In 2 clinical pharmacology studies (total n=24) ropivacaine and bupivacaine were infused (10 mg/min) in human volunteers until the appearance of CNS symptoms, eg, visual or hearing disturbances, perioral numbness, or paresthesia.

Elimination

Ropivacaine is eliminated primarily in the urine and is also metabolized by the liver. Unbound plasma concentrations decline in a biphasic manner with a terminal half-life of about 1 hour. Total plasma clearance of ropivacaine is not significantly influenced by age, gender, or renal function in patients with normal hepatic function.

CLINICAL PHARMACOKINETICS

Ropivacaine is rapidly and efficiently absorbed following intravenous administration, achieving peak plasma concentrations in 1-3 minutes. Ropivacaine is distributed into peripheral tissues and the cerebrospinal fluid, where it is metabolized. Ropivacaine is extensively metabolized in the liver by cytochrome P450 enzymes, producing inactive metabolites. The major metabolites are unbound PPX, 3-hydroxy and 4-hydroxy ropivacaine, which have a pharmacological activity in animal models less than that of ropivacaine. There is no evidence of accumulation of ropivacaine in plasma after repeated epidural infusions. There is no significant difference between the pharmacokinetics of ropivacaine and bupivacaine in patients with normal hepatic function.

Pharmacokinetic parameters are dependent on the method and concentration of drug administration, the route of administration, the patient's pharmacokinetic parameters, and the duration of administration. For example, ropivacaine hydrochloride is rapidly absorbed after subcutaneous or intramuscular injection, achieving peak plasma concentrations in 1-3 minutes. Ropivacaine is also rapidly absorbed after intravenous injection, achieving peak plasma concentrations in 1-3 minutes. Ropivacaine is also rapidly absorbed after intraarticular injection, achieving peak plasma concentrations in 1-3 minutes.

Ropivacaine readily crosses the placenta and equilibrium in regard to unbound concentration will be rapidly reached.

A total of 9 double-blind clinical studies, involving 240 patients were performed to evaluate ropivacaine hydrochloride for epidural block for management of labor pain. When administered in doses up to 278 mg, ropivacaine produced a significant reduction in the mean duration of labor compared to placebo.

A total of 12 studies were performed with epidural administration of ropivacaine hydrochloride for cesarean section. Eight of these studies involved 218 patients using the concentration of 5 mg/mL (0.5%) in 6 studies and 10 mg/mL (1%) in 6 studies. Higher doses produced a more profound block with a greater duration of effect.

There have been rare reports of cardiac arrest during the use of ropivacaine hydrochloride for epidural anesthesia or peripheral nerve blockade, the majority of which occurred after inadvertent subarachnoid injection. However, a negative aspiration does not protect against this complication. It is essential that aspiration for blood, or cerebrospinal fluid (where applicable), be done prior to injecting any local anesthetic, both the original dose and all subsequent doses, to avoid intravascular or subarachnoid injection.

It is essential that aspiration for blood, or cerebrospinal fluid (where applicable), be done prior to injecting any local anesthetic, both the original dose and all subsequent doses, to avoid intravascular or subarachnoid injection.
The safety and efficacy of ropivacaine hydrochloride in pediatric patients have not been established.

**Epidural Use**

A study (3) that evaluated ropivacaine hydrochloride 2% or bupivacaine 5% (in 3 mL of saline) showed that 3 mL of ropivacaine 2% can be administered safely over 10 minutes in adults. This study did not evaluate the effects of ropivacaine 2% on postoperative cardiovascular and respiratory variables, since the patients were also not monitored for hemodynamic changes. In this study, the incidence of central nervous system and cardiovascular effects was not statistically different between the groups of patients receiving ropivacaine and bupivacaine for the first hour after administration. At the end of the first hour, however, ropivacaine was associated with a lower incidence of cardiovascular effects and a lower incidence of nausea and vomiting than bupivacaine. In the study of simultaneous epidural administration of ropivacaine 2% and bupivacaine 5%, a lower incidence of cardiovascular and respiratory effects was observed in the ropivacaine group, but the difference was not statistically significant. In this study, the duration of surgery was longer in the ropivacaine group, which may explain the differences in the incidence of cardiovascular and respiratory effects. The incidence of central nervous system and cardiovascular effects was not statistically different between the groups of patients receiving ropivacaine and bupivacaine for the first hour after administration.

