OFIRMEV®
(acetaminophen) injection

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OFIRMEV® safely and effectively. See full prescribing information for OFIRMEV.

Initial U.S. Approval: 1951

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 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 (5.1).

INDICATIONS AND USAGE
OFIRMEV (acetaminophen) injection is indicated for:

• Management of mild to moderate pain
• Management of moderate to severe pain with adjunctive opioid analgesics
• Reduction of fever

DOSEAGE AND ADMINISTRATION

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

OFIRMEV should be administered only as a 15-minute intravenous infusion. (2.4)

Adults and Adolescents Weighing 50 kg and Over:

1000 mg every 6 hours or 650 mg every 4 hours to a maximum of 4000 mg per day. Minimum dosing interval of 4 hours. (2.2)

Adults and Adolescents Weighing Under 50 kg:

15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours to a maximum of 75 mg/kg per day. Minimum dosing interval of 4 hours. (2.2)

Children:

Children 2 to 12 years of age: 15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours to a maximum of 75 mg/kg per day. Minimum dosing interval of 4 hours. (2.2)

Injection for intravenous infusion.

Each 100 mL glass vial contains 1000 mg acetaminophen (10 mg/mL). (3)

CONTRAINDICATIONS

Acetaminophen is contraindicated:

• In patients with known hypersensitivity to acetaminophen or to any of the excipients in the IV formulation. (4)

• In patients with severe hepatic impairment or severe active liver disease. (4)

WARNINGS AND PRECAUTIONS

• Administration of acetaminophen in doses higher than recommended (by all routes of administration and from all sources) does not exceed the maximum daily limits, and often involve more than one acetaminophen-containing product. (see Warnings and Precautions [5.1]).

ADVERSE REACTIONS

The most common adverse reactions in patients treated with OFIRMEV were nausea, vomiting, headache, and insomnia in adult patients and nausea, vomiting, constipation, pruritus, agitation, and atelectasis in pediatric patients. (6.1)

DRUG INTERACTIONS

Substances that induce or regulate hepatic cytochrome P450 enzyme CYP2E1 may alter the metabolism of acetaminophen and increase its hepatotoxic potential. (7.1)

Chronic oral acetaminophen use at a dose of 4000 mg/day has been shown to cause an increase in international normalized ratio (INR) in some patients who have been stabilized on sodium warfarin as an anticoagulant. (7.2)

USE IN SPECIFIC POPULATIONS

• Pregnancy: Category C. (8.1)

• Labor and Delivery: Use with caution in labor and delivery. (8.2)

• Pediatrics: Use with caution in pediatric patients. (8.3)

• Geriatric Use: Use with caution in elderly patients. (8.5)

• Renal Impairment: Use with caution in patients with renal impairment. (8.7)

• Hepatic Impairment: Use with caution in patients with hepatic impairment or severe active liver disease. (8.6)

• Overdose: Use with caution in patients with overdose. (8.9)

FULL PRESCRIBING INFORMATION: CONTENTS *
WARNING: RISK OF MEDICATION ERRORS AND HEPATOTOXICITY

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FULL PRESCRIBING 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 maximum daily limits, and often involve more than one acetaminophen-containing product (see Warnings and Precautions [5.1]).

1 INDICATIONS AND USAGE

OFIRMEV® (acetaminophen) injection is indicated for:

• the management of mild to moderate pain
• the management of moderate to severe pain with adjunctive opioid analgesics
• the reduction of fever

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

OFIRMEV may be given as a single or repeated dose for the treatment of acute pain or fever. No dose adjustment is required when converting between oral acetaminophen and OFIRMEV dosing in adults and adolescents who weigh 50 kg and above. Calculated maximum daily dose of acetaminophen is based on all routes of administration (i.e., intravenous, oral, and rectal) and all products containing acetaminophen. Exceeding the maximum mg/kg daily dose of acetaminophen as described in Tables 1 and 2 may result in hepatic injury, including the risk of liver failure and death. To avoid the risk of overdose, ensure that the total amount of acetaminophen from all routes and from all sources does not exceed the maximum recommended dose.

