Australian Government
Department of Health
Therapeutic Goods Administration

ACCM 15th Advisory Committee on Complementary Medicines

Ratified Minutes

6th December 2013

TGA Health Safety Regulation

R13/987115

Abbreviations

ACCM	Advisory Committee on Complementary Medicines
ADR	Adverse Drug Reactions
ANZTPA	Australia New Zealand Therapeutic Products Agency
ARGCM	Australian Regulatory Guidelines for Complementary Medicines
ARTG	Australian Register of Therapeutic Goods
BP	British Pharmacopoeia
CG	Compositional Guideline
CMEC	Complementary Medicines Evaluation Committee
CSU	Committee Support Unit
EFSA	European Food Safety Authority
EU	European Union
FSANZ	Food Standard Authority Australia and New Zealand
GRAS	Generally Recognized as Safe
[redacted]	
MAG	Marketing Authorisation Group
NOAEL	No Observable Adverse Effect Level
OCM	Office of Complementary Medicines
OPR	Office of Product Review
[redacted]	
TGA	Therapeutic Goods Administration
USP-NF	United States Pharmacopeia and National Formulary

The Advisory Committee on Complementary Medicines (ACCM) held its fifteenth meeting at the Stamford Plaza, Sydney from 9:30 am to 4:00 pm on 5 December 2013.

Members of ACCM present

[redacted]

Present from the Therapeutic Goods Administration

Ms Jenny Burnett (ACCM Secretary)
Ms Trisha Garrett (Head, OCM)
Ms Kaylene Raynes (Acting ACCM Secretary) (present for part of the meeting)
Dr Anthony Hobbs (Principal Medical Advisor) (present for part of the meeting)
Shannon Blewitt (OCM Secretariat support)

