Thoracotomy

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CASE PRESENTATION
A 71-year-old female with long-standing chronic obstructive pulmonary disease (COPD) found to have left lung cancer (T2aN0M0) requiring a left pneumonectomy for curative intent. Past medical history included a recent diagnosis of Non-Hodgkin’s Lymphoma involving the T12 vertebrae diagnosed during a kyphoplasty. Social history consisted of tobacco abuse for 60 pack years. Patient continues to smoke.

Test results
- Pre-operative evaluation included PET scan, brain MRI, cardiac evaluation, and pulmonary function testing (PFT)
  - Left ventricular ejection fraction: 75%
  - PFTs indicated poor results with an FEV1 of 1.52L and a D LCO of 43% of predicted, making patient high risk for PostOp pulmonary dysfunction

DESCRIPTION OF PROCEDURE
- Left thoracotomy; Left pneumonectomy; Mediastinal lymphadenectomy
- Repair of intra-op rib fracture using plate and screws
- Surgical time: 2 hours and 34 minutes

PATIENT’S PERIOPERATIVE ANALGESIC PROTOCOL

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</thead>
<tbody>
<tr>
<td>OFIRMEV® (acetaminophen) injection</td>
<td>1 g</td>
<td>1 g q6h for 24h (Three doses)</td>
<td>1 g q6h for 24h (One dose)</td>
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<tr>
<td>Bupivacaine 0.5%</td>
<td>30 cc</td>
<td>Initiated 7 h after surgery</td>
<td>Continued through 48 h</td>
<td></td>
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<tr>
<td>Hydromorphone PCA</td>
<td></td>
<td>upon complaint of pain</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>IV ketorolac</td>
<td></td>
<td>15 mg q6h prn (Two doses)</td>
<td>1-2 tabs q6h prn (One dose)</td>
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<td></td>
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<tr>
<td>PO hydrocodone bitartrate/acetaminophen (5 mg/325 mg)</td>
<td></td>
<td></td>
<td></td>
<td>1-2 tabs q6h prn (One dose)</td>
<td>1-2 tabs q6h prn (One dose)</td>
<td>1-2 tabs q6h prn (One dose)</td>
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</tr>
</tbody>
</table>

- Do not exceed the recommended maximum daily limits of acetaminophen by all routes.

INDICATIONS AND USAGE
OFIRMEV® (acetaminophen) injection is indicated for the management of mild to moderate pain, management of moderate to severe pain with adjunctive opioid analgesics, and reduction of fever.

IMPORTANT RISK INFORMATION

WARNING: RISK OF MEDICATION ERRORS AND HEPATOTOXICITY
Take care when prescribing, preparing, and administering OFIRMEV Injection to avoid dosing errors which could result in accidental overdose and death. In particular, be careful to ensure that:
- the dose in milligrams (mg) and milliliters (mL) is not confused;
- the dosing is based on weight for patients under 50 kg;
- infusion pumps are properly programmed; and
- the total daily dose of acetaminophen from all sources does not exceed maximum daily limits.

OFIRMEV contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed the recommended maximum daily limits, and often involve more than one acetaminophen-containing product.

Please see additional Important Risk Information on reverse and in accompanying Full Prescribing Information.

* This case study is intended only to provide healthcare professionals with an example of the use of OFIRMEV (acetaminophen) injection in the treatment of one specific patient. The outcomes described may not be representative of, and may differ significantly from, outcomes that may be obtained in treating other patients. This case study is not intended to provide specific treatment advice, recommendations, or opinions, and should not replace a clinician’s judgment with respect to the treatment of any particular patient.
## PostOp Outcomes

<table>
<thead>
<tr>
<th>PAIN ASSESSMENT*</th>
<th>OPIOID CONSUMPTION</th>
<th>PATIENT SATISFACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PostOp Day 0 (at end of procedure): Patient had adequate pain relief and was extubated</td>
<td>PostOp Day 0: total IV hydromorphone PCA - 3 mg</td>
<td>“Excellent” rating for pain control on a 4-point categorical scale</td>
</tr>
<tr>
<td>PostOp Day 0 (at 90 minutes PostOp): 5/10</td>
<td>PostOp Day 1: total IV hydromorphone PCA - 5.4 mg (assessed every 8 hours)</td>
<td></td>
</tr>
<tr>
<td>PostOp Day 1: 5/10</td>
<td>PostOp Day 2-7: PO hydrocodone bitartrate/acetaminophen - 1 tablet (5 mg/325 mg) per day</td>
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</tr>
</tbody>
</table>

*Based on a 10-point numeric rating scale (NRS).