2.2 Recommended Dosage: Adults and Adolescents

Table 1: Recommended Dosage for Adults and Adolescents

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Dosing Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 kg and over</td>
<td>1000 mg every 6 hours or 650 mg every 4 hours to a maximum of 4000 mg per day. Minimum dosing interval of 4 hours.</td>
</tr>
<tr>
<td>Under 50 kg</td>
<td>15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours to a maximum of 75 mg/kg per day. Minimum dosing interval of 4 hours.</td>
</tr>
</tbody>
</table>

Table 2: Recommended Dosage for Children

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Dosing Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 12</td>
<td>15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours to a maximum of 75 mg/kg per day. Minimum dosing interval of 4 hours.</td>
</tr>
</tbody>
</table>

3 DOSAGE FORMS AND STRENGTHS

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection</td>
<td>10 mg/mL</td>
</tr>
</tbody>
</table>

4 CONTRAINDICATIONS

Acetaminophen is contraindicated:

• In patients with known hypersensitivity to acetaminophen or to any of the excipients in the IV formulation.

• In patients with severe hepatic impairment or severe active liver disease.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatic Injury

Acetaminophen-containing products including combination products). (8.3)

5.2 Serious Skin Reactions

5.3 Risk of Medication Errors

5.4 Allergy and Hypersensitivity

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2.3 Recommended Dosage: Children
Children 2 to 12 years of age: the recommended dosage of OFIRMEV is 15 mg/kg every 6 hours or 12.5 mg/kg every 4 hours, with a maximum single dose of OFIRMEV of 15 mg/kg, a minimum dosing interval of 4 hours, and a maximum daily dose of acetaminophen of 75 mg/kg per day.

2.4 Instructions for Intravenous Administration
For adult and adolescent patients weighing ≥ 50 kg requiring 1000 mg doses of OFIRMEV, administer the dose by inserting a vented intravenous set through the septum of the 100 mL vial. OFIRMEV may be administered without further dilution. Examine the vial contents before dose preparation or administration. DO NOT USE if particulate matter or discoloration is observed. Administer the contents of the vial intravenously over 15-minutes. Use aseptic technique when preparing OFIRMEV for intravenous infusion. Do not add other medications to the OFIRMEV vial or infusion device.

For doses less than 1000 mg, the appropriate dose must be withdrawn from the vial and placed into a separate container prior to administration. Using aseptic technique, withdraw the appropriate dose (650 mg or weight-based) from an intact sealed OFIRMEV vial and place the measured dose in a separate, sterile container (e.g., glass bottle, plastic intravenous container, or syringe) for intravenous infusion to avoid the inadvertent delivery and administration of the total volume of the commercially available container. The entire 100 mL vial of OFIRMEV is not intended for use in patients weighing less than 50 kg. OFIRMEV is a single-use vial and the unused portion must be discarded.

Place small volume pediatric doses up to 60 mL in volume in a syringe and administer over 15 minutes using a syringe pump. Monitor the end of the infusion in order to prevent the possibility of an air embolism, especially in cases where the OFIRMEV infusion is the primary infusion.

Once the vacuum seal of the glass vial has been penetrated, or the contents transferred to another container, administer the dose of OFIRMEV within 6 hours.

Do not add other medications to the OFIRMEV solution. Diclofenac and chlorpromazine hydrochloride are physically incompatible with OFIRMEV, therefore do not administer simultaneously.

