

VI.2.2 Summary of treatment benefits

Because Bupivacain Pilum is a generic medicine, the benefits and risks are taken as being the same as those of the reference medicinal product. Bupivacaine is an amide type local anesthetic drug that is in use since the last 50 years in clinical practice. The pharmacological profile of Bupivacaine is well documented in scientific publications and its pharmacokinetics is well understood.

Bupivacain Pilum works by blocking the transmission of pain signals through nerves in or near the spinal cord. It is used to numb or make parts of the body free from pain.

Bupivacain Pilum is used to:

- numb parts of the body during surgery in adults and adolescents above 12 years
- relieve of acute pain in adults, infants and children above 1 year of age

It is used for example in surgical operations and as relief of pain after an operation.

Bupivacain Pilum will be given to you by your doctor by injection. It can be injected subcutaneous (under the skin), intramuscular (into a muscle), intraarterial (into an artery) or as an epidural injection (into your back). Your doctor will decide what doses is right for you. The dose will depend on your size, your state of health, the part of the body that the medicine is injected into, and what the medicine is being used for. Smaller doses are used for elderly people, young children and people who are unwell.

This medicine may be given before minor or major surgery, or during childbirth. For minor surgery, the injection will usually be given near the part of the body to be operated on. The medicine will prevent pain and cause numbness which will gradually wear off once the procedure is over. For major surgery or childbirth, you may be given an injection in your back which will take a few minutes. This will prevent pain and cause numbness in the lower half of your body.

VI.2.3 Unknowns relating to treatment benefits

NA

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Systemic toxicity; Central nervous system and cardiovascular system	Systemic toxic reactions primarily involve the central nervous system	If you notice these symptoms, tell your doctor or nurse immediately.

Risk	What is known	Preventability
	<p>(CNS) and the cardiovascular system. Such reactions are caused by high blood concentrations of a local anaesthetic, which may appear due to (accidental) intravascular injection, overdose or exceptionally rapid absorption from highly vascularised areas.</p> <p>If you are given more Bupivacain Pilum than you should, you may get systemic reactions to the central nervous system (such as light-headedness, circumoral paraesthesia, numbness of the tongue, hyperacusis, tinnitus, visual disturbances, dysarthria, muscular twitching or tremors, generalised convulsions, grand mal convulsions, unconsciousness, hypoxia, hypercarbia, interference with respiration, possible loss of functional airways and in severe cases apnoea) and systemic reactions to the cardiovascular system (such as decreased cardiac output, hypotension, AV block, bradycardia, and occasionally ventricular arrhythmias including ventricular tachycardia, ventricular fibrillation and cardiac arrest).</p>	<p>Bupivacain Pilum should only be used by physicians experienced in regional anaesthesia or under his or her supervision. The lowest dosage needed to provide effective anaesthesia should be administered.</p> <p>The patient should be regularly monitored throughout the infusion duration with respect to blood pressure, heart rate, and any toxic symptoms. If signs of toxic effects are observed the infusion should immediately be discontinued.</p> <p>Adequate resuscitation equipment should be available whenever local or general anaesthesia is administered. Before any major nerve block is attempted, intravenous access for resuscitation purposes should be established.</p>
<p>Accidental intravascular injection, consequences of</p>	<p>Like all local anaesthetic medicinal products, bupivacaine may cause acute toxicity effects on the central nervous and cardiovascular systems if utilised for local anaesthetic procedures resulting in high blood concentrations of the medicinal product. This is especially the case after unintentional intravascular administration. Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions.</p>	<p>Bupivacain Pilum should only be used by physicians experienced in regional anaesthesia or under his or her supervision.</p> <p>In order to avoid intravascular injection, aspiration should be repeated prior to and during administration of the main dose.</p> <p>An inadvertent intravascular injection may be recognised by a temporary increase in heart rate and an accidental intrathecal injection by signs of a spinal block.</p>
<p>Neurological damage</p>	<p>Neurological damage is a rare but well known side effect of regional anaesthesia especially in epidural and spinal anaesthesia.</p>	<p>Bupivacain Pilum should only be used by physicians experienced in regional anaesthesia or under his or her supervision.</p>
<p>Interaction with medicines to control your heartbeat</p>	<p>Bupivacaine should be used with caution in patients receiving class IB</p>	<p>Tell your doctor if you are taking medicines to control your irregular</p>

Risk	What is known	Preventability
(Interaction with anti-arrhythmics)	anti- arrhythmics since the toxic effects are additive. Specific interaction studies with bupivacaine and other local anaesthetics or anti-arrhythmic medicinal product class III (e.g. amiodarone) have not been performed, but caution should be advised.	heartbeat (such as dronedaron or amiodarone). Patients treated with anti-arrhythmic medicinal products class III (e.g. amiodarone) should be under close surveillance and ECG monitoring.
Low blood pressure (Hypotension)	Hypotension is a very common side effect of bupivacaine.	Do not use Bupivacaine Pilum for epidural anaesthesia in case you have severe hypotension such as in cardiogenic or hypovolemic shock. Talk to your doctor or nurse before you are given Bupivacain Pilum if you have very low blood pressure Your doctor can monitor your blood pressure.
Not being able to urinate (Urinary retention)	Urinary retention is a common side effect of bupivacaine.	Like all medicines, this medicine can cause side effects, although not everybody gets them.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Necrosis and destruction of cartilage (Chondrolysis)	Patients treated with bupivacaine may be at an increased risk of developing chondrolysis. There have been post-marketing reports on chondrolysis in patients treated post-operatively with local anaesthetics via continuous intraarticular infusion. The majority of the reported cases involve chondrolysis in the shoulder joint. Due to several contributing factors it has not been possible to establish a causal relationship. There is also inconsistency in the scientific literature regarding the mechanism of action. Continuous intraarticular infusion is not an approved indication for Bupivacain Pilum.
Limited information on use in paediatric patients	In children < 12 years some injections of Bupivacain Pilum in order to numb parts of the body during surgery are not established, in younger children Bupivacain Pilum is not established in children < 1 year. The safety and efficacy of Bupivacain Pilum in children < 1 year of age have not been established. Only limited data are available. The use of bupivacaine for intra-articular block and for major nerve block in children 1 to 12 years of age has not been documented.

Missing information

Risk	What is known

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Bupivacain Pilum can be found in the authority's EPAR page.

This medicine has no additional risk minimisation measures

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	At time of submission 21/08/2014	Systemic toxicity; CNS and cardiovascular Accidental intravascular injection Neurological damage Interaction with anti-arrhythmics Hypotension Urinary retention Chondrolysis Use in paediatric patients	
2.0	12/02/2015	Use in paediatric patients moved from Missing information to Important potential risks Accidental intravascular injection changed to Accidental intravascular injection, consequences of	Update after comments in assessment report, and updates to SmPC and PL.