UNIVERSITY HEALTH SYSTEM
PHARMACY & THERAPEUTICS COMMITTEE
Guidelines for Use
Tramadol (Ultram®)
Revised December 2009

OVERVIEW:

Tramadol is a centrally-acting analgesic with low affinity for μ-opioid receptors. Its minimal propensity to induce typical opioid adverse effects is an advantage over other morphine-like agents.

It appears to have at least two complementary mechanisms of action:

1. **binding of μ-opioid receptors; and**
2. **weak inhibition of reuptake of norepinephrine and serotonin (activity weaker, but similar, to tricyclic antidepressants)**

P&T GUIDELINES FOR USE

1. **Not recommended for first-line treatment of pain.**

May be beneficial in patients with:

2. a contraindication to NSAIDs
3. fibromyalgia
4. mixed somatic / neuropathic pain

***IMPORTANT NOTES CONCERNING POTENTIAL DEPENDENCE & ABUSE*:**

Tramadol may induce psychic and physical dependence of the morphine (μ-opioid) type, thus should not be used in patients that are currently opioid-dependent. Methadone is a reasonable alternative.

Tramadol has been associated with craving, drug-seeking behavior, and development of tolerance. Tramadol has been shown to reinitiate physical dependence in some patients that have been previously dependent on other opioids.

Dependence and abuse, including drug-seeking behavior & taking illicit action to obtain the drug, are not limited to those patients with prior history of opioid dependence.

FDA-APPROVED USES:

Moderate to moderately-severe pain in adults.

P&T RESTRICTIONS:

As of March, 2004, tramadol is no longer restricted to specific services.

P&T has restricted the prescribing quantities of tramadol to the FDA-approved maximums for safety reasons. The maximum daily dose is 400mg. In patients receiving an SSRI, use extreme caution, titrate more slowly and do not exceed a maximum of 300mg.

RECOMMENDED DOSING:

Adults (not approved in patients less than 17 years of age):

Tolerability is improved by a slow titration regimen. The manufacturer recommends the following:

- Start with 25mg q day (at bedtime).
- Titrate in 25mg increments as separate doses every 3 days to 25mg q.i.d.
- Thereafter, increase the daily dose by 50mg every 3 days to 50mg q.i.d.
- After titration, 50mg to 100mg may be given q 4 to 6 hours prn, **not to exceed 400mg/day.**

Impaired renal function: In patients with CrCl < 30ml/min, adjust dosing interval to **q 12 hours; max dose should not exceed 200mg/day**. Dialysis patients can receive their dose on dialysis days.

Impaired liver function: In patients, with cirrhosis, dose should be adjusted to **50mg q 12hours.**

The Elderly: In patients over 65, titrate more cautiously. In patients over 75, **max dose is 300mg.**

Discontinuation: Withdrawal symptoms may occur if tramadol is discontinued abruptly. Symptoms may include anxiety, sweating, insomnia, rigors, pain, nausea, tremors, diarrhea, upper respiratory symptoms, piloerection, and rarely hallucination. Clinical experience suggests that withdrawal symptoms may be relieved by tapering the dose.

CONTRAINDICATIONS:

1. Tramadol should not be administered to patients who have previously demonstrated **hypersensitivity** to tramadol, any other component of this product or opioids.
2. Tramadol is **contraindicated in any situation where opioids are contraindicated**, including acute intoxication with any of the following: alcohol, hypnotics, narcotics, centrally acting analgesics, opioids or psychotropic drugs. Tramadol may worsen central nervous system and respiratory depression in these patients.

WARNINGS:

1. **Seizures** have been reported in patients receiving tramadol within the recommended dosage range, and even following the first dose.
2. Concomitant use of tramadol **increases risk of seizures** in patients taking SSRIs, anorectics, neuroleptics, tricyclics, cyclobenzaprine, promethazine, opioids, MAOIs or any other drugs that lower the seizure threshold.
3. **Risk of convulsions may also increase** in patients with epilepsy, those with a history of seizures, or in patients with a recognized risk of seizure (head trauma, metabolic disorders, alcohol and drug withdrawal, CNS infections).
4. Because tramadol may **potentiate the effects of other CNS depressants** (e.g., alcohol, anesthetics, phenothiazines, sedative/hypnotics, analgesics, opiates), the drug should be used with caution and in reduced dosage in patients receiving such drugs.
5. **Tramadol decreases the synaptic reuptake of the monoamine neurotransmitters norepinephrine and serotonin**. Animal studies have reported increased deaths when tramadol was given with MAOIs.
6. **Serotonin syndrome** – characterized by atypical chest pain, sinus tachycardia, confusion, psychosis, sundowning, agitation, diaphoresis, and tremor – has been reported when tramadol was administered with an **SSRI.**
7. **Prolongation of the INR and PT** and extensive ecchymoses have been reported in patients receiving tramadol with warfarin.
8. Tramadol should be used with caution in patients with increased intracranial pressure or head injury. Pupillary changes (miosis) from tramadol may obscure the existence, extent, or course of intracranial pathology.

References:

1. Ultram® package insert. Ortho-McNeil; last revision August 2001
2. Tramadol monograph. *AHFS Drug Information*, 2003 edition.