Table 1. Dosing for Adults and Adolescents

<table>
<thead>
<tr>
<th>Age group</th>
<th>Dose given every 4 hours</th>
<th><strong>Dose given every 6 hours</strong></th>
<th>Maximum single dose</th>
<th>Maximum total daily dose of acetaminophen (by all routes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents (13 years and older) weighing ≥ 50 kg</td>
<td>650 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
<td>4000 mg in 24 hours</td>
</tr>
<tr>
<td>Adults and adolescents (13 years and older) weighing &lt; 50 kg</td>
<td>12.5 mg/kg</td>
<td>15 mg/kg</td>
<td>15 mg/kg (up to 750 mg)</td>
<td>75 mg/kg in 24 hours (up to 3750 mg)</td>
</tr>
</tbody>
</table>

Table 2. Dosing for Children

<table>
<thead>
<tr>
<th>Age group</th>
<th>Dose given every 4 hours</th>
<th><strong>Dose given every 6 hours</strong></th>
<th>Maximum single dose</th>
<th>Maximum total daily dose of acetaminophen (by all routes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 2 to 12 years of age</td>
<td>12.5 mg/kg</td>
<td>15 mg/kg</td>
<td>15 mg/kg (up to 750 mg)</td>
<td>75 mg/kg in 24 hours (up to 3750 mg)</td>
</tr>
</tbody>
</table>

6 ADVERSE REACTIONS
The following serious adverse reactions are discussed elsewhere in the labeling:
- Hepatic Injury [see Warnings and Precautions (5.1)]
- Serious Skin Reactions [see Warnings and Precautions (5.2)]
every 8 hours schedule. The maximum exposure was 7.7, 6.4, 6.8, and 7.1 days in neonates, infants, children, and adolescents, respectively.

The most common adverse events (incidence ≥ 5%) in pediatric patients treated with OFIRMEV were nausea, vomiting, constipation, pruritus, agitation, and atelectasis.

Other Adverse Reactions Observed During Clinical Studies of OFIRMEV in Pediatrics

The following additional treatment-emergent adverse reactions were reported by pediatric subjects treated with OFIRMEV (n=355) that occurred with an incidence of at least 1%:

- Blood and lymphatic system disorders: anemia
- Cardiac disorders: tachycardia
- Gastrointestinal disorders: abdominal pain, diarrhea
- General disorders and administration site conditions: injection site pain, edema peripheral, pyrexia
- Investigations: hepatic enzyme increase
- Metabolism and nutrition disorders: hypoalbuninemia, hypokalemia, hypomagnesemia, hypophosphatemia, hypervolemia
- Musculoskeletal and connective tissue disorders: muscle spasm, pain in extremity
- Nervous system disorders: headache
- Psychiatric disorders: insomnia
- Renal and urinary disorders: oliguria
- Respiratory, thoracic and mediastinal disorders: pulmonary edema, hypoxia, pleural effusion, stridor, wheezing
- Skin and subcutaneous tissue disorders: peri-orbital edema, rash
- Vascular disorders: hypertension, hypotension

7 DRUG INTERACTIONS

7.1 Effects of other Substances on Acetaminophen

Substances that induce or regulate hepatic cytochrome enzyme CYP2E1 may alter the metabolism of acetaminophen and increase its hepatotoxic potential. The clinical consequences of these effects have not been established. Effects of ethanol are complex, because excessive alcohol usage can induce hepatic cytochromes, but ethanol also acts as a competitive inhibitor of the metabolism of acetaminophen.

7.2 Anticoagulants

Chronic oral acetaminophen use at a dose of 4000 mg/day has been shown to cause an increase in international normalized ratio (INR) in some patients who have been stabilized on sodium warfarin as an anticoagulant. As no studies have been performed evaluating the short-term use of OFIRMEV in patients on oral anticoagulants, more frequent assessment of INR may be appropriate in such circumstances.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C:

There are no studies of intravenous 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 IV acetaminophen, and it is not known whether OFIRMEV can cause fetal harm when administered to a pregnant woman. OFIRMEV should be given to a pregnant woman only if clearly needed. The results from a large population-based prospective cohort, including data from 26,424 women with live born singletons who were exposed to oral acetaminophen during the first trimester, indicate no increased risk for congenital malformations, compared to a control group of unexposed children. The rate of congenital malformations (4.3%) was similar to the rate in the general population. A population-based, case-control study from the National Birth Defects Prevention Study showed that 11,610 children with prenatal exposure to acetaminophen during the first trimester had no increased risk of major birth defects compared to 4,500 children in the control group. Other epidemiological data showed similar results.

