

MEDICINES CONTROL COUNCIL



COMPLEMENTARY MEDICINES CAFFEINE AND MENTHOL

This guideline is intended to provide recommendations to applicants wishing to submit applications for the registration of Complementary Medicines containing menthol and caffeine. In addition to this guideline, Council reserves the right to request any additional information to establish the safety, quality and efficacy of a medicine in keeping with the knowledge current at the time of evaluation. The MCC is committed to ensure that all registered medicines will be of the required quality, safety and efficacy.

Guidelines and application forms are available from the office of the Registrar of Medicines and the website.

Publication for comment	April 2017
Due date for comment	31 May 2017

Use the *Guideline Comments Form*¹ available on the MCC website when submitting comments.

Submit comments in hard copy to the Registrar of Medicines, Civitas Building, Thabo Sehume Street, Pretoria.

Comments may also be submitted by e-mail to Dr J Lotter at Jeanette.Lotter@health.gov.za

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REGISTRAR OF MEDICINES

¹ 6.13 Guideline Comments Form Dec08 v1.doc

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1 INTRODUCTION

The Medicines Control Council (MCC) is responsible for regulating all medicines and medical devices in South Africa by ensuring that they meet standards of safety, efficacy and quality. The MCC operates in terms of the Medicines and Related Substances Act, 1965 (Act 101 of 1965), the Regulations issued in terms of that Act, and associated guidelines.

The MCC has noted that a number of Complementary medicines (CMs) contain amounts of Caffeine or Menthol – some may by default exist as an integral part of any formulation (e.g.: Caffeine in *Paullinia cupana*, *Camellia sinensis* or Menthol in *Mentha arvensis*, *Juniperus communis*) while other products may be inappropriately loaded with either of these two ingredients.

This presents particular challenges related to patient safety but also yields significant questions as to the intended efficacy of the medicine. As a number of herbs used within the Discipline-Specific sub-category of Complementary Medicines may contain these ingredients and considering the addition of these ingredients to Health Supplements and their close association to DS medicines, it is considered imperative to provide guidance on the use of either substance which may inform the development of CM products suitable for registration.

After comparisons of international policies and monographs and South Africa's existing policy, the attached guidance documents have been developed to guide the use of Caffeine and Menthol in Complementary Medicines (CMs).

2 SCOPE

This guideline applies to all applications for registration of complementary medicines containing caffeine and / or menthol

The guide for the use of Caffeine is reflected in Annex 1.

The guide for the use of Menthol is reflected in Annex 2.

3 UPDATE HISTORY

Date	Reason for update	Version & publication
Feb 2017	New guideline to address caffeine and menthol in CMs published for comment	v1 Apr 2017
31 May 2017	Due date for comment	

Annex 1: CAFFEINE

GUIDANCE FOR USE AS PART OF A COMPLEMENTARY MEDICINE

<p>Caffeine</p> <p><i>1,3,7-Trimethylxanthine</i> <i>3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione</i> <i>guanine</i> <i>methyltheobromine</i></p>	<p>Caffeine is not permitted as a single substance formulation.</p> <p>When used as an active ingredient as part of a multiple substance formulation, it is permitted only in products for oral use where the action of the caffeine will not be responsible for the primary action of a product.</p> <p>The maximum daily dose takes into account the total caffeine content of any product.</p> <p>May only be used as an excipient in topical products.</p> <p>May only be indicated for adults.</p>
<p>Warnings and Special Precautions</p>	<ul style="list-style-type: none"> • Not suitable for children under the age of 18. • The label statement: “CONTAINS CAFFEINE” • Consult a health care practitioner prior to use if you are taking lithium. • Consult a health care practitioner prior to use if you have high blood pressure, glaucoma, and/or detrusor instability (overactive bladder syndrome) • Consumption with other medicines (e.g. bitter orange extract, synephrine, octopamine, ephedra, ephedrine) which increase blood pressure is not recommended. • Consumption with other caffeine-containing products (e.g. medications, coffee, tea, colas, cocoa, guarana, maté) is not recommended. • This product is not intended as a substitute for sleep. <p>Doses greater than or equal to 301 mg per day:</p> <ul style="list-style-type: none"> • Consult a health care practitioner if you are of childbearing age, pregnant or breastfeeding.
<p>Known Adverse Reactions</p>	<ul style="list-style-type: none"> • Hypersensitivity/allergy is known to occur, in which case, discontinue use.
<p>Concentration/Maximum Dose</p>	<p>Maximum Daily Dose: 300 mg</p> <p>Dose(s): up to 200 mg per single dose, not to exceed 300 mg per day.</p> <p>Directions for use: Every 3 - 4 hours, as needed</p>
<p>Health Claim:</p>	<p>Assists (temporarily) to promote alertness and wakefulness.</p> <p>Assists (temporarily) to relieve fatigue.</p>

Annex 2: MENTHOL

GUIDANCE FOR USE AS PART OF A COMPLEMENTARY MEDICINE

Menthol <i>L-menthol</i> <i>Levomenthol</i> <i>(-)-menthol</i> <i>(1R,2S,5R) (-)-5-Methyl-2-(1-methylethyl)cyclohexanol</i> <i>(1R,2S,5R)-5-methyl-2-(propan-2-yl)cyclohexan-1-ol</i> <i>Cyclohexanol, 5-methyl-2-(1-methylethyl)-, (1R,2S,5R)-</i>	<p>The synthetic form (DI-menthol) is not permitted for use in Health Supplements.</p>
<p>Accepted Sources:</p>	<p><i>Juniperus communis</i> (Parts: Fruit) <i>Menthaarvensis</i> (Parts: Herb top) <i>Menthaarvensis</i> (Parts: Herb top flowering) <i>Menthaarvensis</i> (Parts: Leaf) <i>Menthacanadensis</i> (Parts: Herb top) <i>Menthapulegium</i> (Parts: Whole plant) <i>Menthaspicata</i> (Parts: Leaf) <i>Mentha x piperita</i> (Parts: Herb top flowering) <i>Mentha x piperita</i> (Parts: Leaf) <i>Ocimumbasilicum</i> (Parts: Whole plant) <i>Zea mays</i> (Parts: Leaf) <i>Zea mays</i> (Parts: Stigma and style)</p>
<p>Use:</p>	<p>When used as an active ingredient, it is permitted only in topical applications, medicated space sprays or medicated throat lozenges.</p>
<p>Concentration/Maximum Dose:</p>	<p>Products for external use: The concentration must not exceed 16 %. Maximum Daily Dose: 18,5 mg.</p>
<p>Health Claim:</p>	<p>Soothing action for the (skin) (mouth) (throat) [specify area of application].</p>