



**Datum:** 16. März 2016  
**Kontakt:** Mag. pharm. Dr. Ulrike Rehberger  
**Abteilung:** REGA  
**Tel. / Fax:** +43 (0) 505 55 – 36258  
**E-Mail:** pv-implemetation@ages.at  
**Unser Zeichen:** PHV-8546578-A-160316-EUIM  
**Ihr Zeichen:**

## PHV issue Ropivacain

Sehr geehrte Damen und Herren,

basierend auf der Evaluierung des PSURs im EU-HBD-worksharing Projekt (Verfahrensnummer: NL/H/PSUR/0400/002) kommt es zu der Empfehlung, folgende Ergänzungen in die **Fach- und Gebrauchsinformation** aller Ropivacain- hältigen Arzneispezialitäten aufzunehmen.

Sollten diese bereits aufgenommen worden sein, betrachten Sie dieses Schreiben als gegenstandslos.

## Fachinformation

### Ropivacain 5mg/ml:

#### 4.3 Contra-indications

- Hypersensitivity to ropivacaine or to other local anaesthetics of the amide type.
- General contra-indications related to regional anaesthesia, regardless of the local anaesthetic used, should be taken into account.
- Intravenous regional anaesthesia.
- Obstetric paracervical anaesthesia
- Major nerve blocks are contraindicated in hypovolaemic patients.

#### 4.4 Special warnings and precautions for use

Regional anaesthetic procedures should always be performed in a properly equipped and staffed area. Equipment and medicinal products necessary for monitoring and emergency resuscitation should be immediately available.





Patients receiving major blocks should be in optimal condition and have an intravenous line inserted before the blocking procedure.

The clinician responsible should take the necessary precautions to avoid intravascular injection and be appropriately trained and familiar with diagnosis and treatment of undesirable effects, systemic toxicity and other complications. After intrathecal administration, systemic toxicity is not expected to occur, due to the low dose administered. An excessive dose administered into the subarachnoid space may give rise to a total spinal block (see section 4.9).

### **Cardiovascular**

Patients treated with anti-arrhythmic drugs class III (eg, amiodarone) should be under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

### **Hypersensitivity**

A possible cross – hypersensitivity with other amide – type local anaesthetics should be taken into account, (see section 4.3).

### **Hypovolaemia**

Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during intrathecal anaesthesia, regardless of the local anaesthetic used.

### **Patients in poor general health**

Patients in poor general condition due to ageing or other compromising factors such as partial or complete heart conduction block, advanced liver disease or severe renal dysfunction require special attention, however regional anaesthesia is frequently indicated in these patients.

### **Patients with hepatic and renal impairment**

Ropivacaine is metabolised in the liver and should therefore be used with caution in patients with severe liver disease. Repeated doses may need to be reduced due to delayed elimination. Normally there is no need to modify the dose in patients with impaired renal function when used for single dose or short-term treatment. Acidosis and reduced plasma protein concentration, frequently seen in patients with chronic renal failure, may increase the risk of systemic toxicity.

### **Acute porphyria**

Ropivacain solution for injection is possibly porphyrinogenic and should only be prescribed to patients with acute porphyria when no safer alternative is available. Appropriate precautions should be taken in the case of vulnerable patients, according to standard textbooks and/or in consultation with disease area experts.

### **Excipients with recognised action/effect**

This medicinal product contains maximum 3.5 mg sodium per mL. To be taken into consideration by patients on a controlled sodium diet.

### **Prolonged administration**

Prolonged administration of ropivacaine should be avoided in patients concomitantly treated with strong CYP1A2 inhibitors, such as fluvoxamine and enoxacin, (see section 4.5).

### **Paediatric population**

Intrathecal administration for use in infants, toddlers or children has not been documented.





The safety and efficacy of ropivacaine 5 mg/ mL for peripheral nerve blocks in infants below 1 year has not been established

Ropivacain 5 mg/mL is not approved for use in children <1 year. Neonates would need special attention due to immaturity of metabolic pathways. The larger variations in plasma concentrations of ropivacaine observed in clinical trials in neonates suggest that there may be an increased risk of systemic toxicity in this age group.