While animal reproduction studies have not been conducted with intravenous acetaminophen, studies in pregnant rats that received oral acetaminophen during organogenesis at doses up to 0.85 times the maximum human daily dose (MHDD = 4.4 grams/day, based on a body surface area comparison) showed evidence of fetotoxicity (reduced fetal weight and length) and a dose-related increase in bone variations (reduced ossification and rudimentary rib changes). Offspring had no evidence of external, visceral, or skeletal malformations. When pregnant rats received oral acetaminophen throughout gestation at doses of 1.2 times the MHDD (based on a body surface area comparison), areas of necrosis occurred in both the liver and kidney of pregnant rats and fetuses. These effects did not occur in animals that received oral acetaminophen at doses 0.3 times the MHDD, based on a body surface area comparison.

In a continuous breeding study, pregnant mice received 0.25, 0.5, or 1.0% acetaminophen via the diet (357, 715, and 1430 mg/kg/day). These doses are approximately 0.43, 0.87, and 1.7 times the MHDD, respectively, based on a body surface area comparison. A dose-related reduction in body weights of fourth and fifth litter offspring of the treated mating pair occurred during lactation and post-weaning at all doses. Animals in the high dose group had a reduced number of litters per mating pair, male offspring with an increased percentage of abnormal sperm, and reduced birth weights in the next generation pups.

8.2 Labor and Delivery

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

8.3 Nursing Mothers

While studies with OFIRMEV have not been conducted, acetaminophen is secreted in human milk in small quantities after oral administration. Based on data from more than 15 nursing mothers, the calculated infant daily dose of acetaminophen is approximately 1 – 2% of the maternal dose. There is one well-documented report of a rash in a breast-fed infant that resolved when the mother stopped acetaminophen use and recurred when she resumed acetaminophen use. Caution should be exercised when OFIRMEV is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of OFIRMEV for the treatment of acute pain and fever in pediatric patients ages 2 years and older is supported by evidence from adequate and well-controlled studies of OFIRMEV in adults. Additional safety and pharmacokinetic data were collected in 355 patients across the full pediatric age strata, from premature neonates (≥ 32 weeks post menstrual age) to adolescents. The effectiveness of OFIRMEV for the treatment of acute pain and fever has not been studied in pediatric patients < 2 years of age [see Dosage and Administration (2.3) and Pharmacokinetics (12.3)].

8.5 Geriatric Use

Of the total number of subjects in clinical studies of OFIRMEV, 15% were age 65 and over, while 5% were age 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Patients with Hepatic Impairment

Acetaminophen is contraindicated in patients with severe hepatic impairment or severe active liver disease and should be used with caution in patients with hepatic impairment or active liver disease [see Warnings and Precautions (5.1) and Clinical Pharmacology (12)]. A reduced total daily dose of acetaminophen may be warranted.

8.7 Patients with Renal Impairment

In cases of severe renal impairment (creatinine clearance ≤ 30 mL/min), longer dosing intervals and a reduced total daily dose of acetaminophen may be warranted.

10 OVERDOSAGE

Signs and Symptoms

In acute acetaminophen overdose, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur. Plasma acetaminophen levels > 300 mcg/mL at 4 hours after oral ingestion were associated with hepatic damage in 90% of patients; minimal hepatic damage is anticipated if plasma levels at 4 hours are < 150 mcg/mL or < 37.5 mcg/mL at 12 hours after ingestion. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diarrhea, and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion.

