

Product Information

Local AnGel® 4% 5g, 30g

1. Name

Local AnGel® RCH (Amethocaine gel 4%)

CAS number: 94-24-6.

Molecular formula: C(15)H(24)N(2)O(2)

2. Description

Amethocaine base 4% w/w in a white opalescent gel formulation.

3. Pharmacology

Amethocaine is an ester type local anaesthetic and shares the pharmacological effects of other local anaesthetics. It has high lipid solubility and high affinity for neural tissue. A high protein binding capacity (76%) maintains the drug at the receptor site with formation of a long-lasting depot in the stratum corneum and clearance by esterases in the skin and bloodstream. It inhibits the initiation and transmission of nerve impulses by stabilising the neuronal membrane (by blocking sodium ion influx across the axon). Neuronal conduction is first blocked in the autonomic, then in sensory and finally in motor nerve fibres. The mechanism of membrane stabilisation is similar to that of benzocaine.

Pharmacokinetics

Amethocaine has been shown to have a local anaesthetic action after 30 minutes application (median duration 1.5 hours with a range 0.5-3.5hrs), but application for 60 minutes results in longer duration of action (median duration 3 hours with a range of 1-5 hours (p<0.001)). Amethocaine gel is thought to act more rapidly in children than in adults.

Amethocaine is reported to be about 15% bioavailable when applied as a 4% gel to intact skin, with a mean absorption and elimination half-life of about 75 minutes. It is hydrolysed by non-specific tissue esterases in the dermis, to p-n-butyl-aminobenzoic acid (BBA). This cutaneous metabolism decreases the potential for systemic toxicity of dermally applied amethocaine. Plasma concentrations of amethocaine measured after topical application (2g of 5%w/w amethocaine applied for 240 minutes) to the dorsum of the hand, revealed plasma concentrations up to 0.2mg/L in 3 subjects. In the other 7 subjects there was no detectable amethocaine or BBA in the plasma measured at 30, 60, 120, 240 and 360 minutes. It has been demonstrated that the topical application of the maximum recommended dose (100mg) produces neither significant plasma concentrations nor clinical evidence of toxicity. When amethocaine is applied to the skin, as opposed to mucous membranes, both the speed and degree of systemic absorption are reduced.

4. Clinical Trials

Volunteers

Five randomised controlled studies, cited in a review by O'Brien et al 2005, have established the efficacy of 4% amethocaine gel in adult volunteers. In summary these have demonstrated that amethocaine produces more effective anaesthesia when compared to placebo and is as equally effective as lignocaine-prilocaine (EMLA® cream) with a shorter onset of action.

Children

Eight randomised studies cited in a review by O'Brien et al 2005, have evaluated the use of amethocaine 4% in children for its use in venepuncture, intravenous cannulation, vaccination and accessing centrally placed devices. The majority of the comparative studies examined the efficacy of amethocaine compared to EMLA® cream. Two of four studies (comparing amethocaine to EMLA® cream for reducing pain of venepuncture) found amethocaine and EMLA® cream equally efficacious; one study found amethocaine superior and the other study found amethocaine inferior.

When amethocaine was compared to EMLA® cream for efficacy for intravenous cannulation both studies reported greater anaesthesia with amethocaine. The first study though, used a 40 minute application time for both anaesthetics, when it is known that EMLA® cream requires at least 60 minutes to achieve acceptable anaesthesia.

When compared with EMLA® cream for accessing centrally placed devices, both preparations were found to produce clinically acceptable anaesthesia at 30 minutes (amethocaine) and 60 minutes (EMLA® cream). The final study found that a 30 minute application of amethocaine significantly reduced the pain of vaccination when compared to placebo.

The above evidence suggests that 4 % amethocaine gel is an effective topical anaesthetic. It can reduce pain of intravenous cannulation, venepuncture and centrally placed venous devices within 30-45 minutes of application and produces anaesthesia equivalent to EMLA® cream, however anaesthesia is achieved more quickly and lasts longer.

Neonates

Six randomised controlled trials cited in a review by O'Brien et al 2005, have analysed the topical use of amethocaine 4% in neonates between 27-42 weeks of gestational age at birth (some trials performed within 2 weeks after delivery). Cutaneous anaesthesia was assessed in two trials and venepuncture, intravenous cannulation, heel prick blood sampling and peripherally placed intravenous catheters (PICC) in the other four studies. Amethocaine was found to produce safe and clinically acceptable anaesthesia in these neonates within 30 to 60 minutes for venepuncture and intravenous cannulation, however it was found to be ineffective at reducing pain of heel prick blood sampling and PICC insertion.

