SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Bupivacaine Hydrochloride 0.25%w/v Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml contains bupivacaine hydrochloride BP equivalent to 0.25% w/v anhydrous Bupivacaine Hydrochloride.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless aqueous sterile solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Bupivacaine 0.25% and 0.5% solutions are used for the production of local anaesthesia by percutaneous infiltration, peripheral nerve block(s) and central neural block (caudal or epidural), that is, for specialist use in areas where prolonged anaesthesia is indicated. Bupivacaine without adrenaline may also be used for intradural spinal anaesthesia. Bupivacaine is particularly useful for pain relief e.g. during labour, as its sensory nerve block is more marked than its motor block. A list of indications and suggested dose and strength of solution appropriate for each are shown in the table under 'Posology and method of administration'.

- Surgical anaesthesia in adults and children above 12 years of age.
- Acute pain management in adults, infants and children above 1 year of age.

4.2 Posology and method of administration

Great care must be taken in order to prevent an accidental intravascular injection, always including careful aspirations. For epidural anaesthesia, a test dose of 3 - 5ml of bupivacaine containing adrenaline should be administered,

since an intravascular injection of adrenaline will be quickly recognised by an increase in heart rate. Verbal contact and frequent measurements of the heart rate, preferably by electrographic (ECG) monitoring, should be maintained throughout a period of 5 minutes following the test dose.
Aspiration should be repeated prior to the administration of the total dose.
The main dose should be injected slowly, 25 - 50mg/min., in incremental doses under constant contact with the patient. If mild toxic symptoms develop, the injection must be immediately stopped.
The lowest dosage required to achieve effective anaesthesia should be given. However, the dose will vary, and will be dependent on the area to be anaesthetised, the vascularity of the tissues, the number of neuronal segments to be blocked, individual tolerance and the technique of anaesthesia used. For most indications, the duration of anaesthesia with bupivacaine solutions is such that a single dose is sufficient.
The maximum dosage must be determined by evaluating the size and physical status of the patient and considering the usual rate of systemic absorption from a particular injection site. Experience to date indicates a single dose of up to 150mg bupivacaine hydrochloride. Doses of up to 50mg 2-hourly may subsequently be used. The dosages in the following table are recommended as a guide for use in the average adult. For young, elderly or debilitated patients, these doses should be reduced.

Type of block	***Each dose***		***Motor block***[+]
	% Conc	***ml***	***mg***
LOCAL INFILTRATION	0.25	Up to 60	Up to 150	-
LUMBAR EPIDURAL				
Surgical operations	0.50	10 to 20	50 to 100	Moderate to complete
Analgesia in labour	0.50	6 to 12	30 to 60	Moderate to complete
	0.25	6 to 12	15 to 30	Minimal
CAUDAL EPIDURAL				
Surgical operations	0.50	15 to 30	75 to 150	Moderate to complete
Analgesia in labour	0.50	10 to 20	50 to 100	Moderate to complete
	0.25	10 to 20	25 to 50	Moderate
PERIPHERAL NERVES	0.50	Up to 30	Up to 150	Moderate to complete
	0.25	Up to 60	Up to 150	Slight to moderate
SYMPATHETIC BLOCKS	0.25	20 to 50	50 to 125	-
*SPINAL ANAESTHESIA FOR SURGERY				
Average Adult	0.5	2 to 4	10 to 20	

[+] With continuous (intermittent) techniques, repeat doses increase the degree of motor block. The first repeat dose of 0.5% may produce complete motor block for intra-abdominal surgery.

* Bupivacaine without adrenaline. 4ml maximum dose.

Paediatric population:

Paediatric patients 1 to 12 years of age

Paediatric regional anaesthetic procedures should be performed by qualified clinicians who are familiar with this population and the technique.

The doses in the table should be regarded as guidelines for use in paediatrics. Individual variations occur. In children with a high body weight a gradual reduction of the dosage is often necessary and should be based on the ideal body weight. Standard textbooks should be consulted for factors affecting specific block techniques and for individual patient requirements. The lowest dose required for adequate analgesia should be used.