Treatment

If an acetaminophen overdose is suspected, obtain a serum acetaminophen assay as soon as possible, but no sooner than 4 hours following oral ingestion. Obtain liver function studies initially and repeat at 24-hour intervals. Administer the antidote N-acetylcysteine (NAC) as early as possible. As a guide to treatment of acute ingestion, the acetaminophen level can be plotted against time since oral ingestion on a nomogram (Rumack-Matthew). The lower toxic line on the nomogram is equivalent to 150 mcg/mL at 4 hours and 37.5 mcg/mL at 12 hours. If serum level is above the lower line, administer the entire course of NAC treatment. Withhold NAC therapy if the acetaminophen level is below the lower line.

For additional information, call a poison control center at 1-800-222-1222.

11 DESCRIPTION

Acetaminophen is a non-salicylate antipyretic and non-opioid analgesic agent. Its chemical name is N-acetyl-p-aminophenol. Acetaminophen has a molecular weight of 151.16. Its structural formula is:
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
The precise mechanism of the analgesic and antipyretic properties of acetaminophen is not established but is thought to primarily involve central actions.

12.2 Pharmacodynamics
Acetaminophen has been shown to have analgesic and antipyretic activities in animal and human studies. Single doses of OFIRMEV up to 3000 mg and repeated doses of 1000 mg every 6 hours for 48 hours have not been shown to cause a significant effect on platelet aggregation. Acetaminophen does not have any immediate or delayed effects on small-vessel hemostasis. Clinical studies of both healthy subjects and patients with hemophilia showed no significant changes in bleeding time after receiving multiple doses of oral acetaminophen.

12.3 Pharmacokinetics

Distribution
The pharmacokinetics of OFIRMEV have been studied in patients and healthy subjects from premature neonates up to adults 60 years old. The pharmacokinetic profile of OFIRMEV has been demonstrated to be dose proportional in adults following administration of single doses of 500, 650, and 1000 mg.

The maximum concentration (Cmax) occurs at the end of the 15 minute intravenous infusion of OFIRMEV. Compared to the same dose of oral acetaminophen, the Cmax following administration of OFIRMEV is up to 70% higher, while overall exposure (area under the concentration time curve [AUC]) is very similar.

Pharmacokinetic parameters of OFIRMEV (AUC, Cmax, terminal elimination half-life [T1/2], systemic clearance [CL], and volume of distribution at steady state (Vss)) following administration of a single intravenous dose of 15 mg/kg for the pediatric population and 1000 mg in adults are summarized in Table 4.

<table>
<thead>
<tr>
<th>Table 4. OFIRMEV Pharmacokinetic Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subpopulations</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Neonates</td>
</tr>
<tr>
<td>Infants</td>
</tr>
<tr>
<td>Children</td>
</tr>
<tr>
<td>Adolescents</td>
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<tr>
<td>Adults</td>
</tr>
</tbody>
</table>

The pharmacokinetic exposure of OFIRMEV observed in children and adolescents is similar to adults, but higher in neonates and infants. Dosing simulations from pharmacokinetic data in infants and neonates suggest that dose reductions of 33% in infants 1 month to < 2 years of age, and 50% in neonates up to 28 days, with a minimum dosing interval of 6 hours, will produce a pharmacokinetic exposure similar to that observed in children age 2 years and older.

At therapeutic levels, binding of acetaminophen to plasma proteins is low (ranging from 10% to 25%). Acetaminophen appears to be widely distributed throughout most body tissues except fat.

Metabolism and Excretion
Acetaminophen is primarily metabolized in the liver by first-order kinetics and involves three principal separate pathways: Conjugation with glucuronide, conjugation with sulfate, and oxidation via the cytochrome P450 enzyme pathway, primarily CYP2E1, to form a reactive intermediate metabolite (N-acetyl-p-benzoquinone imine or NAPQI). With therapeutic doses, NAPQI undergoes rapid conjugation with glutathione and is then further metabolized to form cysteine and mercapturic acid conjugates.

