

Withdrawal Syndrome

What if the patient misses a dose?

- May experience withdrawal syndrome
- Patients maintained chronically are most at risk
- Due to impact on serotonin receptors, there may be psychiatric withdrawal symptoms (including psychosis, insomnia, anxiety, cravings), dizziness, nausea

**Typical symptoms usually seen during withdrawal period & atypical symptoms appear in 1/8 cases*

Typical Symptoms (ie. opioid withdrawal)	<ul style="list-style-type: none"> • Anxiety, depression • Restlessness • Bone pain, body aches • Diarrhea, nausea, GI pain • Insomnia • Agitation • Excessive perspiration • Palpitations • Unexplained fever • Tremors/shivering • Weakness
Atypical Symptoms	<ul style="list-style-type: none"> • Severe anxiety • Panic attacks • Unusual CNS symptoms (eg. confusion, delusion, paranoia) • Numbness/tingling • Visual & auditory hallucinations

Summary

- ❖ Tramadol/Tramacet is an **opioid**
- ❖ Requires regular bedside monitoring (decrease level of consciousness, miosis, changes in behaviour, insomnia, perspiration, and GI symptoms)
- ❖ May cause **serotonin syndrome** (unlike other opioids)
- ❖ Avoid in patients particularly with **epilepsy** or **Parkinson's**, taking SSRIs (eg. sertraline, escitalopram, paroxetine) or MAOIs (eg. rasagiline, selegiline)
- ❖ **TramaCET contains acetaminophen** - so always double check that they're not on any other acetaminophen products
- ❖ Not a P'Care benefit drug and not on formulary
- ❖ Patients using tramadol chronically may bring in their own supply

References

1. Rajabizadeh G, Kheradmand A, Nasirian M. Psychosis following Tramadol Withdrawal. Addict Health. 2009;2009(Summer):58-61.
2. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018 [updated April 2018; cited 2018 Nov 03]. Ultram. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher
3. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; 2018 [updated April 2018; cited 2018 Nov 03]. Tramacet. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher
4. Opioid conversion guide [Internet]. Ww2.health.wa.gov.au. 2016 [cited 13 November 2018]. Available from: https://ww2.health.wa.gov.au/~/_media/Files/Corporate/general%20documents/Health%20Networks/WA%20Cancer%20and%20Palliative%20Care/How-to-use-the-Opioid-Conversion-Guide.pdf
5. Tramacet [Internet]. Toronto; 2018 [cited 4 November 2018]. Available from: https://www.janssen.com/canada/sites/www_janssen_com_canada/files/prod_files/live/tramacet_cpm.pdf
6. Acetaminophen (paracetamol) and tramadol: Drug information [Internet]. UpToDate. 2018 [cited 4 November 2018]. Available from: https://www.uptodate.com/contents/acetaminophen-paracetamol-and-tramadol-drug-information?search=tramacet&source=panel_search_result&selectedTitle=1~26&usage_type=panel&kp_tab=drug_general&display_rank=1
7. Rajabizadeh G, Kheradmand A, Nasirian M. Psychosis following Tramadol Withdrawal [Internet]. 1st ed. 2009 [cited 13 November 2018]. Available from:
8. ZAWN Z. Tramadol Detox Timeline, Protocol, Withdrawal Symptoms & Help [Internet]. Mentalhelp.net. 2018 [cited 7 November 2018]. Available from: <https://www.mentalhelp.net/articles/tramadol-detox/>
9. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3905496/pdf/AHJ-01-058.pdf>fk=1

Tramadol

&

Tramacet

A brief summary for nurses

November 15th, 2018
In-service

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UBC PharmD Candidates 2019

Tramadol vs. Tramacet

Tramacet is a combination pill of tramadol and acetaminophen.

	Tramadol	Tramacet
Brand Names	Ultram, Durela, Raliva, Tridural, Zytram XL	Tramacet
Dosage Forms	Oral tablets and capsules	Oral tablets
Tablet Strengths	ER: 100mg, 200mg, 300mg IR: 50 mg	Tramadol acetaminophen 37.5mg/325mg
Dosage Regimen (Initial)	50mg Q4-6H PRN	1-2 tabs Q4-6H PRN
Dosage Regimen (Max dose)	Max dose 400mg/day	Max dose: 8 tabs/day
Onset of Action	<1 hour	
Time to Peak Effect	2-3 hours	
Duration of Action	4-6 hours	
PRN or Regular?	Can be either PRN or regular depending on type and severity of pain.	

Opioid Dose Equivalency Estimator

*Note: equivalency dosing is controversial

Oral opioid	Practical Equivalency Dose
Morphine	10mg
Hydromorphone	2mg
Oxycodone	5-7.5mg
Codeine	75-90mg
Tramadol	50mg

*adapted from Government of Western Australian Department of Health

Indications

- Management of mod to mod severe pain
- Has not been well studied beyond 12 weeks
 - Should re-evaluate if planning to use for extended periods of time (long-term usefulness unknown)

Mechanism of Action

Unlike other opioids, tramadol has two main actions

- Inhibits mu opioid receptor
- Inhibits reuptake of norepinephrine & serotonin

Mu (μ)	<ul style="list-style-type: none"> - μ1: analgesia, physical dependence - μ2: resp. depression, miosis, euphoria, \downarrow GI motility physical dependence - μ3: vasodilation
Serotonin	Regulates mood, appetite, sleep, memory
Norepinephrine	Released due to stress; constricts blood vessels and increases BP

Cost Concerns

- Not a benefit drug (P'care), not on formulary
- Can be more expensive to patient due to lack of coverage
- Depending on dose & frequency of use, cost varies (roughly \$110/month)
 - 90 tabs Tramadol = \$90
 - 90 tabs Tramacet = \$83
- Physician may switch to other analgesics depending on indication
- If patients were on this regularly prior to admit and it's re-ordered but patient cannot supply, then VGH pharmacy will consider supplying the medication

Common Side Effects to

Monitor Bedside:

- Nausea, constipation
- Drowsiness, fatigue, somnolence

Serious SEs/When to Contact the Physician:

- **Opioid overdose:** unconscious, decreased breathing, miosis (small pupils, disorientated)
- **Serotonin syndrome:** agitation/restlessness, dilated pupils, muscle rigidity, sweating, tachycardia and hypertension, hyperthermia, hyperreflexia
- **Psychiatric:** ~10% of SEs, so monitor for changes in behaviour or mood
- **Allergic reaction:** swelling of mouth, tongue or throat, shortness of breath, skin rashes or hives.
- **Seizures, and movement disorders (eg. tremors)**

Warning/Precautions

- **Surgery:** opioids decrease bowel motility (monitor in post-op patients)
- Use with **other opioids** may result in opioid overdose
Caution giving Tramacet with other **acetaminophen** containing products, as it may cause acetaminophen overdose
- Caution when taking other agents that affect serotonin (eg. SSRIs), as it increases risk of **serotonin syndrome**
- Caution in patients with a history/currently have **epilepsy** as it increases risk of seizures/convulsions
- Caution with patients taking **antiparkinson** agents (eg. MAOIs) as it increases risk of movement disorders