5. Indications

Percutaneous local anaesthetic to produce anaesthesia of the skin prior to venepuncture or venous cannulation in adults and children over 1 month of age.

6. Contraindications

Do not apply to broken or inflamed tissue. Avoid if there is hypersensitivity to amethocaine (or other ester type local anaesthetics) or hydroxybenzoate (parabens) preservatives or any ingredients of the product. Keep away from the eyes. Not for use in premature babies and infants under one month of age.

7. Precautions

Amethocaine should not be applied to broken skin, ears, eyes, inflamed, traumatised or highly vascular surfaces or mucous membranes as absorption is enhanced and there is potential for increased risk of toxicity. Amethocaine can cause allergic contact sensitisation reactions, particularly with repeated contact. Healthcare professionals should take care to avoid or minimise contact with Local AnGel® during application and removal (use gloves – preferably nitrile not latex).

Use in pregnancy

There is no specific information as to the safety of amethocaine in pregnancy.

Use in lactation

It is not known if amethocaine or its metabolites are secreted into breast milk, however there is minimal absorption of amethocaine after topical administration to intact skin.

Use in children

Full term infants are born with structurally mature skin including a fully developed stratum corneum, but the risk of toxicity is not completely eliminated as newborns and infants have greater skin surface area to bodyweight ratios than older children and adults. Therefore, higher rates of dermal absorption are seen in these populations. Preterm infants have poorly developed epidermal barriers for the first 2-3 weeks of life and as such they are more vulnerable to enhanced absorption and therefore toxicity of topical medications during this period. Amethocaine 4 % gel (Ametop™) is licensed for use in the United Kingdom in term infants over one month of age.

8. Adverse Effects

Mild transient erythema at the site of application is frequently seen with topical administration, this may disappear within 20 minutes after removal of the gel or persist for several hours. This is a consequence of the known vasodilator action of amethocaine at the site of application and may be



an advantage in making small veins on the dorsum of the hand more prominent. Slight oedema or pruritus occur less commonly. Blistering of the skin may also occur. Several cases of sensitisation have been described in adults upon repeated exposure to topical amethocaine. The para-aminobenzoic acid metabolite of ester type anaesthetics is thought to be involved in the sensitisation process by acting as a hapten. To the best of our knowledge there have been no reports of methaemoglobinaemia directly associated with amethocaine. It has only been implicated when applied to mucous membranes in a combination topical spray, Cetacaine® (contains benzocaine 14%, butyl aminobenzoate 2% and amethocaine 2%). Methaemoglobinaemia has been well documented in association with the amide anaesthetics, benzocaine, lignocaine and prilocaine.

9. Dosage and Administration

To aid spreadability and ease of application, ensure gel has come to room temperature. Apply 0.5 grams of gel as a thick layer (size of \$2 coin) to the centre of the area to be anaesthetised and cover with an occlusive dressing. Do not spread or rub in. Remove gel and dressing after 30 minutes for venepuncture and after 45 minutes for venous cannulation. Full anaesthesia may take up to 60 minutes. Do not leave on for longer than 60 minutes. A single application generally provides anaesthesia for 4 to 6 hours. Local AnGel® should not be used in premature infants or those less than 1 month of age.

10. Overdosage

Overdosage with Local AnGel® is unlikely to result from application to intact skin (see pharmacology section). If accidentally ingested systemic toxicity may occur. Local anaesthetic toxicity generally involves the cardiovascular, neurologic and haematologic systems. Initial effects include mild hypertension and tachycardia, light-headedness, mild agitation and confusion. In severe cases this may progress to seizures, coma, respiratory depression, bradycardia, ventricular dysrhythmias and asystole.

11. Presentation and Storage Conditions

Topical gel of amethocaine base containing methylcellulose, propylene glycol, methyl hydroxybenzoate, propyl hydroxybenzoate and purified water.

Store between 2 to 8 degrees C to prevent crystallization and oxidation. Protect from light. Once removed from the refrigerator and stored at room temperature the gel has a recommended life of 30 days.

12. Name and Address of Manufacturer

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13. Poison Schedule

Schedule 2

14. Date of Issue

24th August 2005 Code: LOC01004_1_PI

