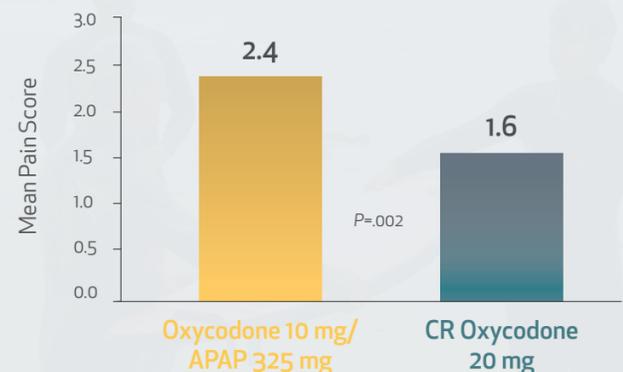


## COMMON COMBINATION THERAPIES Have Been Shown to Deliver

Oxycodone/APAP combinations deliver superior peak pain relief (PPR) vs high-dose monotherapy

### PPR WITH COMBINATION THERAPY\*



\*Patients rated pain relief on a 5-point categorical scale (0=no relief, 4=complete relief).

- Treatment with oxycodone 10 mg/APAP 325 mg produced significantly greater peak pain relief than did single-agent controlled-release (CR) oxycodone 20 mg<sup>7</sup>

### INDICATIONS AND USAGE

PRIMLEV™ (oxycodone and acetaminophen tablets, USP) is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

### IMPORTANT SAFETY INFORMATION

**What is the most important information you should know about PRIMLEV?**

PRIMLEV™ (oxycodone and acetaminophen tablets, CII) is a strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain severe enough to require an opioid medication, and for which alternative treatments such as non-opioid pain medicines do not treat your pain well enough or you cannot tolerate them.

Opioid pain medicines can put you at risk for overdose and death. Even if you take your dose correctly as prescribed, you are at risk for opioid addiction, abuse, and misuse that can lead to death.

**Get emergency help right away if you take too much PRIMLEV (overdose). When you first start taking PRIMLEV, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur.**

**Taking PRIMLEV with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.**

**Never give anyone else your PRIMLEV. They could die from taking it. Store PRIMLEV away from children and in a safe place to prevent stealing or abuse. Selling or giving away PRIMLEV is against the law.**

**Who should not take PRIMLEV?**

**Do not take PRIMLEV if you:**

- Have severe asthma, trouble breathing, or other lung problems
- Have a bowel blockage or have narrowing of the stomach or intestines
- Have a known allergy or hypersensitivity to oxycodone, acetaminophen, or any ingredient in PRIMLEV

**Before you take PRIMLEV, tell your healthcare provider if you:**

- Have a history of head injury or any seizure disorder
- Have or have had liver, kidney, or thyroid problems
- Have problems urinating
- Have or have had pancreas or gallbladder problems
- Have ever abused street or prescription drugs, been addicted to alcohol, or have any history of mental health problems

**Also tell your healthcare provider if you are:**

- **Pregnant or planning to become pregnant.** Using PRIMLEV for long periods during pregnancy can cause withdrawal symptoms in your newborn baby that can be dangerous or life-threatening if not recognized or treated.
- **Breastfeeding.** PRIMLEV passes into breast milk and may harm your baby.

It is important that you tell your healthcare provider about all medicines that you take, including over-the-counter medications and nutritional supplements. Taking PRIMLEV with certain other medicines can cause serious side effects that could lead to death.

**Tell your healthcare provider about all medicines you take, including any of the following:**

- **Medicines that affect an enzyme in your body called CYP3A4**, such as certain antibiotics like erythromycin, anti-fungal medicines like ketoconazole, and antiviral medicines like ritonavir.
- **Benzodiazepines**, or other drugs that affect your central nervous system such as sedatives, tranquilizers, muscle relaxants, or anti-anxiety medicines.
- **Any other medication containing acetaminophen.** Acetaminophen (one of the medicines in PRIMLEV) can cause liver failure, especially at higher doses. Many cases of liver injury from acetaminophen are the result of patients using more than one acetaminophen-containing product.

