



## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **CIATACRURIUM BESYLATE INJECTION** safely and effectively. See full prescribing information for **CIATACRURIUM BESYLATE INJECTION**.

**CIATACRURIUM BESYLATE Injection, for intravenous use**  
Initial U.S. Approval: 1905

## INDICATIONS AND USAGE

Ciatacrurium bescylate injection is a nondepolarizing neuromuscular blocker indicated:

- as an adjunct to general anesthesia to facilitate tracheal intubation in adults and in pediatric patients 1 month to 12 years of age (1)
  - to provide skeletal muscle relaxation during surgery in adults and in pediatric patients 2 to 12 years of age as a bolus or infusion maintenance (1)
  - for mechanical ventilation in the ICU in adults (1)
- Limitations of use**
- Ciatacrurium bescylate injection is not recommended for rapid sequence endotracheal intubation due to the time required for its onset of action (1)

## DOSSAGE AND ADMINISTRATION

Store Ciatacrurium bescylate injection with the cap and ferrule intact and in a manner that minimizes the possibility of selecting the wrong product (2.1).

- Administer intravenously only if or under the supervision of experienced clinicians familiar with drug's actions and possible complications (2.1)
- Use only if personnel and facilities for resuscitation and life support, and a ciatacrurium bescylate antagonist are immediately available (2.1)
- Use a peripheral nerve stimulator to determine adequacy of blockade (e.g., need for additional doses), minimize risk of overdosage or underdosage, assess extent of recovery from blockade, potentially limit exposure to toxic metabolites through dose titration, and facilitate more rapid reversal of ciatacrurium bescylate-induced paralysis (2.1)
- See the Full Prescribing Information for:
  - Dosage and administration instructions in adults, pediatric patients, geriatric patients, patients with neuromuscular diseases, burns, and stage renal disease, and patients undergoing coronary artery bypass graft surgery with induced hypothermia (2.2, 2.3, 2.4, 2.5)
  - Continuous infusion rates (2.6)
  - Preparation instructions (2.7)
  - Drug compatibility (2.8)

## DOSSAGE FORMS AND STRENGTHS

- Injection:**
- 10 mg/mL (2 mg/mL) in single-dose vials (3)
  - 200 mg/10 mL (20 mg/mL) and benzyl alcohol as a preservative in multiple-dose vials (3)
  - 200 mg/20 mL (10 mg/mL) in single-dose vials (3)

## FULL PRESCRIBING INFORMATION-CONTENTS\*

### 1 INDICATIONS AND USAGE

#### 2 INDICATIONS AND ADMINISTRATION

1. Important Dosage and Administration Instructions
2. Recommended Ciatacrurium Bescylate Injection Dose for Performing Tracheal Intubation
3. Recommended Maintenance Bolus Ciatacrurium Bescylate Injection in Adult Surgical Procedures
4. Dosage in Burn Patients
5. Dosage for Continuous Infusion
6. Rate Tables for Continuous Infusion
7. Preparation of Ciatacrurium Bescylate Injection
8. Drug Compatibility

#### 3 DOSSAGE FORMS AND STRENGTHS

#### 4 CONTRAINDICATIONS

#### 5 WARNINGS AND PRECAUTIONS

- 5.1. Residual Paralysis
- 5.2. Risk of Serious Adverse Reactions in Infants due to Benzyl Alcohol Preservative in 10 mL Multiple-Dose Vials
- 5.3. Risk of Severe Hypotension
- 5.4. Hypersensitivity Reactions Including Anaphylaxis
- 5.5. Risk of Death Due to Medication Errors
- 5.6. Risk for Infection
- 5.8. Potential of Neuromuscular Blockade
- 5.9. Resistance to Neuromuscular Blockade with Certain Drugs
- 5.10 Malignant Hyperthermia (MH)

#### 6 ADVERSE REACTIONS

- 6.1. Clinical Studies Experience
- 6.2 Postmarketing Experience

#### 7 DRUG INTERACTIONS

- 7.1 Clinically Significant Drug Interactions
- 7.2 Drugs without Clinically Significant Drug Interactions with Ciatacrurium Bescylate

## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Ciatacrurium Bescylate Injection is indicated:

- as an adjunct to general anesthesia to facilitate tracheal intubation in adults and in pediatric patients 1 month to 12 years of age (1)
- to provide skeletal muscle relaxation in adults during surgical procedures or during mechanical ventilation in the ICU (1)
- to provide skeletal muscle relaxation during surgical procedures via infusion in pediatric patients 2 years and older (1)

### Limitations of Use

Ciatacrurium bescylate injection is not recommended for rapid sequence endotracheal intubation due to the time required for its onset of action.

### 2 DOSSAGE AND ADMINISTRATION

#### 2.1 Important Dosage and Administration Instructions

##### Risk of Medication Errors

Accidental administration of neuromuscular blocking agents may be fatal. Store ciatacrurium bescylate injection with the cap and ferrule intact and in a manner that minimizes the possibility of selecting the wrong product. (See Warnings and Precautions (5.5).)

