The English language text below is provided by Specific Pharma a/s as guidance for healthcare personnel for a better understanding of the original foreign language product information. Specific Pharma a/s cannot be held responsible for any inaccuracies in or misuse of the translation. The translation is for healthcare personnel use only.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BUPISEN CON ADRENALINA 5 mg/ml + 5mcg/ml soluzione iniettabile
1 ml vials; 2 ml vials; 5 ml vials; 10 ml vials; 20 ml vials

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BUPISEN CON ADRENALINA 5 mg/ml + 5mcg/ml soluzione iniettabile

	Content				
	1 ml vial	**2 ml vial**	**5 ml vial**	**10 ml vial**	**20 ml vial**
Active substance: Bupivacaine hydrochloride	5 mg	10 mg	25 mg	50 mg	100 mg
Active substance: Adrenaline acid tartrate (equal to adrenaline base)	9.1 mcg (equal to 5 mcg)	18.2 mcg (equal to 10 mcg)	45.5 mcg (equal to 25 mcg)	91 mcg (equal to 50 mcg)	182 mcg (equal to 100 mcg)

For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Injectable solution

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

BUPISEN CON ADRENALINA can be used in all types of peripheral anaesthesia: local infiltration, troncular, loco-regional, sympathetic block, retrograde intravenous block, caudal epidural, subarachnoid spinal.
BUPISEN CON ADRENALINA is therefore indicated in all general, emergency, orthopaedic, ophthalmological, ENT, stomatological, obstetric-gynaecological and dermatological surgery, whether used alone or in combination with narcosis.

4.2 Posology and method of administration

BUPISEN CON ADRENALINA is usually used in minimum dosages that vary according to the indications, from 2-3 mg to 100-150 mg, as outlined for guidance in the table:

Type of anaesthesia	Dosage		
	Conc. mg/ml	ml	mg
Trigeminal nerve block	2.5	1-5	2.5-12.5
	5	0.5-4	2.5-20
Radial nerve block	2.5	20-40	50-100
	5	10-30	50-150
Stellate ganglion block	2.5	10-20	25-50
Intercostal nerve block	2.5	4-8	10-20
	5	3-5	15-25
	The dose is for every intercostal space		
Epidural	2.5	30-40	75-100
	5	10-20	50-100
Continuous epidural	2.5		
	Start with 10 ml, then 3-5-8 ml every 4-6 hours, depending on the segments to be anaesthetised and the age of the patient.		
Sacral nerve block	2.5	15-40	37.5-100
	5	15-20	75-100
Splanchnic nerve block	2.5	10-40	25-100
Lumbar sympathetic block	2.5	10-40	25-100
Pudendal nerve blocks	5	20-30	100-150
Subarachnoid spinal block	10	2	20

Caution: As the vials do not contain any antimicrobial excipients, they should be used for a single administration. Any remaining product should be discarded.

It is recommended that the maximum dosage for an adult per single administration should not exceed 150 mg, corresponding to 30 ml of the 5 mg/ml solution. More generally, the safe dose not to be exceeded in both adults and children is 2 mg/kg for a single administration.

In long-term analgesic therapy, doses ranging from 0.25 to 1 mg/kg body weight are usually used; administration may be repeated 2-3 times within 24 hours.

4.3 Contraindications

Hypersensitivity to the product components or to other chemically similar substances, specifically to anaesthetics of the same group (amide-type). The product is also contraindicated in intravenous regional anaesthesia (Bier Block). Bupisen con adrenalina, due to its vasoconstrictor content, is contraindicated in cardiac patients, severe arteriopathies, hypertensive patients, subjects displaying any ischaemic manifestations or with TTH, nephropathic patients, hyperthyroidism and diabetes.

Not to be used in the event of known or presumptive pregnancy.

4.4 Special warnings and precautions for use

The total dosage should be adjusted according to the patient's general condition, age and relevant medical history.

If any infiltration under local anaesthesia is carried out in areas where collateral circulation is not possible (fingers, root of the penis, etc.), the anaesthetic should be used without a vasoconstrictor as a precaution in order to avoid ischaemic necrosis.

BUPISEN CON ADRENALINA contains sodium metabisulfite; this substance may cause allergic reactions and severe asthma attacks in sensitive individuals, especially in asthmatics.

The product should be used with scrupulous care in subjects undergoing treatment with MAOIs or tricyclic antidepressants.

Before use, the doctor must ascertain the circulatory status of the subjects to be treated. An overdose of anaesthetic should be avoided and two maximum doses should never be administered without an interval of at least 24 hours.
In any case, the lowest doses and concentrations should be used to achieve the desired effect.
The anaesthetic solution should be injected with caution, in small doses, approximately 10 seconds after prior aspiration. Especially when infiltrating highly vascularised areas, it is advisable to allow about 2 minutes to elapse before proceeding with the actual loco-regional nerve block. The patient should be monitored closely and administration should be stopped immediately at the first alarm symptom (for instance, sensory changes).
It is necessary to have the appropriate equipment, medicinal products and personnel immediately available for emergency treatment, as in rare cases serious and sometimes fatal reactions have been reported following the use of local anaesthetics, even without a history of individual hypersensitivity.

4.5 Interactions with other medicinal products and other forms of interaction
There are no known interactions with other medicinal products.

4.6 Pregnancy and lactation
The product is contraindicated in cases of established or presumed pregnancy (see section 4.3 Contraindications).