Ask your healthcare professional if you are unsure whether any of the medicines you take are in any of the categories listed above.

**Important information about taking PRIMLEV:**

- Do not change your dose. Take PRIMLEV exactly as prescribed by your healthcare provider.
- Take your prescribed dose every 6 hours as needed for pain. Do not take more than your prescribed dose. If you miss a dose, take your next dose at your usual time.

### IMPORTANT SAFETY INFORMATION (cont)

- Call your healthcare provider if the dose you are taking does not control your pain. Do not attempt to take more tablets than prescribed to get additional pain relief.
- If you have been taking PRIMLEV regularly, do not stop taking PRIMLEV without talking to your healthcare provider.
- After you stop taking PRIMLEV, dispose of unused tablets by flushing them down the toilet.

**While taking PRIMLEV, make sure you DO NOT:**

- Drive or operate heavy machinery until you know how PRIMLEV affects you. PRIMLEV can make you sleepy, drowsy, or lightheaded.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with PRIMLEV may cause you to overdose and die.

**What are the possible side effects of PRIMLEV?**

The most common side effects of PRIMLEV are constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, and abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.

**Life-threatening breathing difficulties** are possible with opioid medicines like PRIMLEV, even when used as recommended. The risks for severe breathing problems may be higher in the elderly or in people with other breathing disorders or lung conditions.

**Get emergency medical help if you have any of the following while taking PRIMLEV:**

- Trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue or throat, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

**USE ONLY AS DIRECTED BY YOUR HEALTHCARE PROFESSIONAL**

These are not all the possible side effects of PRIMLEV. Talk to your healthcare provider or pharmacist for more information or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Please see accompanying full Prescribing Information and Medication Guide in pocket.

**References:** 1. National Pharmaceutical Council. Pain: Current Understanding of Assessment, Management, and Treatments. December 2001. 2. Institute of Medicine. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. June 2011. [https://www.nap.edu/catalog/13172/relieving\\_pain\\_in\\_america\\_a\\_blueprint\\_for\\_transforming\\_prevention\\_care\\_education\\_and\\_research](https://www.nap.edu/catalog/13172/relieving_pain_in_america_a_blueprint_for_transforming_prevention_care_education_and_research). Accessed May 9, 2018. 3. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Recommendations for the medical management of osteoarthritis of the hip and knee. *Arthritis Rheum.* 2000;43:1905-1915. 4. Larson AM, Polson J, Fontana RJ, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. *Hepatology.* 2005;42:1364-1372. 5. Graham DJ, Campen D, Hui R, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study. *Lancet.* 2005;365:475-481. 6. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. *J Am Geriatr Soc.* 2009;57:1331-1346. 7. Gammaitoni AR, Galer BS, Bullock S, et al. Randomized, double-blind, placebo-controlled comparison of analgesic efficacy of oxycodone 10 mg/acetaminophen 325 mg versus controlled-release oxycodone 20 mg in postsurgical pain. *J Clin Pharmacol.* 2003;43:296-304. 8. US Food and Drug Administration. Acetaminophen overdose and liver injury—background and options for reducing injury. <http://wayback.archive-it.org/7993/20161022163745/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM179888.pdf>. Accessed May 9, 2018. 9. Perneger TV, Whelton PK, Klag MJ, et al. Risk of kidney failure associated with the use of acetaminophen, aspirin, and nonsteroidal anti-inflammatory drugs. *N Engl J Med.* 1994;331:1675-1679. 10. Tylenol® (acetaminophen) Professional Product Information. <https://www.tylenolprofessional.com>. Accessed May 9, 2018. 11. Bower WA, Johns M, Margolis HS, et al. Population-based surveillance for acute liver failure. *Am J Gastroenterol.* 2007;102:2459-2463. 12. US Food and Drug Administration. Manthripragada A, Zhou E, Ahmad SR, Cao KY. Characterization of acetaminophen overdose and related hepatotoxic events. <http://wayback.archive-it.org/7993/20161022163745/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM179888.pdf>. Accessed May 9, 2018. 13. US Food and Drug Administration. FDA Drug Safety Communication: prescription acetaminophen products to be limited to 325 mg per dosage unit; boxed warning will highlight potential for severe liver failure. January 13, 2011. <http://wayback.archive-it.org/7993/20161022163745/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM174699.pdf>. Accessed May 9, 2018. 14. Krenzelok EP. The FDA Acetaminophen Advisory Board Meeting - what is the future of acetaminophen in the United States? The perspective of a committee member. *Clin Toxicol (Phila).* 2009;47:784-789. 15. Acetaminophen Awareness Coalition. Common Medicines with Acetaminophen. <https://www.knowyourdose.org/common-medicines/>. Accessed May 9, 2018. 16. US Food and Drug Administration. Generale L. OTC and Rx acetaminophen market overview: years 2004-2008. <http://wayback.archive-it.org/7993/20161022163745/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM174699.pdf>. Accessed May 9, 2018. 17. Chen L, Schneider S, Wax P. Knowledge about acetaminophen toxicity among emergency department visitors. *Vet Hum Toxicol.* 2002;44:370-373. 18. Beaver WT. Combination analgesics. *Am J Med.* 1984;77:38-53. 19. Primlev [prescribing information]. Atlanta, GA: Akrimax Pharmaceuticals, LLC; 2012. 20. Oxycodone and Acetaminophen [prescribing information]. Morgantown, WV: Mylan Pharmaceuticals Inc; 2014.