#### 4.5 Interactions with other medicinal products and other forms of interaction

Ropivacain should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, eg, certain antiarrhythmics, such as lidocaine and mexiletine, since the systemic toxic effects are additive. Simultaneous use of Ropivacain with general anaesthetics or opioids may potentiate each other's (adverse) effects. Specific interaction studies with ropivacaine and anti-arrhythmic drugs class III (eg, amiodarone) have not been performed, but caution is advised (see also section 4.4).

Cytochrome P450 (CYP) 1A2 is involved in the formation of 3-hydroxy ropivacaine, the major metabolite. *In vivo* the plasma clearance of ropivacaine was reduced by up to 77% during co administration of fluvoxamine, a selective and potent CYP1A2 inhibitor. Thus strong inhibitors of CYP1A2, such as fluvoxamine and enoxacin, given concomitantly during prolonged administration of Ropivacain, can interact with ropivacaine. Prolonged administration of Ropivacain should be avoided in patients concomitantly treated with strong CYP1A2 inhibitors, (see section 4.4).

*In vivo* the plasma clearance of ropivacaine was reduced by 15% during co administration of ketoconazole, a selective and potent inhibitor of CYP3A4. However the inhibition of this isozyme is not likely to have clinical relevance.

*In vitro* ropivacaine is a competitive inhibitor of CYP2D6 but does not seem to inhibit this isozyme at clinically attained plasma concentrations.

#### 4.6 Pregnancy and lactation

##### **Pregnancy**

Apart from epidural administration for obstetrical use, there are no adequate data on the use of ropivacaine in human pregnancy. Experimental animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

##### **Lactation**

There is no data available concerning the excretion of ropivacaine into human milk.

#### 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Depending on the dose, local anaesthetics may have a minor influence on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

#### 4.8 Undesirable effects

##### **General**

The adverse reaction profile for Ropivacain is similar to those for other long acting local anaesthetics of the amide type. Adverse reactions should be distinguished from the physiological effects of the nerve block itself eg, hypotension and bradycardia during intrathecal anaesthesia, and events caused by needle puncture (eg, spinal hematoma, postdural



puncture headache, meningitis and epidural abscess). Many of the most frequently reported adverse reactions, such as nausea, vomiting and hypotension, are very frequent during anaesthesia and surgery in general and it is not possible to distinguish those caused by the clinical situation from those caused by the medicinal product or the block.

Total spinal block may occur with all local anaesthetics if an epidural dose is inadvertently administered intrathecally, or if a too large intrathecal dose is administered. Systemic and localised adverse reactions of Ropivacain usually occur because of excessive dosage, rapid absorption, or inadvertent intravascular injection. However, due to the low doses used for intrathecal anaesthesia, systemic toxic reactions are not expected.

**Table 3 Table of adverse reactions**

The frequencies used in the table in section 4.8 are: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ) and very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

System Organ Class	Frequency	Undesirable Effect
Psychiatric disorders	Uncommon	Anxiety
Nervous System disorders	Common	Paraesthesia, Dizziness, Headache <sup>c</sup>
	Uncommon	Symptoms of CNS toxicity (Convulsions, Grand mal convulsions, Seizures, Light headedness, Circumoral paraesthesia, Numbness of the tongue, Hyperacusis, Tinnitus, Visual disturbances, Dysarthria, Muscular twitching, Tremor) <sup>*</sup> , Hypoaesthesia <sup>c</sup>
	Not known	Dyskinesia
Cardiac disorders	Common	Bradycardia <sup>c</sup> , Tachycardia
	Rare	Cardiac arrest, Cardiac arrhythmias
Vascular disorders	Very common	Hypotension <sup>a</sup>
	Common	Hypertension
	Uncommon	Syncope <sup>c</sup>
Respiratory, Thoracic and Mediastinal disorders	Uncommon	Dyspnoea <sup>c</sup>
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting <sup>b, c</sup>
Renal and Urinary disorders	Common	Urinary retention <sup>c</sup>
General disorders and Administrative site conditions	Common	Temperature elevation and Chills
	Uncommon	Hypothermia <sup>c</sup>
	Rare	Allergic reactions (anaphylactic reactions, angioneurotic oedema and urticaria)