##### Intravenous Administration

- Ciatacrurium bescylate injection is for intravenous use only.
- Administer ciatacrurium bescylate injection in carefully adjusted dosage by or under the supervision of experienced clinicians who are familiar with the drug's actions and possible complications.
- Use ciatacrurium bescylate injection only when adequate personnel and facilities for resuscitation and life support (tracheal intubation, artificial ventilation, oxygen therapy, and the availability of ciatacrurium bescylate injection. (See Overview (1.2)).
- The dosage information below is intended to serve as an initial guide for individual patients; best subsequent ciatacrurium bescylate injection dosage on the basis of response to the initial doses.
- Use a peripheral nerve stimulator to:
  - Determine the adequacy of neuromuscular blockade (e.g., need for additional ciatacrurium bescylate injection doses, reduction of the infusion rate).
  - Minimize risk of overdosage or underdosage.
  - Assess the extent of recovery from neuromuscular blockade (e.g., spontaneous recovery or recovery after administration of a reversal agent, e.g., neostigmine).
  - Appropriately titrate doses to potentially limit exposure to toxic metabolites.
  - Facilitate more rapid reversal of the ciatacrurium bescylate injection – induced paralysis.

#### 2.2 Recommended Ciatacrurium Bescylate Injection Dose for Performing Tracheal Intubation

##### Tracheal Intubation in Adults

Pro to intubation: The initial ciatacrurium bescylate injection dose should be the desired time to tracheal intubation and the anticipated length of surgery, factors affecting time to onset of complete neuromuscular block such as age and renal function, and factors that may influence intubation conditions such as the presence of co-injection agents (e.g., fentanyl and midazolam) and the depth of anesthesia.

In conjunction with the recommended starting weight-based dose of ciatacrurium bescylate injection in between 0.1 mg/kg and 0.2 mg/kg administered via bolus intravenous injection, the recommended starting weight-based dose of ciatacrurium bescylate injection is between 0.1 mg/kg and 0.2 mg/kg administered via bolus intravenous injection. (See Clinical Studies (14.2)).

##### Patients with Neuromuscular Disease

The maximum recommended initial dose of ciatacrurium bescylate injection is 0.02 mg/kg in patients with neuromuscular diseases (e.g., myasthenia gravis and myasthenic syndrome and congenital myasthenic syndrome). (See Warnings and Precautions (5.1)).

##### Geriatric Patients and Patients with End-Stage Renal Disease

Because the time to maximum neuromuscular blockade is approximately 1 minute slower in geriatric patients compared to younger patients and in patients with end-stage renal disease than in patients with normal renal function, consider extending the interval between administering ciatacrurium bescylate injection and attempting intubation by at least 1 minute to achieve adequate intubation conditions in geriatric patients and patients with end-stage renal disease. A peripheral nerve stimulator should be used to determine the adequacy of muscle relaxation for the purposes of intubation and the timing and amounts of subsequent doses (see Use in Specific Populations (7.2)).

##### Tracheal Intubation in Pediatric Patients

##### Infants < 12 Months of Age

The recommended dose of ciatacrurium bescylate injection for intubation of pediatric patients aged 1 month to 23 months is 0.15 mg/kg administered over 5 to 10 seconds. When administered during stable opioid-induced analgesia, 0.15 mg/kg of ciatacrurium bescylate injection produced maximum neuromuscular blockade in about 2 minutes (range 1 to 3.4 minutes) with a clinically effective block time to 20% recovery for about 43 minutes (range 34 to 58 minutes) (see Clinical Studies (14.2)).

##### Pediatric Patients > 12 Years of Age

The recommended weight-based bolus dose of ciatacrurium bescylate injection for pediatric patients 2 to 12 years of age is 0.1 to 0.15 mg/kg administered over 5 to 10 seconds. When administered during stable opioid-induced analgesia, 0.1 mg/kg ciatacrurium bescylate injection produced maximum neuromuscular blockade in an average of 2.8 minutes (range 1.8 to 4.2 minutes) with a clinically effective block time to 20% recovery for about 38 minutes (range 21 to 53 minutes). When administered during stable opioid-induced analgesia, 0.15 mg/kg ciatacrurium bescylate injection produced maximum neuromuscular blockade in an average of about 3 minutes (range 1.9 to 5.8 minutes) with a clinically effective block for 38 minutes (range 29 to 46 minutes) (see Clinical Studies (14.2)).

#### 2.3 Recommended Maintenance Bolus Ciatacrurium Bescylate Injection Dose in Adult Surgical Procedures

Determine if maintenance bolus doses are needed based on clinical signs indicating the response to peripheral nerve stimulation. The recommended maintenance bolus dose of ciatacrurium bescylate injection is 0.02 mg/kg administered via bolus intravenous injection. Smaller or larger maintenance bolus may be administered based on the required duration of action. Administer the first maintenance bolus dose starting:

- 40 to 60 minutes after an initial dose of ciatacrurium bescylate injection 0.15 mg/kg;
- 60 to 100 minutes after an initial dose of ciatacrurium bescylate injection 0.2 mg/kg.