	Conc. mg/ml	Volume ml/kg	Dose mg/kg	Onset min	Duration of effect hours
ACUTE PAIN MANAGEMENT (per-and postoperative)					
Caudal Epidural Administration	2.5	0.6-0.8	1.5-2	20-30	2-6
Lumbar Epidural Administration	2.5	0.6-0.8	1.5-2	20-30	2-6
Thoracic Epidural Administration[b)]	2.5	0.6-0.8	1.5-2	20-30	2-6
Field Block (eg, minor nerve blocks and infiltration)	2.5		0.5-2.0		
	5.0		0.5-2.0		
Peripheral Nerve Blocks (e.g ilioinguinal –iliohypogastric)	2.5		0.5-2.0	a)	
	5.0		0.5-2.0	)	

[a)]The onset and duration of peripheral nerve blocks depend on the type of block and the dose administered.

[b)]Thoracic epidural blocks need to be given by incremental dosage until the desired level of anaesthesia is achieved.

In children the dosage should be calculated on a weight basis up to 2 mg/kg.

In order to avoid intravascular injection, aspiration should be repeated prior to and during administration of the main dose. This should be injected slowly in incremental doses, particularly in the lumbar and thoracic epidural routes, constantly and closely observing the patient's vital functions.

Peritonsillar infiltration has been performed in children above 2 years of age with bupivacaine 2.5 mg/ml at a dose of 7.5-12.5mg per tonsil.

Ilioinguinal-iliohypogastric blocks have been performed in children aged 1 year or older with bupivacaine 2.5 mg/ml at a dose of 0.1-0.5 ml/kg equivalent to 0.25-1.25 mg/kg. Children aged 5 years or older have received bupivacaine 5 mg/ml at a dose of 1.25-2 mg/kg.

For penile blocks bupivacaine 5 mg/ml has been used at total doses of 0.2-0.5 ml/kg equivalent to 1-2.5 mg/kg.

The safety and efficacy of Bupivacaine Hydrochloride 0.5%w/v solution for Injection in children < 1 year of age have not been established. Only limited data are available.

Safety and efficacy of intermittent epidural bolus injection or continuous infusion have not been established. Only limited data is available.

4.3 Contraindications

Bupivacaine hydrochloride solutions are contraindicated in patients with a known hypersensitivity to local anaesthetic agents of the amide group or to other components of the injectable formulation. Solutions of bupivacaine hydrochloride are contraindicated for intravenous regional anaesthesia (Bier's block).

Epidural anaesthesia, regardless of the local anaesthetic used, has its own contraindications which include: Active disease of the central nervous system such as meningitis, poliomyelitis, intracranial haemorrhage, subacute combined degeneration of the cord due to pernicious anaemia, and cerebral or spinal tumours. Tuberculosis of the spine. Pyogenic infection of the skin at or adjacent to the site of lumbar puncture. Cardiogenic or hypovolaemic shock. Coagulation disorders or ongoing anticoagulant therapy. Epidural and spinal anaesthesia is contraindicated in patients with an expanding cerebral lesion, a tumour, cyst or abscess, which may, if the intracranial pressure is suddenly altered, cause obstruction to the cerebrospinal fluid or blood circulation (the pressure cone).

Injection of adrenaline containing bupivacaine in areas of end arteries (e.g. penile block, Oberst block) may cause ischemic tissue necrosis.

Note: No specific contraindications were identified for paediatric patients.

4.4. Special Warnings and Precautions for Use

There have been reports of cardiac arrest during the use of bupivacaine for epidural anaesthesia. or peripheral nerve blockade where resuscitative efforts have been difficult, and were required to be prolonged before the patient responded. However, in some instances resuscitation has proven impossible despite apparently adequate preparation and appropriate management.

Like all local anaesthetic drugs, 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 drug. This is especially the case after unintentional intravascular administration or injection into highly vascular areas. Ventricular arrhythmia, ventricular fibrillation, sudden cardiovascular collapse and death have been reported in connection with high systemic concentrations of bupivacaine.

Adequate resuscitation equipment should be available whenever local or general anaesthesia is administered. The clinician responsible should take the necessary precautions to avoid intravascular injection (see 4.2).

Before any nerve block is attempted, intravenous access for resuscitation purposes should be established. Clinicians should have received adequate and appropriate training in the procedure to be performed and should be familiar with the diagnosis and treatment of side effects, systemic toxicity or other complications (see 4.9 & 4.8).

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

Overdosage or accidental intravenous injection may give rise to toxic reactions.

Injection of repeated doses of bupivacaine hydrochloride may cause significant increases in blood levels with each repeated dose due to slow accumulation of the drug. Tolerance varies with the status of the patient.

