

# **MORPHINE IR DRUG CLASS**

## **Morphine IR, Dilaudid IR (hydromorphone), Opana IR (oxymorphone)**

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### **RATIONALE FOR INCLUSION IN PA PROGRAM**

#### **Background**

Morphine sulfate immediate release (IR) and its derivatives hydromorphone immediate release (IR) (Dilaudid) and oxymorphone immediate release (IR) (Opana) are Schedule II narcotics prescribed to treat moderate to severe pain. Morphine produces both its therapeutic and adverse effects by interaction with one or more classes of specific opioid receptors located throughout the body. Morphine acts as a full agonist, binding with and activating opioid receptors at sites in brain and spinal cord. In addition to analgesia, the widely diverse effects of morphine include drowsiness, changes in mood, respiratory depression, decreased gastrointestinal motility, nausea, vomiting, and alterations of the endocrine and autonomic nervous system (1-3).

#### **Regulatory Status**

FDA-approved indications:

Morphine sulfate IR, hydromorphone IR and oxymorphone IR are opioid agonists indicated for the relief of moderate to severe acute and chronic pain where an opioid is appropriate (1-3).

Morphine sulfate IR and its derivatives hydromorphone IR (Dilaudid) and oxymorphone IR (Opana) have boxed warnings for the following (1-3):

- Respiratory depression is the chief hazard of opioid agonists, including morphine sulfate, which if not immediately recognized and treated, may lead to respiratory arrest and death. Risk is increased in patients receiving concurrent CNS depressants (including alcohol), patients with chronic obstructive pulmonary disease, orthostatic hypotension, increased intracranial pressure, biliary tract diseases, seizure disorders to reduce the risk of respiratory depression, proper dosing, titration, and monitoring are essential.
- All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.
- Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.

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- Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

Morphine sulfate and oxymorphone are contraindicated in patients with paralytic ileus (1-3).

CDC guidelines find that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (4)

CDC guidelines finds that given uncertain benefits and substantial risks that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue longer than 3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care (4).

The FDA warns that opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity (see Appendix 1 for list of drugs) (5).

The safety and effectiveness of morphine sulfate in pediatric patients below the age of 18 have not been established (1-3).

#### **Summary**

Morphine sulfate IR and its derivatives hydromorphone (Dilaudid) and oxymorphone (Opana) are Schedule II narcotics prescribed to treat moderate to severe pain. In addition to analgesia, the widely diverse effects of morphine include drowsiness, changes in mood, respiratory depression, decreased gastrointestinal motility, nausea, vomiting, and alterations of the endocrine and autonomic nervous system. All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use (1-5).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of

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morphine sulfate IR, hydromorphone IR and oxymorphone IR while maintaining optimal therapeutic outcomes.

#### References

1. Dilaudid [package insert]. Whippany, NJ: Halo Pharmaceutical, Inc.; December 2016.
2. Opana [package insert]. Malvern, PA: Endo Pharmaceuticals; December 2016.
3. Morphine sulfate [package insert]. Columbus, OH: Roxane Laboratories, Inc.; December 2016.
4. Dowell D, Haegerich T, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain. CDC Guidelines 2016.
5. FDA Safety Release. FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes. March 22, 2016.

#### Appendix 1 - List of Serotonergic Medications

##### Selective Serotonin Reuptake Inhibitors (SSRIs)

paroxetine	Paxil, Paxil CR, Pexeva, Brisdelle
fluvoxamine	Luvox, Luvox CR
fluoxetine	Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax
sertraline	Zoloft
citalopram	Celexa
escitalopram	Lexapro

##### Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

venlafaxine	Effexor XR
desvenlafaxine	Pristiq, Khedezla
duloxetine	Cymbalta
milnacipran	Savella

##### Tricyclic Antidepressants (TCAs)

amitriptyline	No brand name currently marketed
desipramine	Norpramin
clomipramine	Anafranil
imipramine	Tofranil, Tofranil PM
nortriptyline	Pamelor, Aventyl
protriptyline	Vivactil
doxepin	Zonalon, Silenor
trimipramine	Surmontil

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### Monoamine Oxidase Inhibitors (MAOIs)

isocarboxazid	Marplan
phenelzine	Nardil
selegiline	Emsam, Eldepryl, Zelapar
tranylcypromine	Parnate

### Other Psychiatric Medicines

amoxapine	No brand name currently marketed
maprotiline	No brand name currently marketed
nefazodone	No brand name currently marketed
trazodone	Oleptro
bupirone	No brand name currently marketed
vilazodone	Viiibryd
mirtazapine	Remeron, Remeron Soltab
lithium	Lithobid

### Migraine Medicines

almotriptan	Axert
frovatriptan	Frova
naratriptan	Amerge
rizatriptan	Maxalt, Maxalt-MLT
sumatriptan	Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet
zolmitriptan	Zomig, Zomig-ZMT

### Antiemetics

ondansetron	Zofran, Zofran ODT, Zuplenz
granisetron	Kytril, Sancuso
dolasetron	Anzemet
palonosetron	Aloxi

### Other Serotonergic Medicines

dextromethorphan	Bromfed-DM, Delsym, Mucinex DM, Nuedexta
linezolid	Zyvox
cyclobenzaprine	Amrix
methylene blue	
St. John's wort	
tryptophan	