PRESCRIBING INFORMATION

AMETOP GEL 4%

Tetracaine Hydrochloride Gel

4% w/w Topical Analgesic

Valeo Pharma Inc.
16667 Hymus Blvd.
Kirkland, Québec
Canada H9H 4R9

Date of Revision:
July 8, 2020

Table of Contents

AMETOP Gel 4%
Tetracaine Hydrochloride Gel

HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Topical	Gel 4% w/w	Potassium phosphate, purified water, sodium chloride, sodium hydroxide, sodium methylparaben, sodium propylparaben and xanthan gum.

INDICATIONS AND CLINICAL USE

AMETOP Gel 4% (Tetracaine Hydrochloride Gel) is indicated for the following:

- Percutaneous local anaesthetic to produce anaesthesia of the skin prior to venepuncture or venous cannulation, including intravenous injections of medications.

Geriatrics:
There is no significant difference in pseudocholinesterase activity in men between the ages of 16 – 94 years and women aged 40 – 99 years.

Pediatrics:
Literature references support its use in this population after one month of age and in the case of premature babies 1 month after the expected delivery date (44 gestation weeks).

CONTRAINDICATIONS

Use in premature babies or full term infants less than one month of age, in whom the metabolic pathway for tetracaine may not be fully developed. **For premature babies use of AMETOP Gel 4% is not recommended before 1 month after the expected delivery date (44 weeks gestation).**

Known hypersensitivity **to any of the ingredients** or local anaesthetics of the ester type.

Do not apply AMETOP Gel 4% to broken skin, mucous membranes or to the eyes or ears.

WARNINGS AND PRECAUTIONS

General
Only apply to intact, unbroken skin. Not to be taken internally.

Ear/Nose/Throat
Do not apply AMETOP Gel 4% to broken skin, mucous membranes or to the eyes or ears. AMETOP Gel 4%, like other local anaesthetics may be ototoxic and should not be instilled into the middle ear or used for procedures which might involve penetration into the middle ear.

Immune
Do not use AMETOP Gel 4% to anaesthetize skin prior to immunization.

Neurologic
Although the systemic availability of tetracaine by percutaneous absorption of AMETOP Gel 4% is low, caution should be exercised in patients with epilepsy.

Special Populations

Pregnant Women: The product is not recommended for use by pregnant women. The rapid hydrolysis of tetracaine by plasma pseudocholinesterase suggests that it is unlikely to present a significant hazard to the foetus when used as indicated.

Nursing Women: It is not known whether tetracaine or its metabolites are secreted in breast milk. Therefore the product is not recommended for use by breastfeeding mothers.

Pediatrics: Use of AMETOP Gel 4% in premature babies before 1 month after the expected delivery date (44 weeks gestation) and in full term infants less than one month of age is not recommended because the metabolic pathway for tetracaine may not be fully developed.

Geriatrics: No special warning.

ADVERSE REACTIONS

Adverse Drug Reaction Overview
Slight erythema is frequently seen at the site of application and is due to the pharmacological action of tetracaine dilating capillary vessels. This may help in delineating the anaesthetised area. Slight oedema or itching are less frequently seen at the site of application. More severe erythema, oedema and/or itching have rarely been reported.
In very rare instances, blistering of the skin at the site of application may be apparent; in these cases, remove the gel immediately and treat the affected area symptomatically.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

Cardiovascular: N/A
Digestive: N/A
Gastrointestinal: N/A

Abnormal Hematologic and Clinical Chemistry Findings

N/A

Post-Market Adverse Drug Reactions

Common: Erythema (slight), Oedema (slight), Pruritus (slight)

Slight erythema is frequently seen at the site of application and is due to the pharmacological action of amethocaine (tetracaine) in dilating capillary vessels.

Slight oedema or itching are less frequently seen at the site of application. This may be due to the local release of histamine and 5-HT.

Rare:	Erythema (severe) Oedema (severe) Pruritus (severe)
Very rare:	Blistering. In cases of blistering of the skin at the site of application, remove the gel immediately and treat the affected area symptomatically.

DRUG INTERACTIONS

Overview

N/A

Drug-Drug Interactions

Do not use AMETOP Gel 4% to anaesthetize skin prior to immunization.

Drug-Food Interactions

N/A

Drug-Herb Interactions
N/A

Drug-Laboratory Interactions
N/A

DOSAGE AND ADMINISTRATION

Missed Dose
N/A

Administration
Apply the contents of the tube to the skin starting from the centre of the area to be anaesthetised and cover with an occlusive dressing. The contents expellable from one tube (approximately one gram) are sufficient to cover and anaesthetise an area of up to 30 cm^2 (6 x 5 cm). Smaller areas of anaesthetised skin may be adequate.