Although regional anaesthesia is frequently the optimal anaesthetic technique, some patients require special attention in order to reduce the risk of dangerous side effects:

- The elderly and patients in poor general condition should be given reduced doses commensurate with their physical status.
- Patients with partial or complete heart block – due to the fact that local anaesthetics may depress myocardial conduction
- Patients with advanced liver disease or severe renal dysfunction.
- Patients in the late stages of pregnancy
- Patients treated with anti-arrhythmic drugs class III (e.g. amiodarone) should be under close surveillance and ECG monitoring, since cardiac effects may be additive.

Only in rare cases have amide local anaesthetics been associated with allergic reactions (with anaphylactic shock developing in most severe instances).

Patients allergic to ester-type local anaesthetics drugs (procaine , tetracaine, benzocaine, etc) have not shown cross-sensitivity to agents of the amide-type such as bupivacaine.

Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of the local anaesthetic drug used.

- Local anaesthetics should be used with caution for epidural anaesthesia in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs.
- The physiological effects generated by a central neural blockade are more pronounced in the presence of hypotension. Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during epidural anaesthesia. Epidural anaesthesia should therefore be avoided or used with caution in patients with untreated hypovolaemia or significantly impaired venous return.
- Retrobulbar injections may very rarely reach the cranial subarachnoid space causing temporary blindness, cardiovascular collapse, apnoea, convulsions etc.
- Retro- and peribulbar injections of local anaesthetics carry a low risk of persistent ocular muscle dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves. The

severity of such tissue reactions is related to the degree of trauma, the concentration of the local anaesthetic and the duration of exposure of the tissue to the local anaesthetic. For this reason, as with all local anaesthetics, the lowest effective concentration and dose of local anaesthetic should be used.

- Vasoconstrictors may aggravate tissue reactions and should be used only when indicated.
- Small doses of local anaesthetics injected into the head and neck, including retrobulbar, dental and stellate ganglion blocks, may produce systemic toxicity due to inadvertent intra-arterial injection.
- Paracervical block may have a greater adverse effect on the foetus, than other nerve blocks used in obstetrics. Due to the systemic toxicity of bupivacaine, special care should be taken when using bupivacaine for paracervical block.
- There have been post-marketing reports of chondrolysis in patients receiving post-operative intra-articular continuous infusion of local anaesthetics. The majority of reported cases of chondrolysis have involved the shoulder joint. Due to multiple contributing factors and inconsistency in the scientific literature regarding mechanism of action, causality has not been established. Intra-articular continuous infusion is not an approved indication for Bupivacaine.

Local anaesthetics should be used with caution for epidural or spinal anaesthesia in the following situations: marked obesity, senility, cerebral atheroma, myocardial degeneration and toxaemia.

Epidural and spinal anaesthesia with any local anaesthetic can cause hypotension and bradycardia which should be anticipated and appropriate precautions taken. These may include preloading the circulation with crystalloid or colloid solution. If hypotension develops it should be treated with a vasopressor such as ephedrine 10-15mg intravenously. Severe hypotension may result from hypovolaemia due to haemorrhage or dehydration or aorto-caval occlusion in patients with massive ascites, large abdominal tumours or late pregnancy. Marked hypotension should be avoided in patients with cardiac decompensation.

Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during epidural anaesthesia.

Epidural anaesthesia can cause intercostal paralysis and patients with pleural effusions may suffer respiratory embarrassment. Septicaemia can increase the risk of intraspinal abscess formation in the postoperative period.

When bupivacaine is administered as intra-articular injection, caution is advised when recent major intra-articular trauma is suspected or extensive raw surfaces within the joint have been created by the surgical procedure, as that may accelerate absorption and result in higher plasma concentrations.

Epidural and spinal anaesthesia, properly performed, is generally well tolerated by obese patients and by those with obstructive lung disease. However, patients with a splinted diaphragm which interferes with breathing,

such as those with hydramnios, large ovarian or uterine tumours, pregnancy, ascites or omental obesity are at risk from hypoxia due to respiratory inadequacy and aortocaval compression due to tumour mass. Lateral tilt, oxygen and mechanical ventilation should be used when indicated. Dosage should be reduced in such patients.

Paediatric population:

The use of bupivacaine for intra-articular block in children 1 to 12 years of age has not been documented.

The use of bupivacaine for major nerve block in children 1 to 12 years of age has not been documented.

For Epidural anaesthesia children should be given incremental doses commensurate with their age and weight as especially epidural anaesthesia at a thoracic level may result in severe hypotension and respiratory impairment.