System Organ Class	Frequency	Undesirable Effect
Immune System Disorders	Rare	Allergic reactions (anaphylactic reactions, angioneurotic oedema and urticaria)
Musculoskeletal and Connective Tissue	Common	Back pain

a Hypotension is less frequent in children (>1/100).

b Vomiting is more frequent in children. (>1/10).

c These reactions are more frequent than indicated after intrathecal administration

\*These symptoms usually occur because of inadvertent intravascular injection, overdose or rapid absorption, (see section 4.9)

### **Class-related adverse reactions**

#### ***Neurological complications***

Neuropathy and spinal cord dysfunction (eg, anterior spinal artery syndrome, arachnoiditis, cauda equina), which may result in rare cases of permanent sequelae, have been associated with regional anaesthesia, regardless of the local anaesthetic used.

#### ***Total spinal block***

Total spinal block may occur if too large an intrathecal dose is administered.

#### ***Acute systemic toxicity***

Systemic toxic reactions primarily involve the central nervous system (CNS) and the cardiovascular system (CVS). Such reactions are caused by high blood concentration of a local anaesthetic, which may appear due to (accidental) intravascular injection, overdose or exceptionally rapid absorption from highly vascularized areas. CNS reactions are similar for all amide local anaesthetics, while cardiac reactions are more dependent on the drug, both quantitatively and qualitatively.

#### ***Central nervous system toxicity***

Central nervous system toxicity is a graded response with symptoms and signs of escalating severity. Initially symptoms such as visual or hearing disturbances, perioral numbness, dizziness, light-headedness, tingling and paraesthesia are seen. Dysarthria, muscular rigidity and muscular twitching are more serious and may precede the onset of generalised convulsions. These signs must not be mistaken for neurotic behaviour. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly during convulsions due to the increased muscular activity, together with the interference with respiration. In severe cases even apnoea may occur. The respiratory and metabolic acidosis increases and extends the toxic effects of local anaesthetics.

Recovery follows the redistribution of the active substance from the central nervous system and subsequent metabolism and excretion. Recovery may be rapid unless large amounts of the medicinal product have been injected.

#### ***Cardiovascular system toxicity***

Cardiovascular toxicity indicates a more severe situation. Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anaesthetics. In volunteers the intravenous infusion of ropivacaine resulted in signs of depression of conductivity and contractility.





Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system, unless the patient is receiving a general anaesthetic or is heavily sedated with medicinal products such as benzodiazepines or barbiturates.

#### **Paediatric population**

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults except for hypotension which happens less often in children (< 1 in 10) and vomiting which happens more often in children (> 1 in 10).

In children, early signs of local anaesthetic toxicity may be difficult to detect since they may not be able to verbally express them. (See also section 4.4)

#### **Treatment of acute systemic toxicity**

See section 4.9.

### 4.9 Overdose

#### **Symptoms**

Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, peak plasma concentrations may not be reached for one to two hours, depending on the site of the injection, and signs of toxicity may thus be delayed. (See section 4.8).

After intrathecal administration, systemic toxicity is not expected to occur, due to the low dose administered. An excessive dose administered into the subarachnoid space may give rise to a total spinal block.

#### **Treatment**

If signs of acute systemic toxicity appear, injection of the local anaesthetic should be stopped immediately and CNS symptoms (convulsions, CNS depression) must promptly be treated with appropriate airway/respiratory support and the administration of anticonvulsant drugs.

If circulatory arrest should occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

If cardiovascular depression occurs (hypotension, bradycardia), appropriate treatment with intravenous fluids, vasopressor, and or inotropic agents should be considered.

Should cardiac arrest occur, a successful outcome may require prolonged resuscitative efforts.

## **Ropivacain 2mg/ml**

## **Ropivacain 7,5mg/ml**

## **Ropivacain 10mg/ml**

### **4.3 Contraindications**

Hypersensitivity to ropivacaine or to other local anaesthetics of the amide type.

General contra-indications related to epidural anesthesia, regardless of the local anaesthetic used, should be taken into account.

Intravenous regional anaesthesia.