Adequate anaesthesia can usually be achieved for venepuncture following a thirty minute application time, and for venous cannulation following a forty-five minute application time; after which the gel should be removed with a gauze swab and the site prepared with an antiseptic wipe in the normal manner.

Is it not necessary to apply AMETOP Gel 4% for longer than the above recommended times and anaesthesia is maintained for 4 to 6 hours in most patients after a single application.

Recommended Dose and Dosage Adjustment
Adults (including the elderly): No more than the contents of 1 tube (approximately 1g) should be applied per site of venepuncture or venous cannulation. In certain circumstances anaesthesia of more than one site may be necessary (e.g., where cannulation is difficult). In such cases, a maximum of 5 sites may be anaesthetized at the outset of a course of treatment, if required to ensure that a series of sites are available for cannulation in the event that venous access cannot be achieved at the first site. The maximum cumulative dose in a 24 hour period should not exceed 7 tubes.

Children (over 1 month of age): The contents of no more than 1 tube (approximately 1 g) should be applied in a single application. The maximum cumulative dose in a 24 hour period should not exceed 2 tubes.

Reconstitution:

Oral Solutions : N/A

Parenteral Products: N/A

OVERDOSAGE

Overdosage with AMETOP Gel 4% is unlikely to result from application to intact skin. If accidentally ingested systemic toxicity may occur, and signs will be similar to those observed after administration of other local anaesthetics.

Systemic effects of overdose of tetracaine have been described as: signs of inebriation, tingling, numbness of the tongue, tinnitus, nystagmus, nausea or vomiting, twitching and ultimately convulsions. Oxygen is recommended as the first line treatment for systemic toxicity.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

N/A

Pharmacodynamics

Tetracaine is a local anaesthetic and is believed to act by blocking nerve conduction mainly by inhibiting sodium ion influx across the axon membrane. Tetracaine achieves this by acting upon specific receptors that control gating mechanisms responsible for conductance changes in specialised proteinaceous sodium channels

Pharmacokinetics

Absorption: *In vivo* (pigs) data has demonstrated that AMETOP Gel 4% is 15± 11% bioavailable when administered to intact normal skin, with mean absorption and elimination half lives of 1.23±0.28hours. No un-metabolised tetracaine has been conclusively detected in human plasma following topical administration.

Distribution: In vitro **s**tudies using human plasma show that **A**METOP Gel 4% is metabolised rapidly in the blood by plasma pseudocholinesterase, suggesting that AMETOP Gel 4% will have an effect only at the site of application and will have no systemic effects.

Metabolism: The ester type "caine" anaesthetics are rapidly metabolised in human blood mainly by plasma pseudocholinesterase. In an *in vitro* study, an initial concentration of tetracaine 3.33 μM (1 μg/ml) in human plasma was found to have been fully metabolised within 20 seconds.

Excretion: Twelve subjects (6 Females / 6 Males) received topical applications of 10g of AMETOP Gel 4% (400 mg of amethocaine) which was spread over 300 cm^2 on both thighs, and covered with a dressing for one hour. No quantifiable amethocaine was found in plasma samples. However, p-(n-butylamino) benzoic acid (BABA), the major metabolite of tetracaine, was found in most samples, and had a mean lag time of 1.5 ± 0.9 hours, tmax of 4.6 ± 2.3 hours and Cmax of 65 ± 50 ng/mL. Low levels of amethocaine, 11 to 78 ng / mL, were found in seven of ten urine samples (4 – 10 hours).

Special Populations and Conditions

Pediatrics: N/A

Geriatrics: N/A

Gender: N/A

Race: N/A

Hepatic Insufficiency: N/A

Renal Insufficiency: N/A

Genetic Polymorphism: N/A

STORAGE AND STABILITY

Keep refrigerated at 2º to 8º. Do not freeze. Protect from heat. Keep in a safe place out of the reach of children.

SPECIAL HANDLING INSTRUCTIONS

Repeated exposure to AMETOP Gel 4% may increase the risk of sensitisation reactions to tetracaine.

DOSAGE FORMS, COMPOSITION AND PACKAGING

1.5g internally lacquered, aluminum collapsible tubes, designed to deliver 1.0g of AMETOP Gel 4% on squeezing.

AMETOP Gel 4% Composition

Medicinal Ingredient: Tetracaine

Non-medicinal ingredients: Potassium phosphate, purified water, sodium chloride, sodium hydroxide, sodium methylparaben, sodium propylparaben and xanthan gum.

CONSUMER INFORMATION

AMETOP Gel 4%
Tetracaine Hydrochloride Gel

This leaflet is part of "Prescribing Information" published when AMETOP Gel 4% was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about AMETOP Gel 4%. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
AMETOP Gel 4% is used to create a temporary loss of feeling or numbness of the skin for preventing / reducing the pain experienced when needles are given to obtain a blood specimen or when an intravenous drip is inserted. AMETOP Gel 4% is for external use only.