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Bupivacaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, e.g. certain anti-arrhythmics, such as lidocaine and mexiletine, since the systemic toxic effects are additive.

Specific interaction studies with Bupivacaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution should be advised. (Refer section 4.4)

4.6 Pregnancy and lactation

Pregnancy

There is no evidence of untoward effects in human pregnancy. In large doses there is evidence of decreased pup survival in rats and an embryological effect in rabbits if bupivacaine is administered in pregnancy. Bupivacaine should not therefore be given in early pregnancy unless the benefits are considered to outweigh the risks.

Foetal adverse effects due to local anaesthetics, such as foetal bradycardia, seem to be most apparent in paracervical block anaesthesia. Such effects may be due to high concentrations of anaesthetic reaching the foetus. (see also Section 4.4)

Breast-feeding
Bupivacaine enters the mother's milk, but in such small quantities that there is no

risk of affecting the child at therapeutic dose levels.

4.7 Effects on ability to drive and use machines

In general, it is sufficient to allow 2 - 4 hours post nerve block or until full functions have returned following regional nerve block. In many situations, patients receive a sedative or other C.N.S. depressant drug e.g. diazepam, midazolam to allow the block to be performed. One must allow adequate time for the effects of these drugs to clear.

Depending on dosage, local anaesthetics may have a very mild effect 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

Accidental sub-arachnoid injection can lead to very high spinal anaesthesia possibly with apnoea and severe hypotension.

The adverse reaction profile for Bupivacaine hydrochloride is similar to those for other long acting local anaesthetics. Adverse reactions caused by the drug per se are difficult to distinguish from the physiological effects of the nerve block (e.g., decrease in blood pressure, bradycardia), events caused directly (e.g., nerve trauma) or indirectly (e.g., epidural abscess) by needle puncture.

Neurological damage is a rare but well recognised consequence of regional and particularly epidural and spinal anaesthesia. It may be due to several causes, e.g. direct injury to the spinal cord or spinal nerves, anterior spinal artery syndrome, injection of an irritant substance, or an injection of a non-sterile solution. These may result in localised areas of paraesthesia or anaesthesia, motor weakness, loss of sphincter control and paraplegia. Occasionally these are permanent.

The adverse reactions considered at least possibly related to treatment with Bupivacaine hydrochloride from clinical trials with related products and post-marketing experience are listed below by body system organ class and absolute frequency. Frequencies are defined as very common (1/10), common (1/100, < 1/10), uncommon (1/1,000, < 1/100), rare (1/10,000, < 1/1,000), including isolated reports, or not known (identified through post-marketing safety surveillance and the frequency cannot be estimated from the available data).

Table of Adverse Drug Reactions (ADR)

System Organ Class	Frequency Classification	Adverse Drug Reaction
Immune system disorders	Rare	Allergic reactions, anaphylactic reaction/shock (see section 4.4)

Nervous system disorders	Common	paraesthesia, dizziness Following epidural injection of some local anaesthetic agents including bupivacaine, high sympathetic blockade may occasionally result in ocular and other symptoms similar to those seen in Horner's syndrome. These effects are encountered more commonly in pregnant women.
	Uncommon	Signs and symptoms of CNS toxicity (convulsions, circumoral paraesthesia, numbness of the tongue, hyperacusis, visual disturbances, loss of consciousness, tremor, light headedness, tinnitus, dysarthria, muscle twitching)
	Rare	Neuropathy, peripheral nerve injury, arachnoiditis, paresis and paraplegia
Eye disorders	Rare	Diplopia
Cardiac disorders	Common	Bradycardia (see section 4.4)
	Rare	Cardiac arrest (see section 4.4), cardiac arrhythmias
Vascular disorders	Very Common	Hypotension (see section 4.4)
	Common	Hypertension (see section 4.5)
Respiratory disorders	Rare	Respiratory depression
Gastrointestinal disorders	Very Common	Nausea

	Common	Vomiting
Renal and Urinary	Common	Urinary retention

Hepatic dysfunction, with reversible increases of SGOT, SGPT, alkaline phosphatase and bilirubin, have been observed following repeated injections or long-term infusions of bupivacaine. If signs of hepatic dysfunction are observed during treatment with bupivacaine, the drug should be discontinued.

Paediatric population

Adverse drug reactions in children are similar to those in adults, however, in children, early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during sedation or general anaesthesia.

