SUMMARY OF PRODUCT CHARACTERISTICS

PRODUCT SUMMARY

1. NAME OF THE MEDICINAL PRODUCT

SEPTANEST 1:200,000
ARTIKENT 1:200,000 (Own label for Kent Express)
BARTINEST 1:200,000
ISONEST 1:200,000 (Own label for Henry Schein Procare)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<table>
<thead>
<tr>
<th>Per cartridge</th>
<th>1.7 ml</th>
<th>2.2 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine hydrochloride</td>
<td>88.000 mg</td>
<td>88.000 mg</td>
</tr>
<tr>
<td>Epinephrine bitartrate</td>
<td>15.47 mcg</td>
<td>20.02 mcg</td>
</tr>
<tr>
<td>Adrenaline tartrate (expressed as base)</td>
<td>8.50 mcg</td>
<td>11.00 mcg</td>
</tr>
</tbody>
</table>

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

FOR USE IN DENTAL ANAESTHESIA ONLY.

SEPTANEST is indicated for local or loco-regional dental anaesthesia in patients of at least 4 years who are to undergo the following procedures:

- Classic operations:
  - Single extractions with no complications,
  - Multiple extractions,
  - Extractions of impacted teeth, trephination,
  - Apical resections, removal of cysts, alveolectomies,
  - Preparation of cavity, biopulpectomies,
  - Maxillo-facial surgery,
  - Crown and bridge procedures,

- Muco-gingival operations.

SEPTANEST 1:100,000 is also available and may be more appropriate for procedures of longer duration and when there is a risk of significant bleeding into the operative field.

(See section 5.1 for more information on duration of analgesia).

4.2 Posology and Method of Administration

For most common operations, one infiltration with 1.7 ml SEPTANEST is sufficient. In all cases, the injection must be done slowly (about 1 ml/min).

For an infiltration in the interdental septum, a quantity of 0.3 to 0.5 ml is indicated as generally sufficient.

Higher volumes should rarely be required.

Do not exceed the equivalent of 7 mg articaine hydrochloride per kilo of weight which corresponds, for a subject weighing 60 kg, to six (6) standard 1.7 ml cartridges or five (5) standard 2.2 ml cartridges (doses of 7 mg/kg were not exceeded in clinical trials). Anaesthesia is obtained rapidly (2 to 5 minutes).

**Dosage in children should be commensurate with their weight.**

The duration of anaesthesia during which an operation can be performed is about one hour (pulpal analgesia) depending on the technique used, and on the procedure.
Do not use under 4 years of age.

<table>
<thead>
<tr>
<th>Maximum Dose: 0.175 ml/kg</th>
<th>20 kg child</th>
<th>40 kg child</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.5 ml, i.e.</td>
<td>7.0 ml, i.e.</td>
</tr>
<tr>
<td></td>
<td>= 2 cartridges of 1.7 ml</td>
<td>= 4 cartridges of 1.7 ml</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>or</td>
</tr>
<tr>
<td></td>
<td>= 1.5 cartridge of 2.2 ml</td>
<td>= 3 cartridges of 2.2 ml</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Recommended dose: 0.06 ml/kg for simple procedure</th>
<th>0.07 ml/kg for complex procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>1.2 ml</td>
<td>= ¼ cartridge of 1.7 ml or</td>
</tr>
<tr>
<td></td>
<td>i.e.</td>
<td>= ½ cartridge of 2.2 ml</td>
</tr>
<tr>
<td></td>
<td>Complex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4 ml</td>
<td>= ¾ cartridge of 1.7 ml or</td>
</tr>
<tr>
<td></td>
<td>i.e.</td>
<td>= ½ cartridge of 2.2 ml</td>
</tr>
<tr>
<td></td>
<td>Simple</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.4 ml</td>
<td>= 1 ½ cartridge of 1.7 ml or</td>
</tr>
<tr>
<td></td>
<td>i.e.</td>
<td>= 1 cartridge of 2.2 ml</td>
</tr>
<tr>
<td></td>
<td>Complex</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.8 ml</td>
<td>= 1 ½ cartridge of 1.7 ml or</td>
</tr>
<tr>
<td></td>
<td>i.e.</td>
<td>= 1 cartridge of 2.2 ml</td>
</tr>
</tbody>
</table>

4.3 Contra-Indications

- Hypersensitivity to any local anaesthetic agent.
- Hypersensitivity to any other component of SEPTANEST.
- Patients who have experienced bronchospasm after administration of any product which contains sulphites should not be given SEPTANEST.
- Patients who are known, or who have a history which suggests a deficiency in plasma cholinesterase activity (see section 5.2.).
- Patients receiving monoamine oxidase inhibitors (or who have received such an agent within two weeks) or tricyclic antidepressants.
- Patients in whom there is a possibility that general anaesthesia might be required to complete the procedure.
- Do not use under 4 years of age.