1. Procedural matters

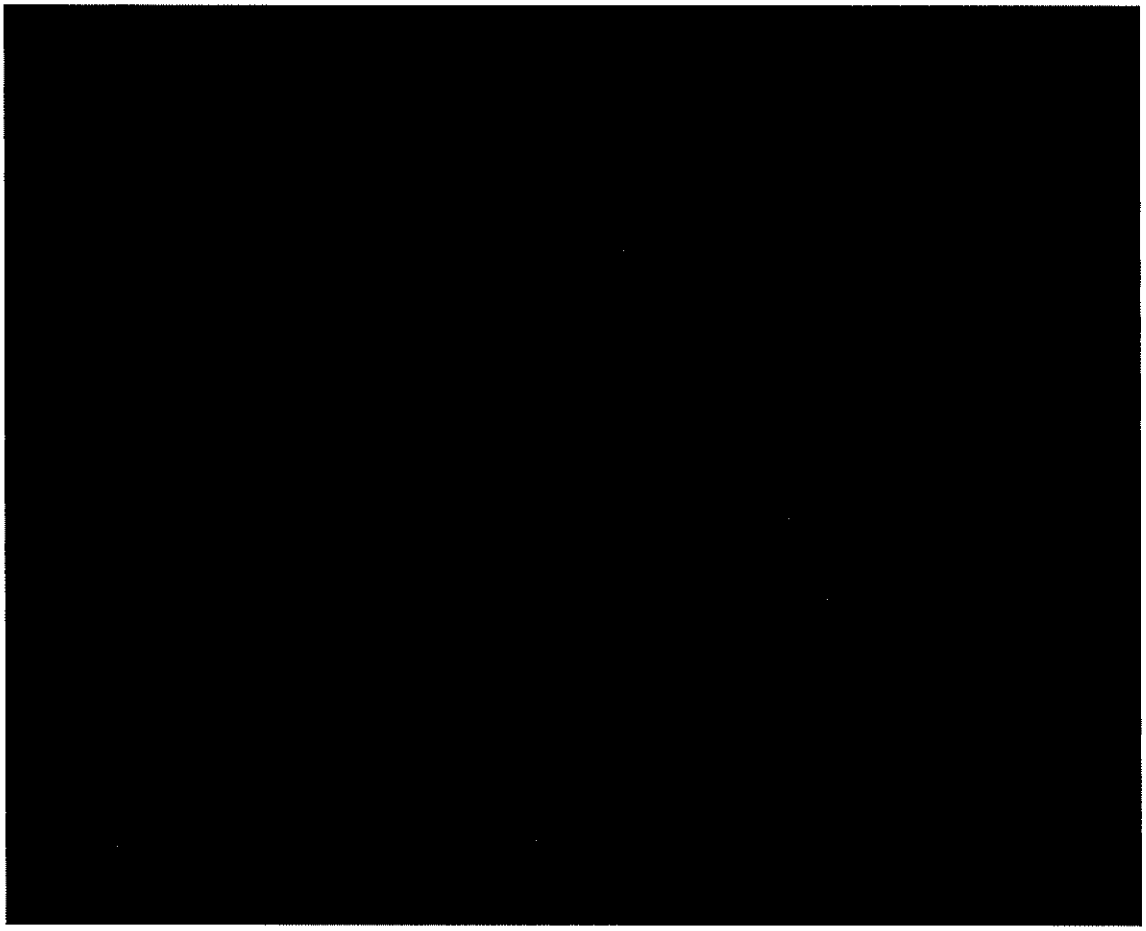
1.1 Opening of meeting

The Chair opened the meeting at 9:30am, welcoming ACCM members, particularly those attending their first meeting, and TGA staff including the Principal Medical Adviser.

[redacted]

1.2 Apologies

[redacted]



5.4 Cognizin® Citicoline

Background

A TGA officer provided an update on the outcome of an application for a new complementary medicine substance that had previously been considered by the committee.

At the ACCM 14 meeting, members advised the TGA that the submitted data package was not sufficient to establish safe use of citicoline in listed oral medicines. The committee acknowledged the extensive use of the substance in other jurisdictions, and the safety of choline component of citicoline, but in the absence of detailed use and adverse effect data and the outcome of the EFSA considerations, appropriate safety had not been established at that time.

EFSA has now published their scientific opinion on the safety of citicoline as a novel food ingredient (NFI), concluding that the NFI, citicoline, is safe under the proposed use as an ingredient in food supplements and in foods formulated for specific medicinal purposes, at use levels of 500mg/day in adults (EFSA, 2013).

Citicoline has been used clinically in a number of countries, mainly for the treatment of stroke, brain injury and as an adjunctive therapy to Parkinson's disease. In some countries (Japan, Spain, France and Italy), it is regulated as a prescription medicine primarily for the treatment of cerebral vascular deficiencies. In the US, Cognizin® citicoline has self-affirmed GRAS status for use in food since 2009. In the current application, citicoline is stated to be intended as a source of choline supplementation at doses of 250-500mg/day.

The human diet is stated to contain very low levels of citicoline but actual intake data could not be found. Once ingested, citicoline is hydrolysed to choline and cytidine, with an additional rapid deamination of cytidine to uridine. At the proposed maximum dose of 500 mg/day, citicoline will provide ~ 107 mg choline and ~ 250 mg cytidine/day.

Dietary exposure levels of choline are reported as 300-400 mg/day, which exceeds the equivalent choline intake (~107 mg) from the proposed dose of 500 mg/day of citicoline but is well below the recommended Upper Level of dietary intake of 3.5 g/day in Australia. Choline, as choline bitartrate, is currently available for use as both an active and an excipient ingredient in listed medicines.

Cytidine is present in any food containing RNA. However, the information supplied to the TGA was inadequate to establish the amount of cytidine in the typical Australian diet; therefore it was not possible to compare the dietary intake of cytidine with the amount provided by the proposed maximum daily dose of citicoline. It is not known whether the daily dose of cytidine from citicoline (if approved for use in listed medicines ~250 mg) would exceed dietary intake.

Neither cytidine nor its metabolite uridine is currently available for use in listed medicines and their safety for use in listed medicines has not been previously established by the TGA.

ACCM was asked to note the outcomes of the EFSA review, including the statement that citicoline is intended to be used in certain target populations only and advise on whether the EFSA review on citicoline addresses the data gaps previously identified by ACCM members (ACCM 14).

Discussion:

The committee noted the extensive clinical data and wide use of citicoline, particularly in food, and the indication that it is generally well tolerated in humans.

ACCM noted the outcome of the EFSA review and acknowledge that citicoline is intended to be used as a medicinal food supplement for adults at a maximum dose of 500mg/day. Members agreed that based on the information contained within the EFSA review, there is now sufficient data to establish safe use in adults at the specified dose. However, the safety data for use in children and pregnant women has not been established and as such all members agreed that use in children and pregnant women is not recommended.