4.8.1 Acute systemic toxicity

Systemic toxic reactions primarily involve the central nervous system (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 (see 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 is a graded response with symptoms and signs of escalating severity. The first symptoms are usually light-headedness, circumoral paraesthesia, numbness of the tongue, hyperacusis, tinnitus and visual disturbances. Dysarthria, muscular twitching or tremors are more serious and 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 following convulsions due to the increased muscular activity, together with the interference with respiration and possible loss of functional airways. In severe cases apnoea may occur. Acidosis, hyperkalaemia and hypoxia increase and extend the toxic effects of local anaesthetics.

Recovery is due to 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 may be seen in severe cases and is generally preceded by signs of toxicity in the central nervous system. In patients under heavy sedation or receiving a general anaesthetic, prodromal CNS symptoms may be absent. Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anaesthetics, but in rare cases cardiac arrest has occurred without prodromal CNS effects.

4.8.2 Treatment of acute toxicity

If signs of acute systemic toxicity appear, injection of the local anaesthetic should be immediately stopped.

Treatment of a patient with systemic toxicity consists of arresting convulsions and ensuring adequate ventilation with oxygen, if necessary by assisted or controlled ventilation (respiration).

Once convulsions have been controlled and adequate ventilation of the lungs ensured, no other treatment is generally required.

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.

Cardiac arrest due to bupivacaine can be resistant to electrical defibrillation and resuscitation must be continued energetically for a prolonged period.

High or total spinal blockade causing respiratory paralysis and hypotension during epidural anaesthesia should be treated by ensuring and maintaining a patent airway and giving oxygen by assisted or controlled ventilation.

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.

Reporting of suspected adverse reactions

Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, systemic toxicity appears later (15-60 minutes after injection) due to the slower increase in local anaesthetic blood concentration. (See sections 4.8.1 & 4.8.2)

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): N01B B51

Bupivacaine has a similar mechanism of action to other local anaesthetics in nerve axons in the peripheral nervous system. It also interferes with the function of all organs in which conduction or transmission of impulses occur. These include effects on the C.N.S, the autonomic ganglia, the neuromuscular junction and all forms of muscle fibres. At high doses it produces surgical anaesthesia, while at lower doses it produces sensory block (analgesia) with less pronounced motor block. Following absorption, bupivacaine may cause stimulation of the C.N.S followed by depression

and, in the cardiovascular system, it acts primarily on the myocardium where it may decrease electrical excitability, conduction rate, force of contraction and eventually cardiac arrest.

5.2 Pharmacokinetic properties

Absorption

Like other local anaesthetics, the rate of systemic absorption of bupivacaine is dependent upon the total dose and concentration administered, the route of administration and the vascularity of the tissue locally. Bupivacaine is about 95% bound to plasma proteins, mainly to alpha-1-acid glycoprotein at low concentrations and to albumin at high concentrations. In adults, the terminal half-life of Bupivacaine is 2.7 hours. In neonates and some young infants, terminal elimination half-lives could be as long as 8 to 12 hours. The maximum blood concentration varies with the site of injection.

Distribution

Amide local anaesthetics including Bupivacaine have been shown to have diminished clearance in neonates and infants less than 3 months of age, with steady maturation until they reach levels of adult clearance at about 8 months of age. Foetal concentrations are lower than maternal concentrations because only the free, unbound drug is available for placental transfer. Local anaesthetics are distributed to some extent to all body tissues, with higher concentrations found in highly perfused organs such as liver, heart and brain. In children the pharmacokinetics is similar to that in adults.

Elimination

Bupivacaine is metabolised in the liver and is excreted in the urine mainly as metabolites, with only 5 to 6% as unchanged drug.

5.3 Preclinical safety data

Bupivacaine hydrochloride is a well established active ingredient.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride, Sodium hydroxide, Water for injections.

6.2 Incompatibilities

Bupivacaine Injection should not be mixed with other drugs. The solution must not be stored in contact with metals, e.g. needles or metal parts of syringes, as dissolved metal ions may cause swelling at the site of injection.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Protect from light.
Store below 25°C.

6.5 Nature and contents of container

Clear One point cut (OPC) glass ampoules, glass type 1 Ph Eur. packed in cardboard cartons to contain 10 unwrapped or sterile wrapped ampoules.

Pack sizes: 10 x 10ml sterile wrapped ampoules
10 x 20ml sterile wrapped ampoules
10 x 10ml unwrapped ampoules
10 x 20ml unwrapped ampoules.

6.6 Special precautions for disposal

If only part used, discard the remaining solution.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

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