What it does:
AMETOP Gel 4% is a topical anaesthetic used to cause a temporary loss of feeling or numbness of the skin at the place it is applied.

When it should not be used:
• in premature babies or full term infants less than one month of age.
• if you or your child is allergic to tetracaine, or any other "caine" type of anaesthetics, or any of the non-medicinal ingredients (see non-medicinal ingredients below).
• prior to immunization.
• do not apply AMETOP Gel 4% to broken skin, large areas of the body, mucous membranes or to the eyes or ears.
• if you are pregnant or breastfeeding.

What the medicinal ingredient is:
Tetracaine 4%

What the important nonmedicinal ingredients are:
Potassium phosphate, purified water, sodium chloride, sodium hydroxide, sodium methylparaben, sodium propylparaben and xanthan gum.

What dosage forms it comes in:
AMETOP Gel 4% is available as a gel in 1.5g tubes.

WARNINGS AND PRECAUTIONS

- Carefully read the product label and this insert before use. If you are not sure about how to use this product, ask your doctor or pharmacist for guidance.
- Children should be closely observed during and after use of AMETOP Gel 4% as they are at greater risk for serious side effects.
- Consult a doctor immediately if the following symptoms appear: weakness, confusion, headache, difficulty breathing and/or discoloured skin.
- Do not use more than the recommended dose. Larger amounts should be applied only under the direct supervision of a medical doctor.
- Side effects are more likely to occur if you apply large amounts of this product to irritated or broken skin, or if you apply large amounts of this product and cover the treated area with a dressing.

BEFORE you use AMETOP Gel 4% talk to your doctor or pharmacist if:
- You are either pregnant or breastfeeding.
- You or your child is allergic to any ingredients contained in this product or any other "caine" type anaesthetics.
- You are a patient with epilepsy.

INTERACTIONS WITH THIS MEDICATION

Do not use AMETOP Gel 4% to anaesthetize skin prior to immunization.

Tell your doctor or pharmacist about any other drugs you take or have recently taken, including the ones you can buy without a prescription.

PROPER USE OF THIS MEDICATION

Administration:
Apply the contents of the tube to the skin starting from the centre of the site where the skin is to be punctured by a needle and cover with an occlusive dressing. The contents from one tube (approximately 1g) are sufficient to cover and anaesthetise an area of up to 30cm2 (6 x 5 cm). Smaller areas of anaesthetised skin may be adequate. Adequate anaesthesia can usually be achieved for getting a needle or having blood taken following a thirty minute application time, and for inserting an intravenous drip following a forty-five minute application time; after which the gel should be removed with a gauze swab and the site prepared with an antiseptic wipe in the normal manner. It is not necessary to apply AMETOP Gel 4% for longer than the above recommended times and anaesthesia is maintained for 4 to 6 hours in most patients after a single application.

Usual dose:
Adults (including the elderly): No more than the contents of 1 tube (approximately 1g) should be applied per site where a needle or an intravenous drip is to be inserted. In certain circumstances anaesthesia of more than one site may be necessary. In such cases, a maximum of 5 sites may be anaesthetized at the outset of a course of treatment, if required to ensure that a series of sites are available in the event that venous access cannot be achieved at the first site. The maximum cumulative dose in a 24hour period should not exceed 7 tubes.

Children (over 1 month of age): No more than 1 tube should be applied in a single application. The maximum cumulative dose in a 24hour period should not exceed 2 tubes.

Overdose:
In case of AMETOP Gel 4% overdose or if you think you or anyone else are experiencing any of the side effects described

below, telephone your doctor or go to the nearest hospital right away.

Missed Dose:

N/A

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Slight redness is frequently seen at the site of application and is due to the action of tetracaine dilating small blood vessels. This may help in identifying the anaesthetised area.

Slight swelling or itching are less frequently seen at the site of application.

More severe redness, swelling and/or itching have rarely been reported.

In very rare instances, blistering of the skin at the site of application may be apparent; in these cases, remove the gel immediately and treat the symptoms of the affected area.

This is not a complete list of side effects. For any unexpected effects while taking AMETOP Gel 4%, contact your doctor or pharmacist.

HOW TO STORE IT

Keep refrigerated at 2° to 8° C. Do not freeze. Protect from heat.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full prescribing information, prepared for health professionals can be found by contacting the sponsor, Valeo Pharma Inc., at:
16667 Hymus Blvd.
Kirkland, Quebec
Canada H9H 4R9

Phone: 1-855-694-0151

This leaflet was prepared by Valeo Pharma Inc.

Last revised: July 8, 2020