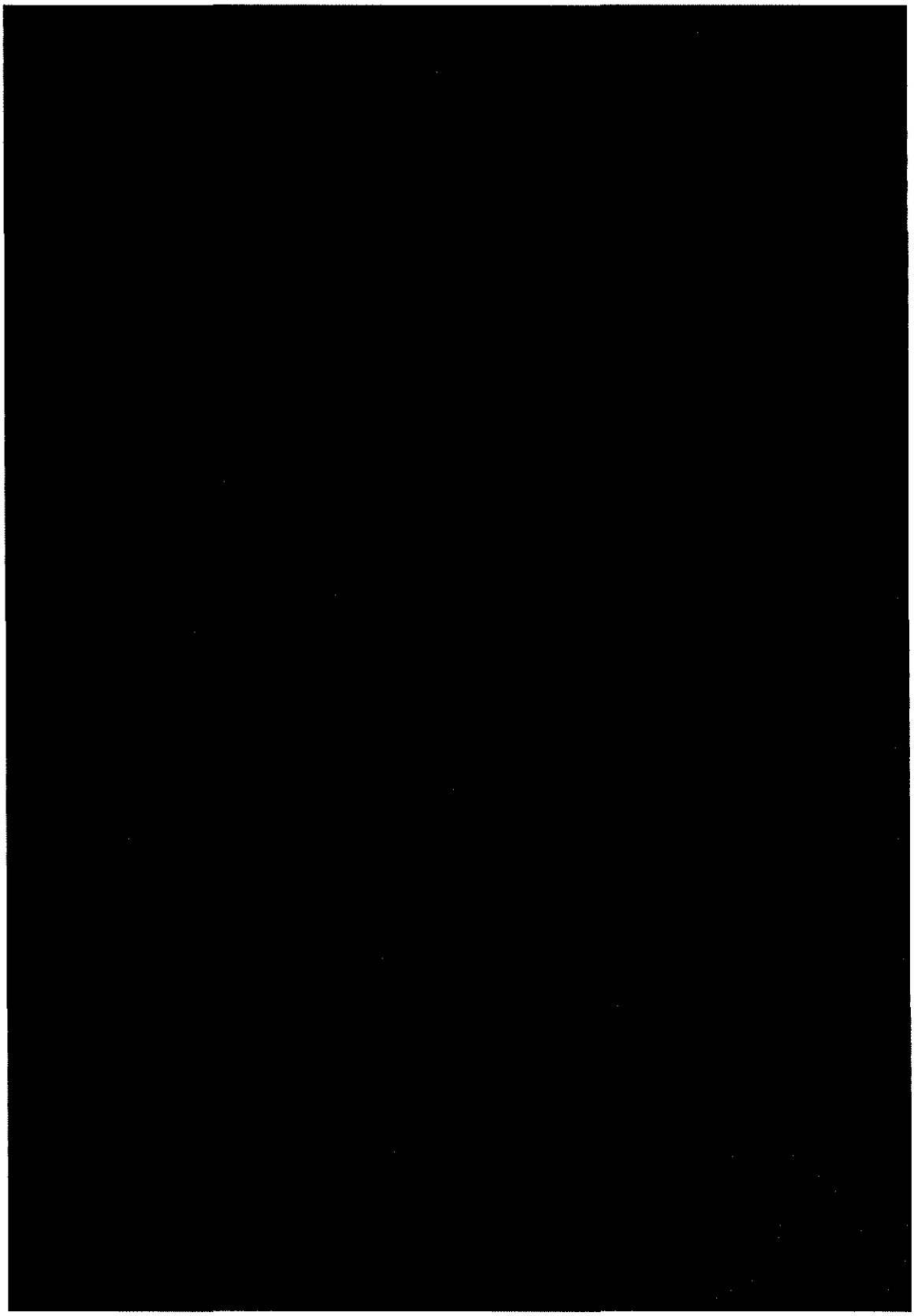
Members discussed the mechanisms by which restrictions could limit its use in children and pregnant women using the current listed medicine regulatory framework. A TGA member indicated there a couple of general mechanisms available using the current regulatory framework, which could include restrictions on its use, such that the medicine is not directed for use in children or by pregnant women.

Advice 15.7

The ACCM notes the outcomes of the EFSA review, its recommendations and considers that the previously identified concerns (ACCM 14) have been addressed. ACCM advises that there is sufficient data to establish the safe use of Citicoline in listed medicines in adults with a maximum daily dose of 500 mg.

Advice 15.8

The ACCM advises the TGA that there is insufficient data to establish the safe use of citicoline in children.



15.7 ACCM advice

The ACCM notes the outcomes of the EFSA review, its recommendations and considers that the previously identified concerns (ACCM 14) have been addressed. ACCM advises that there is sufficient data to establish the safe use of citicoline in listed medicines in adults with a maximum daily dose of 500 mg.

15.8 ACCM advice

The ACCM advises the TGA that there is insufficient data to establish the safe use of citicoline in children.

[redacted]