4.7 Effects on the ability to drive and use machinery
Not relevant.

4.8 Undesirable effects
Toxic and allergic reactions may occur. Among the former, CNS stimulation phenomena are reported with excitement, tremor, disorientation, dizziness, mydriasis, increased metabolism and body temperature and, at very high doses, trismus and convulsions; if the medulla oblongata is affected, there is cardiovascular, respiratory and emetic involvement with sweating, arrhythmias, hypertension, tachypnoea, bronchodilation, nausea and vomiting. Peripheral effects may affect the cardiovascular system with bradycardia and vasodilation.
Allergic reactions mostly occur in hypersensitive individuals, but many cases are reported with no history of individual hypersensitivity. Local manifestations include various types of skin rashes, urticaria, itching; general manifestations include bronchospasm, laryngeal oedema and even cardiorespiratory collapse due to anaphylactic shock.
Due to its action on the circulation, the vasoconstrictor can cause various abnormal effects, especially in cardiac subjects: asthma, sweating, wheezing, cardiac arrhythmias, hypertension (particularly serious in subjects who already have hypertension and hyperthyroidism), acute headache, photophobia, retrosternal and pharyngeal pain, vomiting.

4.9 Overdose
In the event of an overdose, stop administration at the first alarm symptom, place the patient in a horizontal position and ensure airway patency, administering oxygen in the event of severe dyspnoea or performing artificial ventilation (Ambu bag). The use of bulbar analeptics should be avoided so as not to aggravate the situation by increasing oxygen consumption. Convulsions can be controlled with intravenous Diazepam. Barbiturates, on the other hand, are not recommended as they can accentuate PBA. The circulation can be supported with the administration of liquids, e.g. Ringer's lactate solution, or corticosteroids in appropriate doses for intravenous administration; diluted solutions of α-ß-stimulants with a vasoconstrictive action (mephentermine, metaraminol and others) or atropine sulphate can be added.

Sodium bicarbonate in an appropriate concentration can be used intravenously as an antacid.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

BUPISEN CON ADRENALINA*:* pharmacotherapeutic group: amide-type local anaesthetic (bupivacaine with adrenaline), ATC code: N01BB51

Bupivacaine is a long-acting amide-type local anaesthetic. Experimental research conducted in mice, guinea pigs and rabbits has proven the greater analgesic potency and duration of action of Bupivacaine as compared to other local anaesthetics. Anaesthesia induced by bupivacaine lasts, depending on the conditions of use, between 4 and 20 hours. At the end of the anaesthesia itself, there is a long-lasting decrease in pain sensitivity, which makes it possible to significantly reduce the administration of analgesics over the next 24 hours.

5.2 Pharmacokinetic properties

The blood peak of bupivacaine depends on various factors: type of nerve block, concentration of the solution, presence or absence of adrenaline. Used without a vasoconstrictor at doses of 125-150 mg, maximum concentrations in whole venous blood (0.64 µg/ml) are obtained 15-30 minutes after epidural and caudal block. In arterial blood, simultaneous sampling gives 20-40% higher concentrations. Bupivacaine is distributed throughout the body's fluids and tissues and its plasma half-life is over 2 hours. Hepatically metabolised, bupivacaine is primarily excreted renally, either as such or as a metabolite.

5.3 Preclinical safety data

Acute toxicity of bupivacaine with adrenaline 1:200,000

- DL_{50} in mice: 2,1 mg/kg (i.v.); 95 mg/kg (s.c.)
- DL_{50} in rabbits: 50 mg/kg (s.c.)

Repeat-dose toxicity

- Prolonged administration in rats of 10 mg/kg bupivacaine combined with adrenaline for 4 weeks did not cause any pathological findings in organs or weight loss.

6. PHARMACEUTICALINFORMATION

6.1 List of excipients

Bupisen with adrenaline: Sodium chloride, sodium metabisulfite, water for injectable preparations.

6.2 Incompatibilities

Incompatibilities with other medicines are not known.

6.3 Shelf life

2 years in unopened packaging, properly stored.

6.4 Special precautions for storage

Do not store at a temperature above 25°C.

6.5 Nature and content of the container

Bupisen with adrenaline: 1, 2, 5 and 10 ml neutral glass vials of solution for injection in boxes of 10 vials. 20 ml neutral glass vials of solution for injection in boxes of 10 vials.

6.6 Instructions for use and handling

No particular instructions.

7. MARKETING AUTHORISATION HOLDER

Industria Farmaceutica Galenica Senese

8. MARKETING AUTHORISATON NUMBERS

Bupisen con adrenalina 5 mg/ml + 5 mcg/ml soluzione iniettabile 10 fiale da 1 ml - MA No. 034849012
Bupisen con adrenalina 5 mg/ml + 5 mcg/ml soluzione iniettabile 10 fiale da 2 ml - MA No. 034849024
Bupisen con adrenalina 5 mg/ml + 5 mcg/ml soluzione iniettabile 10 fiale da 5 ml - MA No. 034849036
Bupisen con adrenalina 5 mg/ml + 5 mcg/ml soluzione iniettabile 10 fiale da 10 ml - MA No. 034849048
Bupisen con adrenalina 5 mg/ml + 5 mcg/ml soluzione iniettabile 5 fiale da 20 ml - MA No. 034849051

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

BUPISEN CON ADRENALINA: September 2000 / September 2010

10. DATE OF REVISION OF THE TEXT

May 2007