1.3. Product labelling

1.3.1. Summary of product characteristics

1. NAME OF MEDICINAL PRODUCT

ARTICAINA CON ADRENALINA PIERREL
"40 mg / ml soluzione iniettabile con adrenalina 1:100.000“
"40 mg / ml soluzione iniettabile con adrenalina 1:200.000“

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Articaine 40 mg/ml solution for injection with adrenaline 1:100.000
Each mL of solution contains:

Articaine hydrochloride	40.00 mg
Adrenaline bitartrate	18.20 mcg

equivalent to 10 mcg of adrenaline

Articaine 40 mg/ml solution for injection with adrenaline 1:200.000
Each mL of solution contains:

Articaine hydrochloride	40.00 mg
Adrenaline bitartrate	9.10 mcg

equivalent to 5 micrograms of adrenaline

Excipient with known effect: Sodium metabisulfite

3. PHARMACEUTICAL FORM

Solution for injection in cartridges for specialized use.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Articaine 40 mg/ml solution for injection with adrenaline 1:100.000. Dental surgery on the bone and mucous membranes that require intense ischemia; surgery on the dental pulp (amputation and extirpation); extraction of teeth with apical periodontitis and fractured (osteotomy); surgery of long-duration (for example: Caldwell-Luc surgery, percutaneous osteosynthesis, cystectomy, mucogingival operations, cavity preparation and abutments for the implantation of crowns).
Articaine 40 mg/ml solution for injection with adrenaline 1:200,000. Routine intervention, such as extraction of individual teeth or in series, preparations of cavities and abutments for the application of crowns, in particular in patients suffering from severe systemic diseases.

4.2. Posology and method of administration

For normal uncomplicated extractions of the upper teeth in a non-inflammatory state, it is generally sufficient injecting into the vestibular fornix 1.8 ml (a cartridge) of product for each tooth. Exceptionally, a further injection of 1 to 1.8 ml is necessary. This way you can avoid the pain of the palatal injection.
In cases where it is necessary to make an incision or a suture in the palate, it is sufficient to inject into the palate about 0.1 ml at a time.
In case of multiple extractions of adjacent teeth, the number of injections vestibular can be reduced in most cases.
For normal uncomplicated extractions of the mandibular premolars, (nerve block) truncal anesthesia may be waived, it is sufficient plexus anesthesia with a cartridge (1.8 ml) of product per tooth. If you are not establishing full anesthesia, it is advisable to do another injection of 1 to 1.8 ml in the buccal cavity. Only if also in this case the analgesic effect is not complete, the usual mandibular foramen injection is indicated.
For the preparation of cavities and demolition of abutments for crowns, depending on the extent and duration of treatment, (with the exception of the molars of the mandible) from 0.5 to 1.8 ml of the product for each tooth in the vestibular are indicated.

For the Instructions of the injector use, see the paragraph 6.6.

4.3. Contra-indications

Known hypersensitivity to the components or closely related substances from a chemical standpoint.
As with all local anesthetics containing adrenaline, intravenous administration is contra-indicated. Classical contra-indications associated with adrenaline as a vasoconstrictor added to local anesthetics are: heart disease, severe arterial disease, hypertension, ischemic events of any kind, essential headache, kidney disease, hyperthyroidism, diabetes and glaucoma of angle of the anterior chamber of the eye, as well as its use in anesthesia of the terminal circulatory district. Known or suspected pregnancy (see 4.6.).

4.4. Special warnings and precautions for use

WARNING. The product contains the preservative sodium metabisulphite: this substance can cause in susceptible individuals, particularly in asthmatics, allergic reactions and serious asthma attacks.
Direct administration into a vein must be absolutely avoided.
To avoid biting the lips, tongue and mucous membranes, the patient should be instructed not to chew anything before normal sensitivity is restaured.
Keep out of reach of children.
Do not use after the expiration date indicated on the package.
Before use, the physician must ensure the health of the patient and his circulatory condition, must also obtain information on current therapies and possible allergic reactions before.
We must avoid any overdose of anesthetic and never give two highest doses of the product without having elapsed a minimum of 24 hours. The lowest doses and concentrations that can

be used to achieve the desired effect must be used. The anesthetic solution should be injected with caution in small doses with 10 seconds intervals and with prior aspiration. Especially when you have to infiltrate highly vascular areas should it is advisable to alow about 2 minutes before proceeding to the loco-regional block. The patient must be kept under careful control immediately suspending the administration at the first sign of alarm (eg change in sensorium).
It 's necessary to have the immediate availability of equipment, personnel and drugs for the treatment of emergencies, since in rare cases following the use of local anesthetics, severe reactions, sometimes with fatal outcome, even in the absence of individual hypersensitivity to history have been reported.
Local anesthesia should be avoided in infected and inflamed areas.

