Regulatory opportunities for improving communications: Safety communications and product labeling

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Dartmouth Medical School, Hanover, NH
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Disclosures

Co-founders of Informulary, Inc., a company that provides data about the benefits, harms and uncertainties of prescription drugs.
No industry funding.
Expert witness in testosterone litigation
Opportunity for FDA: Better communication

Wide concern that doctors prescribe too many opioids to too many people for too long.

Doctors and patients may overestimate the benefits – and underestimate the harms – of these drugs for chronic pain.

FDA might be able to improve prescribing by better communicating the benefits, harms and uncertainties of chronic opioids.
Improving communication

1. Efficacy and the state of the evidence
   Class information
   Specific drug

2. Serious opioid harms

3. Abuse-deterrent properties

4. Summarizing the evidence and basis of approval
Evidence review

No study of opioid therapy versus placebo, no opioid therapy, or non-opioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence is rated as insufficient (0 studies contributing)
DTC websites

No uncertainty about benefit in chronic pain

Extend your expectations about chronic pain with TRUE 12-HOUR CONTROL
Medication guides

ZOHYDRO® ER (zoh-hye-droh)
(hydrocodone bitartrate) extended-release capsules, CIi

ZOHYDRO ER is:
• A strong prescription pain medicine that contains an opioid (narcotic) that is used to treat pain severe enough to require daily, around-the-clock, long-term treatment with an opioid, when other pain treatments such as non-opioid pain medicines or immediate-release opioid medicines do not treat your pain well enough or you cannot tolerate them.
• A long acting extended-release medicine that can take your dose correctly as prescribed.
• Not for use to treat pain that is not severe.

Important information about ZOHYDRO ER:
• Get emergency help right away if you take too much ZOHYDRO ER (overdose). When you first start taking ZOHYDRO ER, when your dose is changed, or if you take too much (overdose), serious or life-threatening

ZOHYDRO ER is:
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Call your healthcare provider if the dose you are taking does not control your pain.
• Do not stop taking ZOHYDRO ER without talking to your healthcare provider.
• After you stop taking ZOHYDRO ER, flush any unused capsules down the toilet.

While taking ZOHYDRO ER DO NOT:
• Drive or operate heavy machinery, until you know how ZOHYDRO ER affects you. ZOHYDRO ER can make you sleepy, dizzy, or lightheaded.
• Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with ZOHYDRO ER may cause you to overdose and die.

The possible side effects of ZOHYDRO ER are:
• Constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain. Call your healthcare provider if you have any of these symptoms and they are severe.
• Get emergency medical help if you have:
  • Trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue or throat, extreme drowsiness, light-headedness when you are changing positions, or you are feeling faint.

These are not all the possible side effects of ZOHYDRO ER. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. For more information go to dailymed.nlm.nih.gov

ZOHYDRO ER is a registered trademark of Zosano, Inc. Manufactured by: Alkermes Gameaville LLC. Gameaville, GA. Distributed by: Zosano, Inc., San Diego.
Professional websites

No uncertainty about benefit in chronic pain

Patients with chronic pain may need more than short-term solutions

Zohydro® ER (hydrocodone bitartrate) Extended-Release Capsules, CI, with BeadTek™ is the ER formulation that delivers true 12-hour pain control, from start to finish.²
**Professional label**

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all of the information needed to use ZOHYDRO® ER safely and effectively. See full prescribing information for ZOHYDRO® ER.

**ZOHYDRO® ER** (hydrocodone bitartrate) extended-release capsules, for oral use, CIII

Initial U.S. Approval: 1945

**WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPiate WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL; AND CYTOCHROME P450 INTERACTION**

See full prescribing information for complete boxed warning.

- ZOHYDRO® ER exposes users to the risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient’s risk before prescribing, and monitor regularly for development of these behaviors or conditions. (5.1)
- Sudden, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow ZOHYDRO® ER whole to avoid exposure to a potentially lethal dose of hydrocodone. (5.2)
- Accidental ingestion of ZOHYDRO® ER, especially in children, can result in fatal overdose of hydrocodone. (5.2)
- Prolonged use of ZOHYDRO® ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.3)
- Instruct patients not to consume alcohol or any products containing alcohol while taking ZOHYDRO® ER because co-ingestion can result in fatal plasma hydrocodone levels. (5.4)
- Initiation of CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of hydrocodone from ZOHYDRO® ER. (5.5)

**RECENT MAJOR CHANGES**

- Revised 8/2014
- Indications and Usage
- Dosage and Administration

**INDICATIONS AND USAGE**

ZOHYDRO® ER is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. (1)

