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13 May 2019

To:
Scheduling Secretariat
TGA

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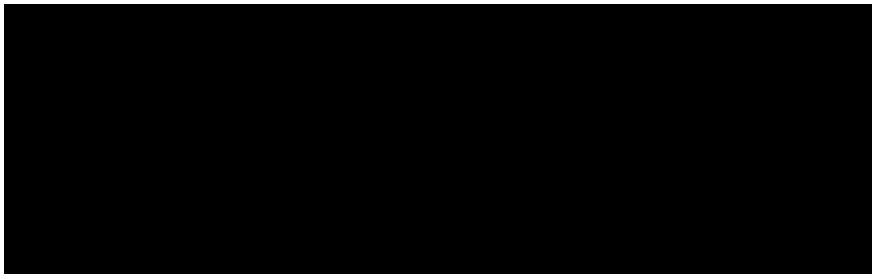


Introduction

Complementary Medicines Australia (CMA) welcomes the opportunity to provide comment on the proposed scheduling amendment, item 1.4, to make the constituent sanguinarine a schedule 10 substance (dangerous substance).

CMA is committed to a vital and sustainable complementary medicines sector, and represents stakeholders across the value chain – including manufacturers, raw material suppliers, distributors, consultants, retailers and allied health professionals.

CMA supports the safe use of medicines and acknowledges the rationale for the scheduling amendment for the component, sanguinarine, noting *Sanguinaria canadensis* (Boodroot) as a key ingredient in the preparation Black Salve, which is marketed and sold on-line, encouraging consumers to treat skin cancer.

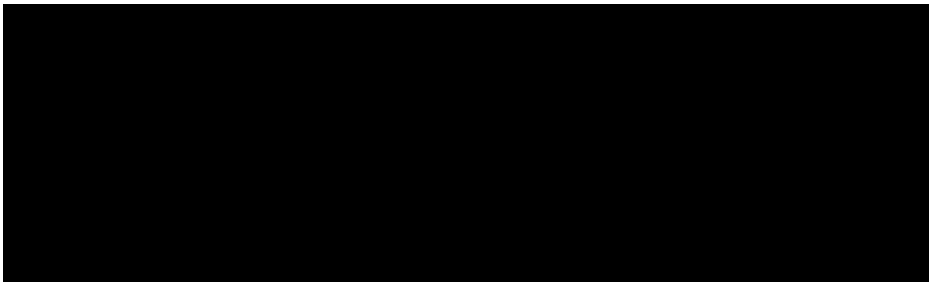
CMA does not support self-diagnosis and self-medication, by consumers, of serious diseases.
However, CMA believes that the upper content limit of sanguinarine of 0.1% would render *S. canadensis* a completely restricted substance, irrespective of plant part, route of administration and professional use.

Furthermore and importantly, the proposed amendment could also impact the accessibility of other herbs such as *Chelidonium majus.*

CMA proposes alternative scheduling and/or regulatory restrictions that could both mitigate the public health risk posed by Black Salve, and allow for use of herbal medicines containing sanguinarine under professional supervision by herbalists and naturopaths.

The CMA submission will

- Outline the herbal medicine products containing sanguinarine
- Discuss the proposed scheduling entry
- Propose alternative regulatory restrictions for sanguinarine.



Use of herbs containing sanguinarine

SANGUINARIA CANADENSIS

In a review by Croaker (2016) et al the authors note the history of use of *S.canadenis* by native American tribes and early European settlers to the north America. [1]

In Australia there are two products listed on the Australian Register of Therapeutic Goods that contain *S. canadensis*. It is also available and supplied as a liquid extract for extemporaneous compounding. These are not required to be listed, but are required to be manufactured under GMP conditions.

Like many plant constituents there is significant natural variability, and sanguinarine content is dependent on harvesting time, ranging between 2.81 – 3.96% in the dried rhizome.[2]

As noted in the public scheduling notice, *S.canadensis* is used in Black Salve, which is primarily supplied on-line as an illegal medicine. That is, a product which is making therapeutic claims but is neither registered or listed on the Australian Register of Therapeutic Goods (ARTG).

Furthermore, Black Salve is promoted and advertised for curing skin cancer, which is a prohibited representation and not permitted to be made about any medicine, whether listed or registered.

