Acetaminophen Injection

Brand names	Ofirmev. Paracetamol is a generic acetaminophen that is used in Europe.
Medication error potential	Care should be taken when prescribing, preparing, and administering to avoid dosing errors that could result in accidental overdose and death.[1,3] Calculating the dosage in milligrams (mg) but then administering the solution in milliliters (mL) has caused a 10-fold dosing error in children.[1] The dose should be based on weight in those <50 kg.[3] Look-alike, sound-alike drug names. Acetaminophen may be confused with acetaZOLAMIDE.[2]
Contraindications and warnings	**U.S. boxed warning:** 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 doses that exceed the recommended maximum daily limits and often involve more than one acetaminophen-containing product. Care should be taken when prescribing, preparing, and administering to avoid dosing errors that could result in accidental overdose and death. (See the Medication Error Potential section.)[3] **Contraindications:** Past hypersensitivity to acetaminophen or any of its components.[3] Severe hepatic impairment or severe active liver disease.[3] **Warnings:** Do not exceed the maximum recommended daily dose of acetaminophen (by all routes of administration and all acetaminophen-containing products including combination products). Discontinue immediately at the first appearance of skin rash and if symptoms associated with allergy or hypersensitivity occur.
Infusion-related cautions	Postmarketing reports of hypersensitivity and anaphylaxis, which includes swelling of the face, mouth, and throat; respiratory distress; urticaria; rash; and pruritus.[3] Life-threatening anaphylaxis has occurred.[3]
Dosage	**Fever/pain in those unable to tolerate oral or rectal administration:** Effectiveness in acute pain and fever has not been studied in patients <2 years of age.[3] Some recommend that acetaminophen not be used in those <32 weeks.[6] A total of 355 pediatric patients (47 neonates, 64 infants, 171 children, and 73 adolescents) have received Ofirmev in active-controlled and open-label clinical trials. Patients received doses up to 15 mg/kg every 4, 6, or 8 hours. The maximum exposure was 7.7, 6.4, 6.8, and 7.1 days in neonates, infants, children, and adolescents, respectively.[3] 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 (7.5 mg/kg q 6 hr), with a minimum dosing interval of 6 hours, will produce a pharmacokinetic exposure similar to that observed in children age 2 years and older.[3] When used for moderate-to-severe pain, acetaminophen should be used in conjunction with opioid analgesics. **Neonates (preterm):** Limited data are available. 7.5 mg/kg q 8 hr for neonates with a postconceptual age (PCA) between 28 and 32 weeks,[8] 10 mg/kg q 12 hr for neonates with a PCA of <31 weeks,[7] 7.5 mg/kg q 6 hr for neonates with a PCA between 33 and 36 weeks,[8] and 10 mg/kg q 8 hr for neonates with a PCA between 31 and 36 weeks.[7] **Neonates (full-term):** Some administer a loading dose of 20 mg/kg[8] followed by 10–15 mg/kg q 6 hr,[7,8] 12.5 mg/kg q 6 hr,[3,4] or 15 mg/kg q 8 hr.[3,4] **Infants to 2 years:** 15 mg/kg q 6 hr or 12.5 mg/kg q 4 hr[4] **2–12 years (<50 kg):** 15 mg/kg q 6 hr or 12.5 mg/kg q 4 hr. Maximum daily dose of 75 mg/kg up to 3750 mg, which includes acetaminophen from all routes and all products.[3] **Adolescents and *adults* ≥50 kg:** 1000 mg q 6 hr or 650 mg q 4 hr with a maximum daily dose of 4000 mg, which includes acetaminophen from all routes and all products.[3]

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Dosage *(cont.)*	**Patent ductus arteriosus (PDA; closure of the ductus arteriosus):** Limited data are available. To date, all reports have involved administration of paracetamol. Acetaminophen should be used in those who have failed or who have a contraindication to an NSAID. Several studies have noted the successful and safe use of *oral* paracetamol for closure of a PDA.[9-12] Ten preterm infants (24–29 weeks gestational age) with a hemodynamically significant PDA were given 15 mg/kg q 6 hr of paracetamol for 3 days. Duration was extended to 6 days if the PDA persisted. The ductus successfully closed in all patients.[13] Another group reported administration of 10 mg/kg q 8 hr in 13 preterm neonates. The PDA closed in 83.3% of patients.[14] Conversely, two letters described failure of the ductus to close in patients given paracetamol. Many patients in these reports had failed ibuprofen.[15,16]
Dosage adjustment in organ dysfunction	Use with extreme caution in those with hepatic impairment as acetaminophen is contraindicated in those with severe hepatic impairment or severe active liver disease.[3] Dosage adjustment may be needed if CrCl is <30 mL/min.[3] If CrCl is <10 mL/min or the patient is receiving intermittent hemodialysis or peritoneal dialysis, administer q 8 hr. No adjustment needed in continuous renal replacement therapy.[3]
Maximum dosage	15 mg/kg up to 1000 mg/dose.[3] The total daily dose from all sources should not exceed a maximum daily dose of 75 mg/kg/day or 4000 mg/day.[3]
Additives	None
Suitable diluents	Does not require further dilution[3] but can be diluted in D5W, D10W, LR, D5LR, NS, and D5NS.[3]
Maximum concentration	1000 mg/100 mL (10 mg/mL)[3]
Preparation and delivery	*Parenteral products should be visually inspected for particulate matter and discoloration before use. Refer to appropriate references for more information on compatibility with other drugs and solutions; compatibility following Y-site delivery, and suggested storage and extended stability.*[5] **Preparation:** For those weighing ≥50 kg, administer without further dilution. For doses <1000 mg, the appropriate dose must be withdrawn from the vial and placed into a separate container (e.g., glass bottle, plastic IV container, or syringe) prior to administration.[3] **Stability:** Store intact vials at room temperature (20°C to 25°C). Do not refrigerate or freeze.[3] Should be used within 6 hours of accessing the vial or transferring the contents to another container.[3] If further diluted, stable for 1 hour.[3] **Compatibility:** Compatible in solutions of D5W and NS and compatible for Y-site administration with D5W, D10W, NS, LR, D5LR, and D5NS. Physically incompatible with diazepam and chlorpromazine hydrochloride.[3] Physically incompatible when admixed with acyclovir, diazepam, and chlorpromazine hydrochloride[3,5] or when infused via Y-site delivery.[5]
IV push	Not recommended[3]
Intermittent infusion	Over 15 minutes[3]
Continuous infusion	Not recommended[3]
Other routes of administration	None