug at a constant rate over time			Taro brand - Non-absorbable shell is passed into the stool after the drug is absorbed	- Although description of these tablet formulations differs, the pharmacokinetics are the same -Interchangeable by some insurance plans ^{10,11}
Zytram XL	CR Tablets - matrix tablet	75mg, 100mg, 150mg, 200mg, 300mg, 400mg	- Tmax ~6 hours. - Css: 3 to 4 days with once daily dosing - At Css, 150mg daily = 50mg IR q8h	- Administered without regard to food - Empty matrix tablet remnants may be visible in the stool, or via colostomy	- Maximum daily dose 400mg - Treatment generally initiated at 150mg with slow titration of dosage adjustments separated by 7 days
CR = controlled release; Css = steady state; ER= extended release; h=hour(s); IR = immediate release; SR = sustained release					

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