In 2012 the TGA released a safety report on its website warning consumers of the risks and dangers of black slave.[3]

CHELIDONIUM MAJUS

C. majus is used in Europe, African and Asian traditions of medicine, primarily for its spasmolytic and choleretic properties which assist in dyspepsia, irritable bowel syndrome and biliary disorders. [4] The ingredient is currently included in 6 listed medicines and 1 registered medicine.

Consistent with the registration process of any medicine, the ingredients and the final product would have been subject to a complete toxicological evaluation. The same product has been clinically trialled in more than 50 000 participants, including children.

C. majus is used by Australian natural health practitioners including western herbal medicine practitioners as well as traditional Chinese medicine practitioners, and is currently used in medicines in the European Union (EU), Australia United States and Canada.

C. majus contains a range of alkaloids including the Benzylisoquinoline type which consists of at least three subgroups:

- Benzophenanthridines: chelerythrine, chelidonine, sanguinarine, isochelidonine
- Protoberberines: berberine, coptisine, dihydrocoptisine, stylopine
- Protopine. [5]

The total content range of all these alkaloids is 0.01-1%, and the individual amounts subject to natural variability. Therefore it is theoretically possible for the sanguinarine content in a preparation containing *C.majus* to exceed the proposed limit of 0.1%

Impact of proposed scheduling entry

The proposed entry is

Schedule 10 - New Entry

SANGUINARINE for therapeutic use **except** in preparations containing 0.1 per cent or less.

Index - New Entry

SANGUINARINE

Schedule 10.

CMA

- agrees with the widespread concerns about the use of Black Salve, given its known risks and unknown therapeutic benefit
- promotes consumers seeking appropriate and responsible medical assistance for serious conditions such as skin cancer
- does not encourage the use of Black Salve or any other illegal medicines

Schedule 10 includes substances of such danger to health as to warrant prohibition of sale, supply and use. This schedule includes very toxic substances such as formaldehyde, coal tar, lead compounds. Given the limited sale, supply (predominantly from international websites) and use of Black Salve, CMA finds that the proposed scheduling entry for sanguinarine, is not commensurate with the level of risk proposed.

Furthermore, the proposed amendment - to restrict the content limit to 0.1% in the final preparation - would likely make both *C. majus* and *S. canadensis,* and completely unavailable for use in medicines for all routes of administration, preparation types and regulatory status (including registered), including for use by practitioners who are trained to use them.

In summary making sanguinarine a dangerous substance is a crude instrument to solve a very specific problem, and is unlikely to achieve the desired outcome of limiting the sale, supply and use of Black Salve in Australia.

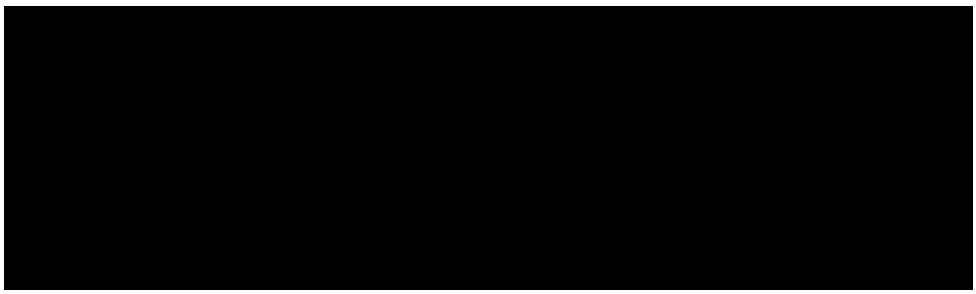
Products called Black Salve are mostly promoted and sold in Australia on the internet and consist of a wide range of ingredients. [6] As the products are illegally manufactured and supplied, the exact identity - that is the ingredients and their quantities within the products - cannot be confirmed. That is to say that, the products supplied may or may not contain *S. Canadensis*. Therefore, the actual risk to those purchasing products called Black Salve is in fact unknown.