4.5. Interactions with other medicaments and other forms of interaction
No impact other than those desires with opioids routinely used for premedication and for additional medication or other analgesics, atropine, psychotropic medication or analeptics peripheral or, in case of additional general anesthesia, barbiturates, inhalation anesthetics, ketamine and analgesic neuroleptics.
The hypertensive action of sympathomimetic vasoconstrictors such as the adrenaline may be potentiated by tricyclic antidepressants or MAOIs. In case of treatment with such drugs, the product must be used with extreme caution. Interactions of this type have been reported with the use of noradrenaline at a concentration of 1:25,000 and adrenaline at a concentration of 1:80,000; The concentrations contained in the two formulations of the product (1:100,000 and 1:200,000) is lower, however, one must consider the possibility of an interference of this type.

4.6. Pregnancy and lactation
Do not use during pregnancy or suspected.

4.7. Effects on ability to drive and use machines
Only the doctor can decide if, after surgery, the patient may drive or operate machinery.

4.8. Undesirable effects
Undesirable effects can be due to high plasma levels and hypersensitivity reactions to anesthetic and to the vasoconstrictor.
Effects of anesthetics: are described side effects resulting from high plasma levels on the CNS and on the cardiovascular system. CNS effects described are: excitement, tremors, disorientation, dizziness, mydriasis, increased metabolism and body temperature, and for very high doses, convulsions and lockjaw, if the brainstem is interested the cardiovascular, respiratory and emetic centres are affected with sweating, arrhythmias, hypertension, tachypnea, bronchodilation, nausea and vomiting. The peripheral-type effect affecting the cardiovascular apparatus are: bradycardia and vasodilation.
Allergic reactions occur mostly in hypersensitive individuals but many cases are reported with the absence of individual hypersensitivity in the amnesis. Local events include rash of various

types, hives, itching, those general bronchospasm, laryngeal edema until cardiorespiratory collapse from anaphylactic shock.
Effects due to the vasoconstrictor: its action on the circulation may cause undesirable effects of various kinds, especially in subjects with subnormal cardio-cirulatory system: anxiety, sweating, difficulty breathing, cardiac arrhythmia, hypertension (especially severe in hypertensive and hyperthyroidic patients), acute headache, photophobia, retrosternal pain and throat, vomiting, if symptoms of this type appear treatment must be immediately discontinued.
In the event of other undesirable effects relating to the use of the drug tell the patient to inform his doctor.

4.9. Overdose
At the first warning sign must stop the administration, placing the patient in a horizontal position and ensure the clear air way, administering oxygen in case of severe dyspnea or performing artificial ventilation (Ambu balloon). The use of analeptics should be avoided so as not to aggravate the situation by increasing the consumption of oxygen. Possible convulsions can be controlled with the use of diazepam at a dose of 10-20 mg intravenously; barbiturates are discouraged since they may accentuate the bulbar depression. The circulation can be supported with the administration of cortisone in appropriate doses intravenously: dilute solutions of of alpha-beta stimulants may be added to the vasoconstrictor (mefentermina, metaraminolo and others) or atropine sulphate. Sodium bicarbonate at targeted concentration can be used intravenously as anti-acid.

5.PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties
The product contains articaine, local anesthetic of the amide type, which is characterized chemically to be the only thiophene derivative of the local anesthetics in use to date. Both formulations of the product are local anesthetics for anesthesia plexus and truncal with rapid analgesic and deep effect. (latency time from 1 to 3 minutes) with optimal tissue tolerability.
The duration of surface anesthesia with Articaine 40 mg/ml solution for injection with adrenaline 1:100,000 is on average 45 minutes; Articaine with 40 mg/ml solution for injection with adrenaline 1:200,000 on average of 53 minutes. The good tissue tolerability and the mild vasoconstriction allow healing of the wounds without complications.

5.2. Pharmacokinetic Properties
The maximum tolerated (MTD) dose of articaine by the intramuscular route in mice is between 50 and 100 mg/kg and in rats up to 50 mg/kg, intravenously, MTD up to 5 mg/kg in rats and up to 10 mg/kg in mice. The results of subacute toxicity tests, conducted in various animal species with different doses, show no deviation from the norm of parameters considered.
The studies, conducted in rats and rabbits, indicate that articaine is devoid of teratogenic activity.

5.3. Preclinical safety data
The adrenaline (1:100.000 - 1:200.000) added to the articaine slows down the passage of the anesthetic into the bloodstream and thus maintains a tissue active concentration more prolonged and thus increases the anesthetic effectiveness of the articaine; Consequently, the adrenaline permits to use the smallest possible amount of anesthetic, obtaining equally favorable plasma concentrations.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Sodium chloride, sodium metabisulfite, water for injections.