**AKRIMAX**  
PHARMACEUTICALS

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AKR-PRIM-201

**PRIMLEV™**

Oxycodone HCl/Acetaminophen Ⓢ  
Available in 5/300, 7.5/300 & 10/300 mg

For severe pain relief...  
**COMBINATION THERAPY**  
+ Affordability



Pay \$0 for co-pays up to \$400 per valid Primlev prescription.\*

\*Offer valid for patients 18 years or older, except for prescriptions reimbursed in whole or in part under Medicaid, a Medicare drug benefit plan or other federal or state programs (such as medical assistance programs or private insurance or HMO insurance plans that reimburse the patient for the entire cost of their prescription).

**PRIMLEV™**

Oxycodone HCl/Acetaminophen Ⓢ  
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### INDICATIONS AND USAGE

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Please see accompanying full Prescribing Information and Medication Guide in pocket.

### IMPORTANT SAFETY INFORMATION (cont)

**Also tell your healthcare provider if you are:**

- **Pregnant or planning to become pregnant.** Using PRIMLEV for long periods during pregnancy can cause withdrawal symptoms in your newborn baby that can be dangerous or life-threatening if not recognized or treated.
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## PAIN CONTROL Is an Important Component of Patient Care

Relieving pain due to surgical procedure and/or other medical conditions has clear benefits for patients

- Improved patient quality of life (QOL)<sup>1</sup>
- Reduced use of hospital/healthcare resources<sup>1</sup>
- Increased patient satisfaction with treatment

“ Pain is a major driver for visits to physicians and other healthcare providers, a major reason for taking medications, a major cause of disability, and a key factor in quality of life and productivity. ”

— Institute of Medicine of the National Academies Report on Pain, 2011

### IMPORTANT SAFETY INFORMATION (cont)

Get emergency help right away if you take too much PRIMLEV (overdose). When you first start taking PRIMLEV, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur.

Taking PRIMLEV with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.

Never give anyone else your PRIMLEV. They could die from taking it. Store PRIMLEV away from children and in a safe place to prevent stealing or abuse. Selling or giving away PRIMLEV is against the law.

Please see accompanying full Prescribing Information and Medication Guide in pocket.