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve ZOHYDRO® ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioid) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
- ZOHYDRO® ER is not indicated as an as-needed (prn) analgesic. (1)

**CONTRAINDICATIONS**

- Significant respiratory depression (4)
- Acute or severe bronchial asthma (4)
- Known or suspected paralytic ileus (4)
- Hypersensitivity to hydrocodone bitartrate (4)

**WARNINGS AND PRECAUTIONS**

See Boxed WARNINGS

- Interactions with CNS depressants: Concomitant use may cause profound sedation, respiratory depression, and death. If discontinuation is required, consider dose reduction of one or both drugs. (5.4)
- Elderly, cachectic, debilitated patients, and those with chronic pulmonary disease: Monitor closely because of increased risk for life-threatening respiratory depression. (5.5, 5.6)
- Reproductive effects: Monitor during dose initiation and titration. (5.7)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of ZOHYDRO® ER in patients with impaired consciousness or coma susceptible to immunoassay of meperidine. (5.8)
- Concomitant use of CYP3A4 inhibitors may increase opioid effects. (5.13)

**ADVERSE REACTIONS**

Adverse reactions in ≥15% of patients in placebo-controlled trials include constipation, nausea, somnolence, fatigue, headache, dizziness, dry mouth, vomiting, pruritus, abdominal pain, oedema peripheral, upper respiratory tract infection, muscle spasm, urinary tract infection, back pain, and nausea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Zogenix, Inc. at 1-866-ZOGENIX or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

- Mixed agonist/antagonist and partial agonist analogs: Avoid use with ZOHYDRO® ER because they may reduce analgesic effect of ZOHYDRO® ER or precipitate withdrawal symptoms. (7.4)
- The use of MAO inhibitors or tricyclic antidepressants with ZOHYDRO® ER may increase the effect of either the antidepressant or ZOHYDRO® ER. (7.5)

**USE IN SPECIFIC POPULATIONS**

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Not recommended. (8.2)
- Hepatic impairment: No adjustment in starting dose with ZOHYDRO® ER is required in patients with mild or moderate hepatic impairment however, in patients with severe hepatic impairment, start with the lowest dose, 10 mg. Monitor these patients closely for adverse events such as respiratory depression. (8.6)
- Renal impairment: Use a lower initial dose of ZOHYDRO® ER in patients with renal impairment and monitor closely for adverse events such as respiratory depression. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

**REVISION HISTORY**

Revised: 01/2015

**DOSEAGE FORMS AND STRENGTHS**

- Extended-release capsules: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg (3)
There is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely. (CDC conclusion)

Long term efficacy and safety of opioids in treating chronic pain for more than 1 year have not been established. Pain is unlikely.” (CDC conclusion)
Improving communication

1. Efficacy and the state of the evidence
   - Class information
   - Specific drug

2. Serious opioid harms

3. Abuse-deterrent properties

4. Summarizing the evidence and basis of approval
14 CLINICAL STUDIES

Zohydro ER provided greater analgesia compared to placebo. There was a significant difference in the mean changes from Baseline to Week 12 in average weekly pain intensity Numeric Rating Scale (NRS) scores between the two groups.
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**Zohydro** (hydrocodone bitartrate) for severe, chronic pain requiring around-the-clock opioids

<table>
<thead>
<tr>
<th></th>
<th><strong>ZOHYDRO</strong></th>
<th><strong>PLACEBO</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>(20-100mg twice a day)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**How did Zohydro help?**

**Change in average pain level**

- 0.5 points less pain on a scale from 0 [no pain] to 10 [worst pain imaginable]
- 0.5 points more pain
- 1.0 points more pain
14 CLINICAL STUDIES

Percentage Improvement in Average Pain Intensity From Screening to Final Visit

- **48%** for ZOHYDRO ER
- **23%** for Placebo
Average pain intensity at baseline was 3 points. 50% improvement corresponds to 1.5 points less pain.
Zohydro (hydrocodone bitartrate) for severe, chronic pain requiring around-the-clock opioids