The data from this study do not allow for a comparison of ropivacaine and bupivacaine with respect to the incidence of cardiovascular and respiratory effects. In this study, the incidence of cardiovascular and respiratory effects was not statistically different between the groups of patients receiving ropivacaine and bupivacaine for the first hour after administration.

**Postoperative Complications**

The incidence of postoperative complications associated with ropivacaine is similar to that of other local anesthetics. Some of the most common complications associated with ropivacaine include hypotension, respiratory depression, and cardiovascular collapse. The incidence of these complications is lower than that observed with bupivacaine, but higher than that observed with lidocaine.

**Use in Ophthalmic Surgery**

In ophthalmic surgery, ropivacaine hydrochloride is used as a topical anesthetic for lid manipulation. The use of ropivacaine in ophthalmic surgery should be restricted to situations in which other local anesthetics are not available or ineffective.

**Intravenous Regional Anesthesia (Bier Block)**

Intravenous regional anesthesia (Bier block) should not be performed due to a lack of clinical experience and the risk of attaining toxic blood levels of ropivacaine.

**Psychiatric Disorders**

Ropivacaine hydrochloride is not indicated for the treatment of psychiatric disorders. The use of ropivacaine in psychiatric disorders is associated with an increased risk of adverse events, including seizures, respiratory depression, and cardiovascular collapse. The use of ropivacaine in psychiatric disorders is associated with an increased risk of adverse events, including seizures, respiratory depression, and cardiovascular collapse.

**Adjunctive Pharmacology**

Ropivacaine hydrochloride is a local anesthetic that is used in the treatment of acute and chronic pain. It is also used in the treatment of dermatologic conditions, such as postherpetic neuralgia, and in the treatment of neuropathic pain.

**Common Events (Optional Administration)**

- Nausea
- Vomiting
- Headache
- Paresthesia
- Hypertension
- Hypotension
- Bradycardia
- Tachycardia
- Pruritus
- Transient numbness
- Local skin or subcutaneous edema
- Intravascular injection
- Allergic-type skin reaction
- Subcutaneous nodules
- Intravascular or intrathecal injection
- Syringe aspirations should also be performed before and during each supplemental injection in continuous (intermittent) catheter techniques.

**Adverse Events**

The most common adverse events associated with ropivacaine hydrochloride are related to the route of administration and the total dose administered. These adverse events include:

- Nausea and vomiting
- Headache
- Paresthesia
- Hypertension
- Hypotension
- Bradycardia
- Tachycardia
- Pruritus
- Transient numbness
- Local skin or subcutaneous edema
- Intravascular injection
- Allergic-type skin reaction
- Subcutaneous nodules
- Intravascular or intrathecal injection
- Syringe aspirations should also be performed before and during each supplemental injection in continuous (intermittent) catheter techniques.

**Intrathecal Use**

Intrathecal use of ropivacaine hydrochloride is associated with a higher incidence of adverse events compared to epidural use. The most common adverse events associated with intrathecal use include:

- Nausea and vomiting
- Headache
- Paresthesia
- Hypertension
- Hypotension
- Bradycardia
- Tachycardia
- Pruritus
- Transient numbness
- Local skin or subcutaneous edema
- Intravascular injection
- Allergic-type skin reaction
- Subcutaneous nodules
- Intravascular or intrathecal injection
- Syringe aspirations should also be performed before and during each supplemental injection in continuous (intermittent) catheter techniques.

**Other Routes of Administration**

Ropivacaine hydrochloride is not indicated for other routes of administration, such as intramuscular, subcutaneous, or intravenous injection.

**Pharmacokinetics**

Ropivacaine hydrochloride is rapidly absorbed following intramuscular, subcutaneous, and intravenous administration. The plasma clearance of ropivacaine is approximately 1.5 L/min/kg, which is similar to that of bupivacaine. The systemic clearance of ropivacaine is reduced in elderly patients, and there is a wide interpatient variability in the pharmacokinetics of ropivacaine.

**Elimination**

Ropivacaine hydrochloride is eliminated primarily by metabolism, and to a lesser extent by renal clearance. The half-life of ropivacaine in adults is approximately 1.5 hours, which is similar to that of bupivacaine.

**Contraindications**

Ropivacaine hydrochloride is contraindicated in patients with known sensitivity to ropivacaine or to any of the excipients in the formulation. Ropivacaine hydrochloride is also contraindicated in patients with known sensitivity to bupivacaine or to any of the excipients in the formulation.