4.4 Special Warnings and Precautions for Use

- Intra-vascular injection is strictly contra-indicated. Accidental injection into a blood vessel may be associated with systemic adverse effects due to the circulating levels of adrenaline and/or articaine. Therefore, it is imperative to ensure that the needle being used for the injection does not go into a vessel.
- Each time a local anaesthetic is used there should be available:
  - Anti-convulsant medicines (benzodiazepines or barbiturates which can be injected), myorelaxants, atropine and vasopressors and benadryl or adrenaline for a severe allergic or anaphylactic reaction.
  - Resuscitating equipment (in particular a source of oxygen) enabling artificial ventilation if necessary.

SEPTANEST should not be used in patients with a deficiency of plasma cholinesterase activity.

- Since amide-type local anaesthetics are also metabolized by the liver, SEPTANEST should be used with caution in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anaesthetics normally, are at greater risk of developing toxic plasma concentration.
- Due to the presence of adrenaline, the product is not advised for diabetic subjects and for patients with thyrotoxicosis.
- The effects of local anaesthetics may be reduced if an injection is made into an inflamed or infected area.

SEPTANEST should be administered with caution to subjects with cardiovascular disease, abnormalities of cardiac conduction, or a history of epilepsy.

4.5 Interactions with Other Medicaments and Other Forms of Interaction

No drug interaction studies have been performed.

Due to the possibility that clinically significant increases in circulating adrenaline concentrations may occur post-injection, SEPTANEST should be administered with caution to any patient receiving drugs with sympathomimetic properties or with agents whose therapeutic actions may be antagonised by adrenaline.

Articaine should be given with caution to any patient receiving an antiarrhythmic agent.

4.6 Pregnancy and Lactation

Use in pregnancy
No clinical experience of the use in pregnant and lactating women is available. Safe use of local anaesthetics during pregnancy has not been established with respect to adverse effects on foetal development. The product should only be used in pregnancy when the benefits are considered to outweigh the risks.

**Use during lactation**

The excretion of articaine or its metabolites in human milk is unknown. Therefore, nursing mothers should not breastfeed 48 hours following anaesthesia with SEPTANESt.

### 4.7 Effects on Ability to Drive and Use Machines

In a controlled study on healthy volunteers articaine was shown to have no effect on the level of attentiveness, reaction time to visual stimulations or motor coordination.

Patients who experience systemic adverse effects during or immediately following administration of SEPTANESt should be advised to avoid driving or operating machinery until resolution of signs or symptoms.

### 4.8 Undesirable Effects

Articaine and adrenaline may reach sufficient concentrations in blood to provoke systemic adverse effects.

- **Toxic reactions due to articaine**

  Toxic reactions (showing an abnormally high concentration of local anaesthetic in the blood) may appear either immediately, by accidental intravascular injection or later, by true overdose following an injection of an excessive quantity of anaesthetic solution. One may observe:

  - **symptoms showing effects on the central nervous system**: nervousness, shaking, yawning, trembling, apprehension, nystagmus, logorrhoea, headache, nausea, buzzing in the ears. These signs, when they appear, require rapid corrective measures to prevent possible worsening.
  
  - **respiratory symptoms**: tachypnea, then bradypnea, which could lead to apnea.
  
  - **cardiovascular signs**: reduction in the contractile power of the myocardium, lowering of heart rate and drop in blood pressure.

- **Other adverse reactions due to articaine**

  **Incidence greater than 1%**
  - Headache, face oedema, gingivitis,
  - Disruption of nerve transmission (para-, hypo- and dysaesthesia) may appear after articaine administration. Resolution usually occurs within eight weeks.

  **Incidence less than 1%**
  - Nausea.

  **Very rare**
  One may observe manifestations of hypersensitivity to articaine as rash, pruritus, urticaria or anaphylaxis.

  The administration of large doses of articaine may produce methaemoglobinemia in patients with subclinical methaemoglobinemia.

  - **Allergic reaction to sulphites**

    Allergic-type reactions may occur in patients with bronchial asthma due to hypersensitivity to the sulphite component and may be manifested by dermatologic reactions, oedema, urticaria and other allergy symptoms.

  - **Adverse events due to adrenaline**

    Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result.

### 4.9 Overdose

The most serious effects of articaine intoxication are on the CNS and cardiovascular system. The type of toxic reaction is unpredictable and depends on such factors as dosage, rate of absorption, and clinical status of the patient. Two types of reactions that effect stimulation and/or depression of the central cortex and medulla may result from systemic absorption.