Obstetric paracervical anaesthesia

Hypovolaemia

### **4.4 Special warnings and precautions for use**

Regional anaesthetic procedures should always be performed in a properly equipped and staffed area. Equipment and drugs necessary for monitoring and emergency resuscitation should be immediately available.

Patients receiving major blocks should be in an optimal condition and have an intravenous line inserted before the blocking procedure.

The clinician responsible should take the necessary precautions to avoid intravascular injection and be appropriately trained and familiar with diagnosis and treatment of side effects, systemic toxicity and other complications (see section 4.8 and 4.9) such as inadvertent subarachnoid injection which may produce a high spinal block with apnoea and hypotension. Convulsions have occurred most often after brachial plexus block and epidural block. This is likely to be the result of either accidental intravascular injection or rapid absorption from the injection site.

Caution is required to prevent injections in inflamed areas.

#### **Cardiovascular**

Patients treated with anti-arrhythmic drugs class III (eg, amiodarone) should be under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

There have been rare reports of cardiac arrest during the use of Ropivacain for epidural anaesthesia or peripheral nerve blockade, especially after unintentional accidental intravascular administration in elderly patients and in patients with concomitant heart disease. In some instances, resuscitation has been difficult. Should cardiac arrest occur, prolonged resuscitative efforts may be required to improve the possibility of a successful outcome.

#### **Head and neck blocks**

Certain local anaesthetic procedures, such as injections in the head and neck regions, may be associated with a higher frequency of serious adverse reactions, regardless of the local anaesthetic used.

#### **Major peripheral nerve blocks**

Major peripheral nerve blocks may imply the administration of a large volume of local anaesthetic in highly vascularized areas, often close to large vessels where there is an increased risk of intravascular injection and/or rapid systemic absorption, which can lead to high plasma concentrations.



## **Hypersensitivity**

A possible cross-hypersensitivity with other amide-type local anaesthetics should be taken into account.

## **Hypovolaemia**

Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during epidural anaesthesia, regardless of the local anaesthetic used.

## **Patients in poor general health**

Patients in poor general condition due to ageing or other compromising factors such as partial or complete heart conduction block, advanced liver disease or severe renal dysfunction require special attention, although regional anaesthesia is frequently indicated in these patients.

## **Patients with hepatic and renal impairment**

Ropivacaine is metabolised in the liver and should therefore be used with caution in patients with severe liver disease; repeated doses may need to be reduced due to delayed elimination. Normally there is no need to modify the dose in patients with impaired renal function when used for single dose or short term treatment. Acidosis and reduced plasma protein concentration, frequently seen in patients with chronic renal failure, may increase the risk of systemic toxicity.

## **Acute porphyria**

Ropivacain solution for injection and infusion is possibly porphyrinogenic and should only be prescribed to patients with acute porphyria when no safer alternative is available. Appropriate precautions should be taken in the case of vulnerable patients, according to standard textbooks and/or in consultation with disease area experts.

## **Chondrolysis**

There have been post-marketing reports of chondrolysis in patients receiving post-operative intra-articular continuous infusion of local anaesthetics, including ropivacaine. The majority of reported cases of chondrolysis have involved the shoulder joint. Intra-articular continuous infusion is not an approved indication for Ropivacain. Intra-articular continuous infusion with Ropivacain should be avoided, as the efficacy and safety has not been established.

## **Excipients with recognised action/effect**

This medicinal product contains maximum 3.7 mg sodium per ml. To be taken into consideration by patients on a controlled sodium diet.

## **Prolonged administration**

Prolonged administration of ropivacaine should be avoided in patients concomitantly treated with strong CYP1A2 inhibitors, such as fluvoxamine and enoxacin, (see section 0).

## **Paediatric patients**

Neonates may need special attention due to immaturity of metabolic pathways. The larger variations in plasma concentrations of ropivacaine observed in clinical trials in neonates suggest that there may be an increased risk of systemic toxicity in this age group, especially during continuous epidural infusion. The recommended doses in neonates are based on limited clinical data. When ropivacaine is used in this patient group, regular monitoring of systemic toxicity (e.g. by signs of CNS toxicity, ECG, SpO<sub>2</sub>) and local neurotoxicity (e.g. prolonged recovery) is required, which should be continued after ending infusion, due to a slow elimination in neonates.