### PATIENT OBSERVATIONS/DISCHARGE
- **PostOp Events:** No PostOp Nausea and Vomiting (PONV) or respiratory depression despite poor pulmonary function
- **Lab Tests:**
  - Liver function tests were unchanged from baseline on PostOp Days 3-4
- **Activities of Daily Living**
  - PostOp Day 1: Chest tube removed, up in chair using incentive spirometry with good cough effort
  - PostOp Day 2: Tolerating general diet, ambulating in room, transferred to telemetry unit
  - PostOp Day 3: Ambulating in hallway short distance
  - PostOp Day 4-7: Increasing ambulation and gradually performing self care activities
- **Patient was discharged on PostOp Day 7**
- **Patient was seen 2 weeks post discharge**

### IMPORTANT RISK INFORMATION

#### CONTRAINDICATIONS
- Acetaminophen is contraindicated in patients with:
  - known hypersensitivity to acetaminophen or to any of the excipients in the intravenous (IV) formulation.
  - severe hepatic impairment or severe active liver disease.

#### WARNINGS AND PRECAUTIONS
- Administration of acetaminophen in doses higher than recommended may result in hepatic injury, including the risk of liver failure and death. Do not exceed the maximum recommended daily dose of acetaminophen. The maximum recommended daily dose of acetaminophen includes all routes of acetaminophen administration and all acetaminophen-containing products administered, including combination products. Dosing errors could result in accidental overdose and death.
- Use caution when administering acetaminophen in patients with the following conditions: hepatic impairment or active hepatic disease, alcoholism, chronic malnutrition, severe hypovolemia (e.g., due to dehydration or blood loss), or severe renal impairment (creatinine clearance ≤ 30 mL/min).
- Rarely, acetaminophen may cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Hypersensitivity and anaphylaxis associated with the use of acetaminophen have been reported. Clinical signs included swelling of the face, mouth, and throat, respiratory distress, urticaria, rash, and pruritus. The antipyretic effects of OFIRMEV may mask fever.
- **Serious adverse reactions** may include hepatic injury, serious skin reactions, hypersensitivity, and anaphylaxis. **Common adverse reactions** in adults include nausea, vomiting, headache, and insomnia. **Common adverse reactions** in pediatric patients include nausea, vomiting, constipation, pruritus, agitation, and atelectasis.

### USE IN SPECIFIC POPULATIONS
- **Pregnancy:** Pregnancy Category C. OFIRMEV should be given to a pregnant woman only if clearly needed.
- **Breast Feeding:** While studies with OFIRMEV have not been conducted, acetaminophen is secreted in human milk in small quantities after oral administration.
- **Pediatrics:** The effectiveness of OFIRMEV for the treatment of acute pain and fever has not been studied in pediatric patients < 2 years of age.

Please see additional Important Risk Information, including boxed warning, on reverse side and in accompanying Full Prescribing Information.
**WARNING: Risk of Medication Errors and Hepatotoxicity**

See full prescribing information for complete boxed warning. Take care when prescribing, preparing, and administering OFIRMEV injection to avoid dosing errors which could result in accidental overdose and death.

**OFIRMEV** contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplantation or death. Some reports suggest the risk of liver injury in patients associated with the use of acetaminophen at doses that exceed the recommended doses, dose forms, and limits, and often involve more than one acetaminophen-containing product (5.1).

**INDICATIONS AND USAGE**

**Acetaminophen** (see Acetaminophen section) is indicated for:

- Management of mild to moderate pain
- Reduction of fever

See full prescribing information for complete prescribing information. See Acetaminophen section.

**DOSE AND ADMINISTRATION**

**OFIRMEV** may be given as a single repeated dose (2.1).

- **OFIRMEV** should be administered only as a 15-minute intravenous infusion. Do not add other medications to the OFIRMEV vial, therefore do not administer in a plastic intravenous container, or syringe.

See full prescribing information for complete prescribing information. See Acetaminophen section.

- **Adults and Adolescents Weighing 50 kg or Greater:**
  
  15 mg/kg of acetaminophen, maximum dose of 1000 mg, administered to a nursing woman. (8.3)

- **Adults and Adolescents Weighing Under 50 kg:**
  
  15 mg/kg of acetaminophen, maximum dose of 1000 mg, administered to a nursing woman. (8.3)

See full prescribing information for complete prescribing information. See Acetaminophen section.

- **Children:**
  
  Ofirmev is contraindicated in patients weighing less than 50 kg. OFIRMEV is a single-use vial intended for intravenous infusion. Each 100 mL glass vial contains acetylsalicylic acid (25 mg/mL) in 4% hydroxyethyl starch (200 kDa) with a total of 1000 mg acetaminophen. Optimal dosing and administration of OFIRMEV in children has not been established. OFIRMEV is for intravenous use only. Dosage of OFIRMEV should be administered only as a 15-minute intravenous infusion. Do not add other medications to the OFIRMEV vial, therefore do not administer in a plastic intravenous container, or syringe.