Slow onset symptoms following overdose include stimulation leading to nervousness, dizziness, blurred vision, nausea, tremors, convulsions, hypotension, cardiovascular depression, and respiratory arrest.
Rapid onset symptoms following overdose include depression, leading primarily to respiratory arrest, cardiovascular collapse, and cardiac arrest. Since cardiac arrest symptoms may occur rapidly and with little warning, treatment should be readily available.

Supportive treatment should be given; specific therapy may be required to counter adverse effects on the cardiovascular and/or respiratory systems and to control convulsions. There is no specific antidote.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Articaine is a local anaesthetic of the amide type. The ATC code is N01BB08.

Preclinical pharmacodynamic studies showed that the mechanism of action of articaine is similar to that of other commonly used anaesthetics (lidocaine, procaine, prilocaine). Inhibition of the generation and the conduction of the action potential but no change in resting potential were shown. Articaine blocked sodium channels and, with lower sensitivity, potassium channels at neutral pH. Inhibition of muscle activation after nerve stimulation and depression of cardiac electrophysiologic measurements demonstrated that articaine had the same pharmacologic activities as other local anaesthetics.

When injected close to the sensitive nerve filaments, articaine has the reversible effect of blocking the conduction of painful sensations. The anaesthesia is obtained rapidly (about 3 minutes); it is deep and lasts about 15 to 30 minutes with articaine alone.

Adrenaline added to the solution reduces bleeding during surgery, slows down the passage of articaine into the general circulation and thus ensures the prolonged maintenance of an active tissular concentration.

SEPTANESE 1:200,000, administered by infiltration or nerve block injection, provides anaesthesia in about 3 minutes. The pulpal analgesia lasts 60 minutes.

SEPTANESE 1:100,000, administered by infiltration or nerve block injection, provide anaesthesia in about 3 minutes. The pulpal analgesia lasts 75 minutes and the bleeding during surgery is significantly reduced.

5.2 Pharmacokinetic Properties

Injected in the mouth by the submucosa route, in a solution containing 1:200,000 adrenaline, peak plasma concentrations of articaine are related to dose and generally occur within 0.5 hour after administration. The half life elimination is about 1.6 to 1.8 hours.

Articaine is rapidly hydrolysed by plasmatic cholinesterases to its primary metabolite articanic acid which is further metabolized to articians acid glucuronide. Articans acid concentration peak is about 30 to 60 minutes after the peak in articaine concentration.

Articaine is cleared from the body within 12 to 24 hours. Approximately 50% of the dose is eliminated in the urine, 95% as articaine acid and 2% as articaine.

5.3 Preclinical Safety Data

In preclinical studies, symptoms of articaine toxicity were independent of the route of administration (IV, IM, SC and PO) and of the animal species and included trembling, vertigo, and tonic and clonic convulsions. The duration and intensity of these symptoms were dose dependent: at high doses (approx 50-100 mg/kg b.w. following single administration) the convulsions resulted in death and at low doses all symptoms dissipated in 5 to 10 minutes. Lethal doses of articaine resulted in pulmonary oedema in mice following intravenous and subcutaneous administration and in rats following intravenous, intramuscular, subcutaneous and oral administration.

Preclinical studies with articaine on rats, rabbits and cats showed no effect on embryo or foetal development in utero and no skeletal or organ abnormalities. The rate of embryonic mortality was similar in treated and control animals.

Pups of lactating rats receiving articaine in high doses (50 mg/kg/bw/day) causing maternal toxicity showed delayed eye opening and increased likelihood failure in the passive avoidance test.

Following IV administration, the presence of 1:100,000 adrenaline increased the toxicity of articaine in the rat and mouse, but not in the rabbit.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium chloride,
Sodium metabisulphite (E223),
Sodium hydroxide solution,
Water for injections.

6.2 Incompatibilities
6.3 Shelf-life
16 months.

6.4 Special Precautions for Storage
Store up to 25 °C. Store in the original container protected from light. Do not freeze.

6.5 Nature and Contents of Container
Box containing 5 blister trays of 10 x 1.7 ml or 2.2 ml (glass cartridges) with rubber closures.

6.6 Instructions for Use/Handling
One or more cartridges should be used on a single patient during each session of treatment. If only a portion of a cartridge is used, the remainder must be discarded.

ADMINISTRATIVE DATA

7. MARKETING AUTHORISATION HOLDER
SEPTODONT UK Ltd.
Units R & S
Orchard Business Centre,
St Barnabas Close,
Allington, Maidstone
Kent ME16 0JZ
ENGLAND

8. MARKETING AUTHORISATION NUMBER
PL 08313/0038

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION
19/08/1998

10. DATE OF (PARTIAL) REVISION OF THE TEXT
August 2003.