<table>
<thead>
<tr>
<th>How did Zohydro help?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in average pain level</strong></td>
</tr>
<tr>
<td>0.5 points less pain on a scale from 0 [no pain] to 10 [worst pain imaginable]</td>
</tr>
<tr>
<td><strong>Percent of people whose pain was ….</strong></td>
</tr>
<tr>
<td>Better by 50% or more (≥ 1.5 pain points)</td>
</tr>
<tr>
<td>Better by 80% or more (≥ 2 pain points)</td>
</tr>
<tr>
<td><strong>Medications for breakthrough pain</strong></td>
</tr>
<tr>
<td><strong>Change in disability</strong></td>
</tr>
<tr>
<td>4 points less disabled on a scale from 0 [none] to 100 [bedridden]</td>
</tr>
<tr>
<td><strong>Quality of life</strong></td>
</tr>
</tbody>
</table>
**Zohydro** (hydrocodone bitartrate) for severe, chronic pain requiring around-the-clock opioids

<table>
<thead>
<tr>
<th>How did Zohydro help?</th>
<th>ZOHYDRO (20-100mg twice a day)</th>
<th>PLACEBO (No drug)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Change in average pain level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 points less pain on a scale from 0 [no pain] to 10 [worst pain imaginable]</td>
<td>0.5 points</td>
<td>1.0 points</td>
</tr>
<tr>
<td></td>
<td>more pain</td>
<td>more pain</td>
</tr>
<tr>
<td><strong>Percent of people whose pain was ....</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better by 50% or more ($\geq 1.5$ pain points)</td>
<td>48%</td>
<td>23%</td>
</tr>
<tr>
<td>Better by 80% or more ($\geq 2$ pain points)</td>
<td>6%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Medications for breakthrough pain</strong></td>
<td>Taken about 69% of days in both groups</td>
<td></td>
</tr>
</tbody>
</table>

Both groups still had “severe” disability. How many people moved to lower disability categories?

| Quality of life | Not measured |
Improving FDA communications about opioids

*Routinely communicate the limits of efficacy of opioids for chronic pain*

Every opioid label, medication guide and FDA drug safety communication should include a “limitation of use” that the long-term benefits on pain, function and quality of life are unknown.

*Quantify the known - and acknowledge the unknown – efficacy of each opioid*
Improving communication

1. Efficacy and the state of the evidence
   Class information
   Specific drug

2. Serious opioid harms

3. Abuse-deterrent properties

4. Summarizing the evidence and basis of approval
ZOHYDRO ER exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient’s risk before prescribing, and monitor regularly for development of these behaviors or conditions. (5.1)

THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL

See full prescribing information

- ZOHYDRO ER exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient’s risk before prescribing, and monitor regularly for development of these behaviors or conditions.

- Serious, life-threatening, or fatal adverse drug reactions: Monitor closely, especially under conditions that may increase. Instruct patients to avoid exposure to a potentially fatal overdose.

- Accidental ingestion of ZOHYDRO ER may result in a fatal overdose of heroin.

- Prolonged use of ZOHYDRO ER may increase the risk of neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available. (5.3)

- Instruct patients not to consume alcohol or any products containing alcohol while taking ZOHYDRO ER because co-ingestion can
# Quantify serious harms – by dose

<table>
<thead>
<tr>
<th></th>
<th>No opioids</th>
<th>Opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low dose</td>
<td>High dose</td>
</tr>
<tr>
<td>Addiction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Car accidents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any overdose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal overdose</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Quantify serious harms – by dose

<table>
<thead>
<tr>
<th></th>
<th>No opioids</th>
<th>Opioids</th>
<th>Low dose</th>
<th>High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction (1.5 yrs)</td>
<td>0.004%</td>
<td>1%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Car accidents</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>Any overdose (1 yr)</td>
<td>?</td>
<td>0.2%</td>
<td>4.2%</td>
<td></td>
</tr>
<tr>
<td>Fatal overdose (1 yr)</td>
<td>?</td>
<td>0.01%</td>
<td>0.26%</td>
<td></td>
</tr>
</tbody>
</table>
Quantify serious harms – by dose

<table>
<thead>
<tr>
<th>Condition</th>
<th>No opioids</th>
<th>Opioids</th>
<th>High dose ≥ 100/120 MME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction (1.5 yrs)</td>
<td>0.004%</td>
<td>1%</td>
<td>6%</td>
</tr>
<tr>
<td>Car accidents</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Any overdose (1 yr)</td>
<td>?</td>
<td>0.2%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Fatal overdose (1 yr)</td>
<td>?</td>
<td>0.01%</td>
<td>0.26%</td>
</tr>
</tbody>
</table>

Accumulates over time
~1% chance by 4 years

NNH=17
National Academies could call on FDA or CDC to...

Reanalyze available data to generate “best” estimates of serious harms

Specific populations/settings

Standardize definitions (high vs low dose, codes for outcomes of interest)

Standardize time frames
Improving FDA communications about opioids

Routinely communicate the limits of efficacy of opioids for chronic pain
Every opioid label, medication guide and FDA drug safety communication should include a “limitation of use” that the long-term benefits on pain, function and quality of life are unknown.