6.2. Incompatibilities
None known.

6.3. Shelf life
Two years in its closed box correctly stored.

6.4. Special precautions for storage
Do not store above 25 °C.

6.5. Nature of primary packaging and contents of container
The cartridges is avaiable in different packages:
Box containing n° 100 sterile cartridges of 1.8 ml clear high hydrolytic resistance (type I) glass with bromobutyl rubber plunger.
Closure of the cartridge consists of an aluminum cap and rubber gasket.
Or
Box containing n° 100 disposable injectors containing a cartridge of 1,8 ml clear high hydrolytic resistance (type I) glass with bromobutyl rubber plunger.
Closure of the cartridge consists of an aluminum cap and rubber gasket.

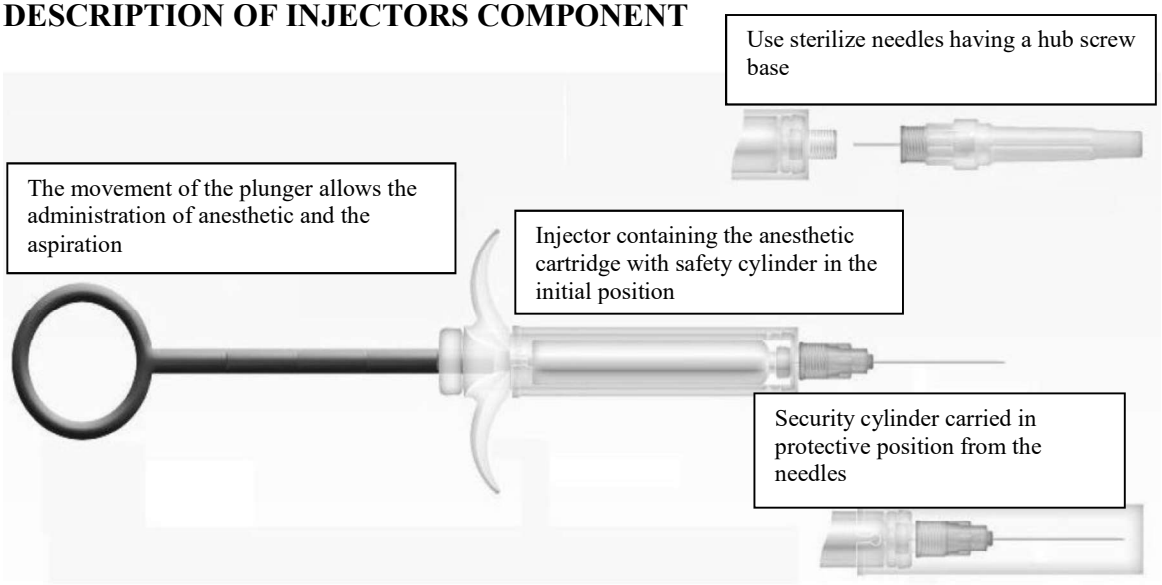
6.6 Special precautions for use and disposal of used injectors
Any unused medicinal product and its waste materials, should be disposed of in compliance with local authorities procedures.

The following informations are intended for healthcare professional

For correct use of the injector by the dentist, please refer to the instructions given below:

CONTENT
Each blistes contains a single disposable injector containing one Pierrel anaesthetic cartridge and ready for use.
General informations are reported on the box cojtaining 100 disposable injectors.

DESCRIPTION OF INJECTORS COMPONENT



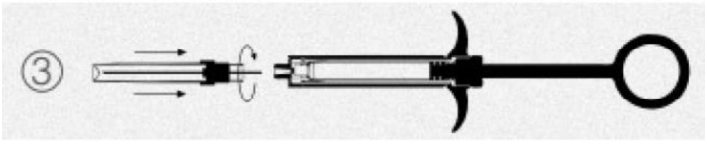
NOTE: needle is not included in the package

INSTRUCTIONS OF USE

Step 1-2: check the integrity of the package and open it carefully without the use of cutting tools.

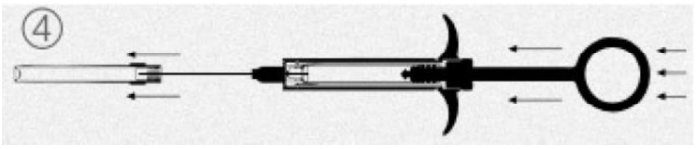
WARNING: do not use the injector if package has not been opened or damaged.

Step 3: select the most appropriate needle for the desired intervention, having a hub screw base; remove the rear protection of needle and insert it into the injector head puncturing the membrane of the cartridge containing the anesthetic; screw the needle on the injector thread until it stops.