Black Salve is sold by businesses that already demonstrate very little regard for the law. As evidenced by the manufacturing, promotion and supply products that are presented as medicines, but in fact illegal therapeutic goods. Therefore it appears unlikely that making a *S. canadensis* a dangerous substance (S10) is going to deter unscrupulous entities from selling and supplying these goods (whether or not they contain *S. Canadensis)* and therefore not guaranteed to limit the use of Black Salve. For example, even if S. Canadensis were scheduled, companies may still market and supply illegal medicines call Black Salve.

Potentially all the proposed scheduling amendment would achieve is impacting those medicines and substances that *are* complying with the regulatory environment.

Alternative regulation of sanguinarine

In order to actually impact the supply chain of Black Salve, as well as retain the use of other therapeutic ingredients that contain sanguinarine (at a safe limit, with an appropriate dosage form and rout of administration) CMA proposes a collection of other measures.



1. That the TGA conduct a survey of products marketed and sold as Black Salve, analysing the actual composition of these preparations. Once this is known, targeted, relevant regulatory action can be taken.

2. That the TGA pursue those companies and individuals manufacturing and supplying medicines that are not registered on the ARTG. There are now sufficient penalty provisions that can be exercised under section 19B of the Therapeutic goods Act to deal with these actions.

3. Regarding *S. candaensis*, the ingredient could be limited by its route of administration and/or dosage form to restrict topical use. This can be implemented at the time of listing or application for registration.

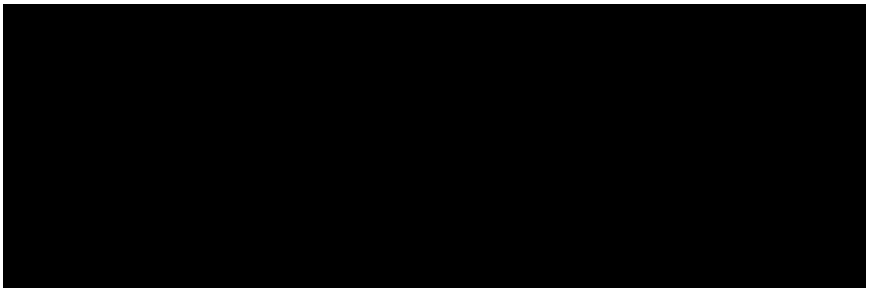
4. Use the Permissible Ingredient Determination to mandate any label warning statements for products containing *S. canadensis* that the committee finds appropriate.

Should the ACMS find the scheduling of sanguinarine necessary, CMA recommends that preparations containing less than 2% of sanguinarine only be appropriate by prescription, and otherwise available for use in herbal medicine preparations.

Conclusion

CMA appreciates the opportunity to comment on the proposed scheduling amendment for *S.canadensis* and is equally concerned by the misuse of Black Salve. However, the proposed amendment will not predictably ameliorate that risk, and at the same restrict uses of herbal medicines that are already on the ARTG, including a registered medicine.

CMA proposes the TGA employ the range of regulatory techniques proposed in the submission to selectively target the sale and supply of Black Salve itself, whilst at the same time creating appropriate provisions that will ensure the safe use of herbal medicines and products that contain sanguinarine.



1 Croaker A et al. Sanguinaria canadensis: Traditional Medicine, Phytochemical Composition, Biological Activities and Current Uses. Int. J. Mol. Sci. 2016: 17, 1414. doi:10.3390/ijms17091414

2 Graf T et al. Variability in the Yield of Benzophenanthridine Alkaloids in Wildcrafted vs Cultivated Bloodroot (Sanguinaria canadensis L.). 2007: J. Agric. Food Chem. 55, 1205 1211. DOI: 10.1021/jf062498f

3 TGA 2012. https://www.tga.gov.au/alert/black-and-red-salves-treating-cancer. Cited 10 May 2019

4 Maji A and Banerji P. Chelidonium majus L. (Greater celandine) A Review on its Phytochemical and Therapeutic Perspectives. 2005: Int. Nat. J. of Herb. Med. 3 (1): 10-27. DOI: 10.22271/flora.2015.v3.i1.03

[5] Committee on Herbal Medicinal Products (HMPC), EMA. Assessment report on Chelidonium majus L., herba. 2013: EMA/HMPC/369801/2009

6 Croaker A. Black salve in a nutshell. Aust. J. Ge. Pract. 20018: 47(2).

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