- The safety and efficacy of ropivacaine 7.5 mg/ml and 10 mg/ml in children up to and including 12 years has not been established.







- The safety and efficacy of ropivacaine 2 mg/ml for field block in children up to and including 12 years has not been established
- The safety and efficacy of ropivacaine 2 mg/ml for peripheral nerve blocks in infants below 1 year has not been established

#### 4.5 Interactions with other medicinal products and other forms of interaction

Ropivacain should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, e.g. certain antiarrhythmics, such as lidocaine and mexiletine, since the systemic toxic effects are additive. Simultaneous use of Ropivacain with general anaesthetics or opioids may potentiate each others (adverse) effects. Specific interaction studies with ropivacaine and anti-arrhythmic drugs class III (eg, amiodarone) have not been performed, but caution is advised (see also section 4.4).

Cytochrome P450 (CYP) 1A2 is involved in the formation of 3-hydroxy ropivacaine, the major metabolite. In vivo the plasma clearance of ropivacaine was reduced by up to 77% during coadministration of fluvoxamine, a selective and potent CYP1A2 inhibitor. Thus strong inhibitors of CYP1A2, such as fluvoxamine and enoxacin, given concomitantly during prolonged administration of Ropivacain, can interact with Ropivacain. Prolonged administration of ropivacaine should be avoided in patients concomitantly treated with strong CYP1A2 inhibitors, see also section 4.4.

In vivo the plasma clearance of ropivacaine was reduced by 15% during co-administration of ketoconazole, a selective and potent inhibitor of CYP3A4. However the inhibition of this isozyme is not likely to have clinical relevance.

In vitro ropivacaine is a competitive inhibitor of CYP2D6 but does not seem to inhibit this isozyme at clinically attained plasma concentrations.

#### 4.6 Pregnancy and lactation

##### **Pregnancy**

Apart from epidural administration for obstetrical use, there are no adequate data on the use of ropivacaine in human pregnancy. Experimental animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

##### **Lactation**

There is no data available concerning the excretion of ropivacaine into human milk.

#### 4.7 Effects on ability to drive and use machines

No data is available. Depending on the dose, local anaesthetics may have a minor influence on mental function and coordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

#### 4.8 Undesirable effects

##### **General**

The adverse reaction profile for Ropivacain is similar to those for other long acting local anaesthetics of the amide type. Adverse drug reactions should be distinguished from the physiological effects of the nerve block itself e.g. a decrease in blood pressure and bradycardia during spinal/epidural block.



**Table 4 Table of adverse drug reactions**

The frequencies used in the table in Section 4.8 are: very common ( $\geq 1/10$ ), common ( $\geq 1/100$  to  $< 1/10$ ), uncommon ( $\geq 1/1,000$  to  $< 1/100$ ), rare ( $\geq 1/10,000$  to  $< 1/1,000$ ) and very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

Page 17 of 29

*(cannot be estimated from the available data)*

System Organ Class	Frequency	Undesirable Effect
Psychiatric disorders	Uncommon	Anxiety
Nervous System disorders	Common	Paraesthesia, Dizziness, Headache
	Uncommon	Symptoms of CNS toxicity (Convulsions, Grand mal convulsions, Seizures, Light headedness, Circumoral paraesthesia, Numbness of the tongue, Hyperacusis, Tinnitus, Visual disturbances, Dysarthria, Muscular twitching, Tremor) *, Hypoaesthesia
	Not known	Dyskinesia
Cardiac disorders	Common	Bradycardia, Tachycardia
	Rare	Cardiac arrest, Cardiac arrhythmias
Vascular disorders	Very common	Hypotension <sup>a</sup>
	Common	Hypertension
	Uncommon	Syncope
Respiratory, Thoracic and Mediastinal disorders	Uncommon	Dyspnoea
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting <sup>b</sup>
Renal and Urinary disorders	Common	Urinary retention
General Disorders and Administrative site conditions	Common	Temperature elevation and Chills
	Uncommon	Hypothermia
Immune System Disorders	Rare	Allergic reactions (anaphylactic reactions, angioneurotic oedema and urticaria)
Musculoskeletal and Connective Tissue	Common	Back pain

a Hypotension is less frequent in children ( $> 1/100$ ).

b Vomiting is more frequent in children. ( $> 1/10$ ).