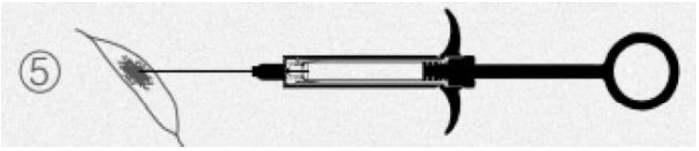


WARNING: Do not remove the needle cap until you are ready to inject.

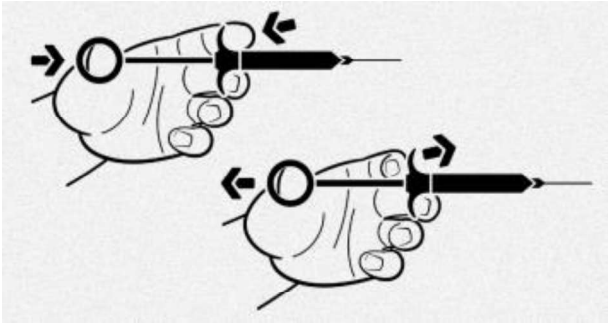
Step 4: grip the injector firmly by inserting the thumb into the thumb ring and place index and middle fingers on the finger grips.



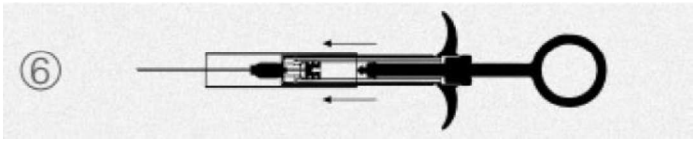
Step 5: remove the needle cap and the injectors is ready to use.



Note: the particular injectors plunger allows to perform the "self-aspirating test“ to check for accidental injection into blood capillares/vessels. To facilitate this action, place your fingers as shown in figure below.

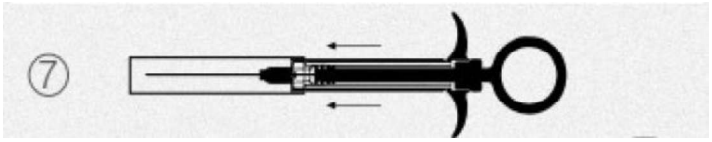


Step 6: administer anaesthetic as required



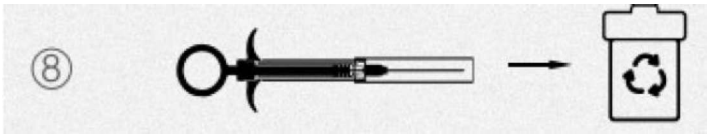
Note:
It is can make multiple injections in the same patient with the same injector.
In case of multiple injections performed with the same injector, in the event that the injector is to be put between one administration and the next, it is advisable to partially activate the protection system carrying the sliding cylinder forward, taking care not to lock it stroke end.
At the time of administration of an additional portion of anesthetic, you must retract the protective cylinder until it will be locked in its initial position.

Step 7: completed the administration and withdrawal of the needle from the injection zone, slide forward the lock cylinder in the final position of the lock-up (the limit shutter is perceptible with a "click").



Note: it is recommended to make sure that the security system has been properly primed (sliding cylinder locked forward), for example by pressing the same gently against a firm surface and checking that the protection system remains firm in its locked position.

Step 8: disposal of used injectors: disposal of components and packaging materials should be done in compliance with local authorities procedures and regulations regardind bio-hazardous waste.



WARNING: single use only. Do not sterilize or reuse.
The sterilization oft he injector may compromise the functional integrity of the device and/or lead to device failure and/or degradation oft he anaesthetic solution, and may result in patient injury, illness or death. Reuse may also create a risk of contamination of the device and cause patient infection or cross infection, including, but not limited to, the transmission of the infectious disease from one patient to another. Contamination of the device may lead to injury, illness or death oft he patient.

7. MARKETING AUTHORIZATION OWNER
PIERREL PHARMA S.R.L.: Strada Statale Appia, 46/48 – 81043 Capua (CE)

8. MARKETING AUTHORIZATION NUMBER
"40 mg / ml soluzione iniettabile con adrenalina 1:100.000“
– 100 cartucce 1.8 ml AIC n°031815018

"40 mg / ml soluzione iniettabile con adrenalina 1:200.000"
– 100 cartucce 1.8 ml AIC n°031815020

"40 mg / ml soluzione iniettabile con adrenalina 1:100.000"
– 100 iniettori monouso precaricati con cartucce da 1,8 ml AIC n° 031815032

"40 mg / ml soluzione iniettabile con adrenalina 1:200.000"

– 100 iniettori monouso precaricati con cartucce da 1,8 ml AIC n° 031815044

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF
13/05/1998 - 13/05/2008

10. DATE OF REVISION OF THE TEXT
February 25th 2016 (Italy)