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- **Administration:**
  
  Children should not be given acetaminophen in doses higher than recommended by all routes of administration and from all acetaminophen-containing products including combination products; may result in hepatic injury, including the risk of liver failure and death. (5.1)

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  Children should not be given acetaminophen in doses higher than recommended by all routes of administration and from all acetaminophen-containing products including combination products; may result in hepatic injury, including the risk of liver failure and death. (5.1)
Drugs are sometimes not effective in pregnant women. While studies with ORIFMEV have not been conducted in pregnant women, there is no known evidence of harm to the fetus. However, due to the risk of maternal toxicity, ORIFMEV should be used only in pregnant women if the potential benefit justifies the potential risk to the fetus.

In a continuous breeding study, pregnant mice received oral acetaminophen during organogenesis at doses up to 0.85 times the maximum human daily dose (MHDD = 650 mg/kg). The safety and effectiveness of ORIFMEV for the treatment of acute pain and fever in pediatric patients 2 years and older is supported by evidence from adequate and well-controlled studies of ORIFMEV in adults. The safety and effectiveness of ORIFMEV have been demonstrated in controlled clinical trials in pregnant women; however, epidemiological data on oral acetaminophen during pregnancy in women have shown that pregnant women who take acetaminophen have an increased risk of major congenital malformations due to a risk of maternal toxicity. Therefore, ORIFMEV should be used only in pregnant women if the potential benefit justifies the potential risk to the fetus.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy (See Contraindications)

There are no studies of intrauterine acetaminophen in pregnant women. However, epidemiological data on oral acetaminophen use in pregnant women show no increased risk of major congenital malformations. Animal reproduction studies have not been conducted with ORIFMEV, and it is not known whether ORIFMEV can cause fetal harm when administered to a pregnant woman. ORIFMEV should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.

The results from a large population-based prospective cohort, including data from 24,424 women with live-born infants born between 1988 and 1998 in California, showed that oral acetaminophen use during pregnancy did not increase the risk of congenital malformations. However, the results did not control for other potential confounders, such as other prescription medications, or congenital malformations.

8.2 Labor and Delivery

There are no adequate and well-controlled studies with ORIFMEV during labor and delivery. Therefore, it should be used in such settings only after a careful benefit-risk assessment.

8.3 Nursing Mothers

Acetaminophen is contraindicated in breastfed infants with severe hepatic or severe active liver disease and should not be used in patients with hepatic disease or a history of chronic active liver disease (see Warnings and Precautions (5.1) and Contraindications (4)). A reduced total daily dose of acetaminophen may be warranted.

8.4 Pediatric Use

Acetaminophen is contraindicated in young children with evidence of hepatic toxicity may not be apparent until 48 to 72 hours after opening. Do not refrigerate or freeze. For single use only. The product should be used within 6 hours after opening. Do not reinject or freeze before opening.

14.1 Adult Fever

OFIRMEV was studied in 353 pediatric patients in two active-controlled, double-blind, and randomized pharmacokinetics trials (see in Specific Populations (4.6)).

14.2 Adult Fever

The efficacy of ORIFMEV 1000 mg in the treatment of adult fever was evaluated in randomized, double-blind, placebo-controlled clinical trials. The study was a 6-hour, single-dose, esmolol-induced fever study in healthy adult males. A statistically significant antipyretic effect of OFIRMEV was demonstrated when treated in comparison to placebo.

15 nursing mothers, the calculated infant daily dose of acetaminophen is approximately 1 – 2% of the maternal dose. While studies with OFIRMEV have not been conducted in pregnant women, the infant daily dose of acetaminophen is approximately 1% of the maternal dose.

Skin and subcutaneous tissue disorders: periorbital edema, hypoxia, pleural effusion, stridor, wheezing

8.3 Nursing Mothers

As the potential for systemic exposure of acetaminophen is approximately 1 – 2% of the maternal dose, the risk to the breastfed infant is likely to be small. Acetaminophen is secreted in human milk in small quantities. The maximum quantity of acetaminophen transferred from the mother to her breastfed infant in a 24-hour period is approximately 2 mg/kg/day. The calculated infant daily dose of acetaminophen is approximately 0.6% of the maternal dose for a 50 kg women.

8.2 Labor and Delivery

The pharmacokinetics of OFIRMEV have been studied in patients and healthy subjects from premature neonates up to adults 65 years of age. The pharmacokinetic profile of OFIRMEV is similar to that observed in children age 2 years and older. The clinical significance of these findings is not known.

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