## PAIN CONTROL Is Not Without Risk

Many agents that effectively control pain can cause potentially serious adverse events (AEs)

DRUGS/CLASS	AEs
Acetaminophen (APAP) <sup>1,3,4</sup>	Liver toxicity
Nonsteroidal anti-inflammatory drugs (NSAIDs) <sup>1,3,5,6</sup>	Gastrointestinal (GI)/cardiovascular (CV)/renal complications Cyclooxygenase-2 reduces GI risk but not CV risk Use with extreme caution in elderly patients
Tricyclic antidepressants <sup>1</sup>	Dry mouth, urinary retention, constipation, sedation, sexual dysfunction, arrhythmias
Antiepileptic drugs <sup>1</sup>	Nausea, dizziness, restlessness
Opioids <sup>1</sup>	Abuse potential Nausea, constipation, somnolence, pruritus Risk of overdose or death

**PRIMLEV™**  
Oxycodone HCl/Acetaminophen   
Available in 5/300, 7.5/300 & 10/300 mg

### Who should not take PRIMLEV?

Do not take PRIMLEV if you:

- Have severe asthma, trouble breathing, or other lung problems
- Have a bowel blockage or have narrowing of the stomach or intestines
- Have a known allergy or hypersensitivity to oxycodone, acetaminophen, or any ingredient in PRIMLEV

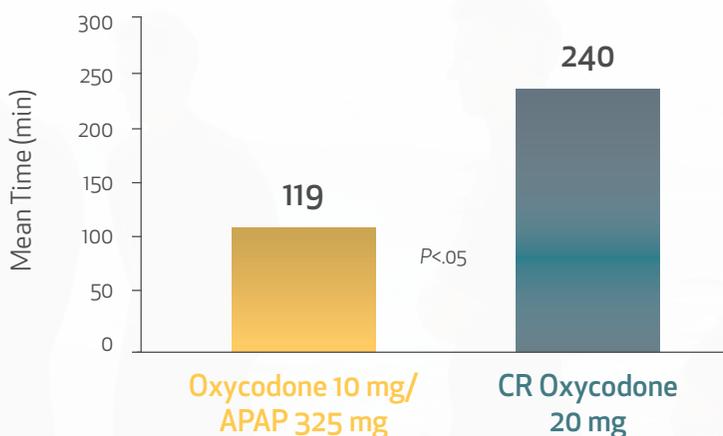
Before you take PRIMLEV, tell your healthcare provider if you:

- Have a history of head injury or any seizure disorder
- Have or have had liver, kidney, or thyroid problems
- Have problems urinating
- Have or have had pancreas or gallbladder problems
- Have ever abused street or prescription drugs, been addicted to alcohol, or have any history of mental health problems

# Effective, Faster-Acting Pain Relief

Oxycodone/APAP combinations provide faster pain relief vs high-dose, controlled-release monotherapy

## TIME TO PPR\*



\*Patients rated pain relief on a 5-point categorical scale (0=no relief, 4=complete relief).

- Patients treated with oxycodone 10 mg/APAP 325 mg experienced PPR significantly faster than did patients treated with CR oxycodone 20 mg<sup>7</sup>

## Tell your healthcare provider about all medicines you take, including any of the following:

- **Medicines that affect an enzyme in your body called CYP3A4**, such as certain antibiotics like erythromycin, anti-fungal medicines like ketoconazole, and antiviral medicines like ritonavir.
- **Benzodiazepines**, or other drugs that affect your central nervous system such as sedatives, tranquilizers, muscle relaxants, or anti-anxiety medicines.
- **Any other medication containing acetaminophen.** Acetaminophen (one of the medicines in PRIMLEV) can cause liver failure, especially at higher doses. Many cases of liver injury from acetaminophen are the result of patients using more than one acetaminophen-containing product.

Ask your healthcare professional if you are unsure whether any of the medicines you take are in any of the categories listed above.

## Important information about taking PRIMLEV:

- Do not change your dose. Take PRIMLEV exactly as prescribed by your healthcare provider.