\*These symptoms usually occur because of inadvertent intravascular injection, overdose or rapid absorption, see section 4.9

## **Class-related adverse drug reactions**

### *Neurological complications*

Neuropathy and spinal cord dysfunction (e.g. anterior spinal artery syndrome, arachnoiditis, cauda equina), which may result in rare cases of permanent sequelae, have been associated with regional anaesthesia, regardless of the local anaesthetic used.

#### *Total spinal block*

Total spinal block may occur if an epidural dose is inadvertently administered intrathecally.

#### *Acute systemic toxicity*

Systemic toxic reactions primarily involve the central nervous system (CNS) and the cardiovascular system (CVS). Such reactions are caused by high blood concentration of a local anaesthetic, which may appear due to (accidental) intravascular injection, overdose or exceptionally rapid absorption from highly vascularized areas, see also section 4.4. CNS reactions are similar for all amide local anaesthetics, while cardiac reactions are more dependent on the drug, both quantitatively and qualitatively.

#### *Central nervous system toxicity*

Central nervous system toxicity is a graded response with symptoms and signs of escalating severity. Initially symptoms such as visual or hearing disturbances, perioral numbness, dizziness, light-headedness, tingling and paraesthesia are seen. Dysarthria, muscular rigidity and muscular twitching are more serious and may precede the onset of generalised convulsions. These signs must not be mistaken for neurotic behaviour. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly during convulsions due to the increased muscular activity, together with the interference with respiration. In severe cases even apnoea may occur. The respiratory and metabolic acidosis increases and extends the toxic effects of local anaesthetics.

Recovery follows the redistribution of the local anaesthetic drug from the central nervous system and subsequent metabolism and excretion. Recovery may be rapid unless large amounts of the drug have been injected.

#### *Cardiovascular system toxicity*

Cardiovascular toxicity indicates a more severe situation. Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anaesthetics. In volunteers the intravenous infusion of ropivacaine resulted in signs of depression of conductivity and contractility.

Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system, unless the patient is receiving a general anaesthetic or is heavily sedated with drugs such as benzodiazepines or barbiturates.

In children, early signs of local anaesthetic toxicity may be difficult to detect since they may not be able to verbally express them. See also section 4.4.

## **Paediatric population**

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults except for hypotension which happens less often in children (< 1 in 10) and vomiting which happens more often in children (> 1 in 10).



In children, early signs of local anaesthetic toxicity may be difficult to detect since they may not be able to verbally express them. (See also section 4.4).

### **Treatment of acute systemic toxicity**

See section 4.9.

## **4.9 Overdose**

### **Symptoms**

Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, peak plasma concentrations may not be reached for one to two hours, depending on the site of the injection, and signs of toxicity may thus be delayed. (See section 4.8).

### **Treatment**

If signs of acute systemic toxicity appear, injection of the local anaesthetic should be stopped immediately and CNS symptoms (convulsions, CNS depression) must promptly be treated with appropriate airway/respiratory support and the administration of anticonvulsant drugs.

If circulatory arrest should occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

If cardiovascular depression occurs (hypotension, bradycardia), appropriate treatment with intravenous fluids, vasopressor, and or inotropic agents should be considered. Children should be given doses commensurate with age and weight.

Should cardiac arrest occur, a successful outcome may require prolonged resuscitative efforts.

Oben angeführte Textabschnitte stellen eine Mindestanforderung dar, zusätzliche nationale Hinweise in diesen Abschnitten sind zu belassen.



Die Zulassungsinhaber werden aufgefordert, auch die Gebrauchsinformationen diesbezüglich anzupassen und bis **spätestens 16. Mai 2016** eine Variation gemäß  
"Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures."

für die Arzneyspezialitäten:

beim Institut Zulassung & Lifecycle Management einzureichen.

In der Begründung ist „**PHV-Issue: Ropivacain** “ sowie die **Geschäftszahl (PHV-8546578-A-160316-EUIM)** anzugeben.

Mit freundlichen Grüßen  
Für das Bundesamt  
Mag. Rudolf Schranz