For long surgical procedures using inhalational anesthesia with nitrous oxide/oxygen at 1.25 MAC level for at least 30 minutes, consider administering less frequent maintenance bolus doses and a lower maintenance bolus dose of ciatacrurium bescylate injection (see Clinical Pharmacology (12.2)). No adjustment to the initial ciatacrurium bescylate injection maintenance bolus dose should be necessary when ciatacrurium bescylate injection is administered during after initiation of volatile agents or when used in patients receiving propofol anesthesia.

#### 2.4 Dosage in Burn Patients

Burn patients have been shown to develop resistance to nondepolarizing neuromuscular blocking agents; therefore, consider increasing the ciatacrurium bescylate injection dosage for intubation and maintenance (see Clinical Studies (14.2)).

#### 2.5 Dosage for Continuous Infusion

##### Continuous Infusion for Surgical Procedures in Adults and Pediatric Patients

During extended endotracheal ventilation, ciatacrurium bescylate injection may be administered by continuous infusion to adults and pediatric patients aged 2 or more years if patients have spontaneous recovery after the initial ciatacrurium bescylate injection bolus dose. Following recovery from neuromuscular blockade, it may be necessary to re-administer a bolus dose to quickly re-establish neuromuscular blockade prior to starting the continuous infusion.

If patients have no evidence of neuromuscular function, the recommended initial ciatacrurium bescylate injection infusion rate is 2 mg/kg/min (see Dosage and Administration (2.6)). Spontaneous recovery to baseline is not necessary to re-administer a bolus dose to quickly re-establish neuromuscular blockade prior to starting the continuous infusion. To assess the level of neuromuscular blockade and to appropriately titrate ciatacrurium bescylate injection infusion rate, if no response is elicited by peripheral nerve stimulation, describe the following with a peripheral nerve stimulator:

- Determine the infusion rate by up to 30% to 40% when ciatacrurium bescylate injection is administered during stable isoflurane anesthesia for at least 30 minutes administered with nitrous oxide/oxygen at 1.25 MAC level (see Clinical Pharmacology (7.2)). Greater resistance in the ciatacrurium bescylate injection infusion rate may be required with longer durations of administration of isoflurane or with the administration of other inhalational anesthetics.

##### Patients Undergoing Coronary Artery Bypass Graft (CABG) Surgery

Consider reducing the infusion rate in patients undergoing CABG with induced hypothermia to half the rate required during normothermia (see Clinical Pharmacology (12.2)). Spontaneous recovery from neuromuscular block following discontinuation of ciatacrurium bescylate infusion is expected to proceed at a rate comparable to that following administration of a single bolus dose.

##### Continuous Infusion for Mechanical Ventilation in the Intensive Care Unit for Adults

During extended need for mechanical ventilation and adequate muscle relaxation in the intensive care unit (ICU), ciatacrurium bescylate injection may be administered by continuous infusion to adults if a patient has spontaneous recovery of neuromuscular function after the initial ciatacrurium bescylate injection bolus dose.

However, recovery from neuromuscular blockade may be necessary to re-administer a bolus dose to quickly re-establish neuromuscular blockade prior to starting the continuous infusion.

The recovery of residual ciatacrurium bescylate injection resistance in adult patients in the ICU is 2 mg/kg/min (range 0.5 to 10.2 mg/kg/min) (see Dosage and Administration (2.6)). Use peripheral nerve stimulation to assess the level of neuromuscular blockade and to appropriately titrate the ciatacrurium bescylate injection infusion rate.

#### 2.6 Rate Table for Continuous Infusion

The infusion infusion rate depends upon the ciatacrurium bescylate concentration, the desired dose, the patient's weight, and the contribution of the infusion solution to the fluid requirements of the patient. Tables 1 and 2 provide guidelines for the ciatacrurium bescylate injection infusion rate, in mL/hour (equivalent to mL/min) for ciatacrurium bescylate injection solutions of 0.1 mg/mL and 0.2 mg/mL.

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	6	9	12	18	30
45 kg	27	41	54	81	135
70 kg	42	63	84	126	210
100 kg	58	87	116	174	300

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

Patient Weight	Drug Delivery Rate (mg/kg/min)				
	1	1.5	2	3	5
10 kg	1.5	2.3	3	4.5	7.5
45 kg	6.8	10.1	13.5	20.3	33.8
70 kg	10.5	15.8	21	31.5	52.5
100 kg	15	22.5	30	45	75

preservative.

- 200 mg of cisatracurium per 20 mL (10 mg/mL) in single-dose vials.

#### 4 CONTRAINDICATIONS