# THE RISKS with Opioid Pain Medication

## Opioid-related risks include:

- Abuse potential
- Nausea, constipation, somnolence, pruritus
- Risk of overdose or death

## APAP Can Also Be Hazardous

Daily exposure >4000 mg is associated with liver toxicity<sup>3,4,8\*</sup>

- APAP poses increased risk for special populations, including:
  - Patients with kidney or liver disease<sup>1,9</sup>
  - Patients on multiple-drug regimens<sup>10</sup>
- APAP overdoses have been linked to acute liver failure and death:
  - **Acute liver failure:** APAP is the leading cause of acute liver failure in the United States<sup>4,11</sup>
  - **Fatal poisoning:** 18% of fatal poisoning calls to the National Poison Data System in 2007 were linked to APAP<sup>12</sup>

In January 2011, the FDA mandated limiting the amount of APAP to 325 mg per dosage in all prescription APAP-containing products by 2014.<sup>13,14\*</sup>

\*APAP is safe and effective when used according to the label.<sup>8</sup>

### IMPORTANT SAFETY INFORMATION

**Warnings:** Read and know all PRIMLEV warnings: addiction, misuse, abuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; hepatotoxicity; risks from concomitant use with benzodiazepines or other CNS depressants; adrenal insufficiency; severe hypertension; skin reactions; hypersensitivity/anaphylaxis; withdrawal.

# PRIMLEV™: Lowest Approved APAP Dose

An additional 25 mg of APAP per dose adds up over time

Cumulative 30-day difference in APAP exposure (PRIMLEV™ 300-mg APAP vs oxycodone/325-mg APAP formulations) <sup>9,19,20</sup>			
PRIMLEV™	Oxycodone/APAP	Maximal daily dosing regimen	Cumulative 30-day difference
5/300	5/325	12 doses per day for 30 days	9000 mg less APAP
7.5/300	7.5/325	8 doses per day for 30 days	6000 mg less APAP
10/300	10/325	6 doses per day for 30 days	4500 mg less APAP

### IMPORTANT SAFETY INFORMATION

**Adverse reactions:** Serious adverse reactions that may be associated with PRIMLEV™ use include respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, and shock (see OVERDOSAGE in full Prescribing Information in pocket).

**PRIMLEV™**  
Oxycodone HCl/Acetaminophen Ⓢ  
Available in 5/300, 7.5/300 & 10/300 mg

### IMPORTANT SAFETY INFORMATION (cont)

- Take your prescribed dose every 6 hours as needed for pain. Do not take more than your prescribed dose. If you miss a dose, take your next dose at your usual time.
  - Call your healthcare provider if the dose you are taking does not control your pain. Do not attempt to take more tablets than prescribed to get additional pain relief.
  - If you have been taking PRIMLEV regularly, do not stop taking PRIMLEV without talking to your healthcare provider.
  - After you stop taking PRIMLEV, dispose of unused tablets by flushing them down the toilet.
- While taking PRIMLEV, make sure you DO NOT:**
- Drive or operate heavy machinery until you know how PRIMLEV affects you. PRIMLEV can make you sleepy, drowsy, or lightheaded.

Please see accompanying full Prescribing Information and Medication Guide in pocket.

- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with PRIMLEV may cause you to overdose and die.

### What are the possible side effects of PRIMLEV?

The most common side effects of PRIMLEV are constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, and abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.

**Life-threatening breathing difficulties** are possible with opioid medicines like PRIMLEV, even when used as recommended. The risks for severe breathing problems may be higher in the elderly or in people with other breathing disorders or lung conditions.

# PRIMLEV™ Provides Balanced Pain Relief

## Balanced pain relief limits APAP exposure

- Dual-action pain relief: contains both centrally and peripherally acting agents<sup>18</sup>
- Combination of oxycodone and APAP is proven to reduce pain more effectively than higher-dose (20 mg) oxycodone monotherapy<sup>7,18</sup>
- Each dose contains 300 mg of APAP, the lowest FDA-approved dose of APAP found in an oxycodone/APAP combination
- Available in 3 convenient doses of oxycodone for initiation and titration (5 mg, 7.5 mg, and 10 mg, each in combination with 300 mg APAP)<sup>19</sup>



## IMPORTANT SAFETY INFORMATION (cont)

### Get emergency medical help if you have any of the following while taking PRIMLEV:

- Trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue or throat, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

### USE ONLY AS DIRECTED BY YOUR HEALTHCARE PROFESSIONAL

These are not all the possible side effects of PRIMLEV. Talk to your healthcare provider or pharmacist for more information or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or by visiting [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

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