Acetaminophen metabolites are mainly excreted in the urine. Less than 5% is excreted in the urine as unconjugated (free) acetaminophen and more than 90% of the administered dose is excreted within 24 hours.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Long-term studies in mice and rats have been completed by the National Toxicology Program to evaluate the carcinogenic potential of acetaminophen. In 2-year feeding studies, F344/N rats and B6C3F1 mice were fed a diet containing acetaminophen up to 6000 ppm. Proliferation of female rats demonstrated increased incidence of carcinogenic activity based on increased incidences of mononuclear cell leukemia at 0.8 times the maximum human daily dose (MHDD) of 4 grams/day, based on a body surface area comparison. In contrast, there was no evidence of carcinogenic activity in male rats (0.7 times) or mice (1.2-1.4 times the MHDD, based on a body surface area comparison).

Mutagenesis
Acetaminophen was not mutagenic in the bacterial reverse mutation assay (Ames test). In contrast, acetaminophen tested positive in the in vitro mouse lymphoma assay and in the in vitro chromosomal aberration assay using human lymphocytes. In the published literature, acetaminophen has been reported to be clastogenic when administered a dose of 1500 mg/kg/day to the rat model (3.6-times the MHDD, based on a body surface area comparison). In contrast, no clastogenicity was noted at a dose of 750 mg/kg/day (1.8-times the MHDD, based on a body surface area comparison), suggesting a threshold effect.

Impairment of Fertility
In studies conducted by the National Toxicology Program, fertility assessments have been completed in Swiss mice via a continuous breeding study. There were no effects on fertility parameters in mice consuming up to 1.7 times the MHDD of acetaminophen, based on a body surface area comparison. Although there was no effect on sperm motility or sperm density in the epididymis, there was a significant increase in the percentage of abnormal sperm in mice consuming 1.7 times the MHDD (based on a body surface area comparison) and there was a reduction in the number of mating pairs producing a fifth litter at this dose, suggesting the potential for cumulative toxicity with chronic administration of acetaminophen near the upper limit of daily dosing.

Published studies in rodents report that oral acetaminophen treatment of male animals at doses that are 1.2 times the MHDD and greater (based on a body surface area comparison) result in decreased testicular weights, reduced spermatogenesis, reduced fertility, and reduced implantation sites in females given the same doses. These effects appear to increase with the duration of treatment. The clinical significance of these findings is not known.

14 CLINICAL STUDIES
14.1 Adult Acute Pain

The efficacy of OFIRMEV in the treatment of acute pain in adults was evaluated in two randomized, double-blind, placebo-controlled clinical trials. The study was a 6-hour, single-dose, endotoxin-induced fever study in 60 healthy adult males. A statistically significant antipyretic effect of OFIRMEV was demonstrated through 6 hours in comparison to placebo. The mean temperature over time is shown in Figure 1.

14.2 Adult Fever

The efficacy of OFIRMEV 1000 mg in the treatment of adult fever was evaluated in one randomized, double-blind, placebo-controlled clinical trial. The study was a 6-hour, single-dose, endotoxin-induced fever study in 60 healthy adult males. A statistically significant antipyretic effect of OFIRMEV was demonstrated through 6 hours in comparison to placebo. The mean temperature over time is shown in Figure 1.

14.3 Pediatric Acute Pain and Fever

OFIRMEV was studied in 355 pediatric patients in two active-controlled and three open-label safety and pharmacokinetic trials [see Use in Specific Populations (8.4)].

16 HOW SUPPLIED/STORAGE AND HANDLING

NDC 43825-102-01 - OFIRMEV® (acetaminophen) Injection is supplied in a 100 mL glass vial containing 1000 mg acetaminophen (10 mg/mL) in cartons of 24 vials.

OFIRMEV should be stored at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature].

For single use only. The product should be used within 6 hours after opening. Do not refrigerate or freeze.

Manufactured for: Mallinckrodt Hospital Products Inc. Hazelwood, MO 63042 USA

Revised: 12/2014

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U.S. PATENT NUMBERS: 6,028,222; 6,992,218
OFV15698K