Quantify the known - and acknowledge the unknown – efficacy of each opioid

Quantify the serious harms – addiction, overdose and death - of chronic use
Generate a current best estimates for these risks and highlight the substantial increased risk with longer use and higher doses in labeling, etc.
Improving communication

1. Efficacy and the state of the evidence
   Class information
   Specific drug

2. Serious opioid harms

3. Abuse-deterrent properties

4. Summarizing the evidence and basis of approval
Does this opioid have FDA–designated abuse-deterrent properties? And if so, what abuses do they deter?
Information Page: FDA approves extended-release, single-entity hydrocodone product with abuse-deterrent properties

[11/20/2014] FDA approved Hysingla ER (hydrocodone bitartrate), an extended-release (ER) opioid analgesic to treat pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Hysingla ER has approved labeling describing the product’s abuse-deterrent properties consistent with the FDA’s 2013 draft guidance for industry, Abuse-Deterrent Opioids – Evaluation and Labeling.

Hysingla ER has properties that are expected to reduce, but not totally prevent, abuse of the drug when chewed and then taken orally, or crushed and snorted or injected.
Does this opioid have FDA–designated abuse-deterrent properties? And if so, what abuse do they deter?
Standard presentation could make it easier to see which opioids do- or do not – have specific properties.

- **Long-acting opioid:**
  - FDA-designated: Chew and crush resistant (snort or inject) properties
  - FDA-designated: No chew or crush resistant properties
How does the label deal with this information?
Improving FDA communications about opioids

Routinely communicate the limits of efficacy of opioids for chronic pain
Every opioid label, medication guide and FDA drug safety communication should include a “limitation of use” that the long-term benefits on pain, function and quality of life are unknown.

Quantify the known - and acknowledge the unknown – efficacy of each opioid

Quantify the serious harms – addiction, overdose and death - of chronic use
Generate a current best estimates for these risks and highlight the substantial increased risk with longer use and higher doses in labeling, etc.

Highlight the abuse deterrent properties of each opioid or specify “None”
Include an explicit statement about which modes of abuse are addressed (e.g. snort, inject) in the label “highlights”, med guide, DTC and professional ads
Improving communication

1. Efficacy and the state of the evidence
   Class information
   Specific drug

2. Serious opioid harms

3. Abuse-deterrent properties

4. Summarizing the evidence and basis of approval
Efficiently communicate benefits and harms

We developed a format called the Drug Facts Box – a table summarizing the results of approval trials.
<table>
<thead>
<tr>
<th>Amount/Serving</th>
<th>Calories</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories from Fat</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% DV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Fat</td>
</tr>
<tr>
<td>Saturated Fat</td>
</tr>
<tr>
<td>Trans Fat</td>
</tr>
<tr>
<td>Cholesterol</td>
</tr>
<tr>
<td>Sodium</td>
</tr>
<tr>
<td>Total Carb.</td>
</tr>
<tr>
<td>Dietary Fiber</td>
</tr>
<tr>
<td>Sugars</td>
</tr>
<tr>
<td>Protein</td>
</tr>
</tbody>
</table>

- Vitamin A: 10% • Vitamin C: 30%
- Calcium: 4% • Iron: 30%
- Vitamin D: 15% • Thiamin: 30%
- Riboflavin: 30% • Niacin: 30%
- Vitamin B6: 30% • Folic Acid: 30%
- Vitamin B12: 30% • Zinc: 10%

*Percent Daily Values (DV) are based on a 2,000 calorie diet.
**ZOHYDRO ER Study Findings**

There was one trial the FDA used to approve ZOHYDRO ER. People who had a pain score of 4 or higher (out of 10) were given ZOHYDRO ER for 6 weeks. Participants were randomly assigned to either keep taking the drug or were given a sugar pill (placebo) for 3 months, and they did not know which they were taking. Here’s what happened:

### How did ZOHYDRO ER help?*

<table>
<thead>
<tr>
<th>Daily pain level: Patient’s rating of pain on an 11-point scale</th>
<th>ZOHYDRO ER</th>
<th>vs.</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average change</td>
<td>0.5 points worse</td>
<td>vs.</td>
<td>1 point worse</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Percent of people with various changes in pain level</th>
<th>ZOHYDRO ER</th>
<th>vs.</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worse, little or no change (pain rating changed by less than 1 point)</td>
<td>32%</td>
<td>vs.</td>
<td>69%</td>
</tr>
<tr>
<td>Moderate relief (pain improved 1 to 1.5 points)</td>
<td>20%</td>
<td>vs.</td>
<td>8%</td>
</tr>
<tr>
<td>Substantial relief (pain improved 1.5 to 2 points)</td>
<td>41%</td>
<td>vs.</td>
<td>12%</td>
</tr>
<tr>
<td>Almost complete relief (pain improved 2 points or more)</td>
<td>6%</td>
<td>vs.</td>
<td>4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disability: patients’ rating of disability on a 100-point scale</th>
<th>ZOHYDRO ER</th>
<th>vs.</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average change</td>
<td>3.2 points worse</td>
<td>vs.</td>
<td>7.6 points worse</td>
</tr>
</tbody>
</table>

### Patient satisfaction:

- Percentage of people “very much” or “completely” satisfied: 54% vs. 35%

### Need for pain rescue medication:

- Days pain rescue medication taken: Both patients in the ZOHYDRO ER and placebo group took additional medication to treat breakthrough pain about 69% of days during the trial.

### What were ZOHYDRO ER’s side effects?**

#### **BLACK BOX WARNING**

**ZOHYDRO ER carries the most serious level of FDA warning because it can cause:**

- Opioid addiction, which can lead to overdose and death – even at recommended doses.
- Breathing to stop, especially when starting or increasing the dose. Crushing, chewing or dissolving ZOHYDRO ER can rapidly release the drug and cause a fatal overdose.
- Fatal overdoses in children – even with a single dose.
- Infants and neonates – exposure to ZOHYDRO ER through breast milk can cause death. Women who have taken ZOHYDRO ER should not breastfeed.
- Dangerous reaction to alcohol – drinking alcohol with ZOHYDRO ER can cause a fatal overdose.

#### Symptom side effects

<table>
<thead>
<tr>
<th>Symptom side effects</th>
<th>ZOHYDRO ER (20-100 mg twice)</th>
<th>vs.</th>
<th>Placebo (No drug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation (8% more people)</td>
<td>8%</td>
<td>vs.</td>
<td>0%</td>
</tr>
<tr>
<td>Nausea (4% more)</td>
<td>7%</td>
<td>vs.</td>
<td>3%</td>
</tr>
<tr>
<td>Vomiting (4% more)</td>
<td>5%</td>
<td>vs.</td>
<td>1%</td>
</tr>
<tr>
<td>Abdominal pain (3% more)</td>
<td>3%</td>
<td>vs.</td>
<td>0%</td>
</tr>
<tr>
<td>Muscle spasms (3% more)</td>
<td>3%</td>
<td>vs.</td>
<td>1%</td>
</tr>
<tr>
<td>Leg swelling (3% more)</td>
<td>3%</td>
<td>vs.</td>
<td>0%</td>
</tr>
<tr>
<td>Urinary tract infections (2% more)</td>
<td>5%</td>
<td>vs.</td>
<td>2%</td>
</tr>
<tr>
<td>Diarrhea (2% more)</td>
<td>3%</td>
<td>vs.</td>
<td>1%</td>
</tr>
<tr>
<td>Stuffy nose (1% more)</td>
<td>1%</td>
<td>vs.</td>
<td>0%</td>
</tr>
</tbody>
</table>
Efficiently communicate benefits and harms

We developed a format called the Drug Facts Box – a table summarizing the results of approval trials.

We conducted a series of studies – including 2 national trials showing the drug facts box led to more accurate consumer perceptions of drug benefit and harm and improved decisions.

FDA confirmed our findings

National Academies consider recommending that FDA include quantitative data summaries like Drug Facts Boxes in labeling and consumer information.
Improving FDA communications about opioids

*Routinely communicate the limits of efficacy of opioids for chronic pain*
Every opioid label, medication guide and FDA drug safety communication should include a “limitation of use” that the long-term benefits on pain, function and quality of life are unknown.

*Quantify the known - and acknowledge the unknown – efficacy of each opioid*

*Quantify the serious harms –addiction, overdose and death - of chronic use*
Present current best estimates for these risks and highlight the substantial increased risk with longer use and higher doses in labeling, etc.

*Highlight the abuse deterrent properties of each opioid or specify “None”*
Include an explicit statement about which modes of abuse are addressed (e.g. snort, inject) in the label “highlights”, med guide, DTC and professional ads

*Summarize the the basis of new opioid approvals, including how public health was taken into account*
Help doctors and patients understand the basis of approval and understand any unique benefit or safety features.