

The use of “as needed” or “PRN” range orders for opioid analgesics is a common clinical practice in the management of acute pain and in care at end-of-life (EOL). This approach provides flexibility in dosing to meet individual patient’s unique analgesic requirements. Range orders enable necessary and safe dose adjustments based on an individual’s response to treatment. However, open-ended analgesic orders, such as “titrate to comfort” are not acceptable (even at EOL in palliative care situations) because they are vague, lack specific parameters, and are prone to variable or unsafe interpretation. Rather, an order should specify an appropriate dose range and frequency of administration based on the pharmacokinetics of the opioid, patient characteristics, adverse effects and the situation, with discernible endpoints.

#### **Key Points for Prescribers:**

- Construct orders that contain a dosage range with a fixed time interval. If PRN range orders are to be used, order a dosage range large enough to permit appropriate and safe dose titration. The maximum dose should not be greater than four times the minimum dose.
- Consider patient and drug characteristics including, but not limited to: type, intensity and duration of pain, patient age and goals, past exposure and prior response to analgesics (both pain relief and side effects), comorbidities, end organ function, concomitant administration of other drugs and pharmacokinetics of the analgesic to be ordered.
- IV loading doses may be used to achieve therapeutic analgesia sooner and to initially relieve acute uncontrolled pain. In order to maintain the analgesic relief achieved by the loading dose, start the hourly basal rate at one-fifth of the total loading dose. Give a bolus dose (equal to the new hourly basal rate) with each increase in the infusion rate.
- Full effects of initiating or increasing a basal rate will not be seen until steady state is reached, approximately 3-5 half-lives (6-15 hours for most opioids). This means that in most situations, the continuous infusion dose (basal rate) should not be increased more frequently than once or twice a day.
- When continuous infusions are used, write a PRN RN bolus order with a dosage and time interval appropriate for the drug, route of administration and situation. Take into account usual distribution characteristics, time to onset, time to peak effect and duration of action. This PRN RN bolus dose is generally ordered at an amount equal to or double the hourly infusion every 60 minutes, but may be allowed as frequently as every 15 minutes.
- Reasonable titration guidelines include: for moderate to severe pain increase by 50-100%, for mild to moderate pain increase by 25-50%, irrespective of starting dose. When increasing doses of IV opioids, do not increase the basal rate by more than 100% at any one time, irrespective of how many bolus/breakthrough doses have been used. These guidelines apply to patients with normal renal and hepatic function. For elderly patients, or those with renal/hepatic disease, percentage increases may need to be reduced.

Examples of Titration to Comfort Orders	
<p>Situation of Palliative Care at EOL</p> <ol style="list-style-type: none"> <li>1. Give morphine 1mg IV loading dose, then start IV morphine infusion at 1mg/hr*</li> <li>2. PRN RN IV bolus 1 to 2 mg morphine every 15 minutes if needed for uncontrolled pain</li> <li>3. If pain is uncontrolled by PRN RN IV boluses, increase continuous infusion by 50-100% every 12 to 24 hours and increase PRN RN IV bolus to amount equal to the new hourly infusion dose.</li> <li>4. Call MD for poorly controlled pain, if more than 3 dose escalations are necessary, if patient is unexpectedly very difficult to arouse, or for questions on how to safely increase dose.</li> </ol>	<p>Situation of Acute Pain Titration</p> <ol style="list-style-type: none"> <li>1. Give loading dose of 2-4mg IV morphine* every 15 minutes until pain is reduced by 50% or maximum of 4 doses have been given</li> <li>2. Then start continuous infusion at 1/5<sup>th</sup> of the total loading dose given</li> <li>3. Patient-initiated dose at ½ of the established hourly infusion dose using a 10min lockout period</li> <li>4. PRN RN IV bolus equal to hourly infusion every 1 hour</li> <li>5. Call MD for uncontrolled pain, side effects, or questions</li> </ol>

*\*Examples given for opioid naïve adult. For tolerant patients calculate equianalgesic dose or consult pharmacist for recommended starting dose. Caution: equianalgesic doses are approximate. Individual patient response must be observed. Doses and intervals between doses are titrated according to the patient’s response.*

**References**

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