Australian Government
Department of Health
Therapeutic Goods Administration

Colourings used in medicines for topical and oral use

Version 2.2, August 2018

TGA Health Safety Regulation

Contents

Introduction

This guidance relates to:

- colourings in medicines for topical and oral use that do not require evaluation of data by the TGA
- the information required to evaluate a colouring that is not:
  - Table 1 Colourings for use as excipients in medicines for topical use only
  - Table 2 Colourings for use in medicines for oral and topical use

Why colourings are used in medicines for topical and oral use

Colourings are inactive substances that may be used in topical or oral formulations of medicines, for various reasons such as:

- to distinguish between strengths, indications or markings
- to assist with identifying the medicine
- to distinguish between other medicines.

Colourings that do not require evaluation

Excipients with colouring characteristics

Generally, ingredients that have colouring characteristics may be used without further evaluation of toxicology data, as long as they are available for excipient use in the relevant medicine type e.g. prescription medicines, listed medicines.

For example, if sponsors wish to use a fruit extract such as *Vaccinium myrtillus* (bilberry) as a natural colouring in medicines, no additional toxicological data is required.

Check the ingredient database in TGA Business services for excipient availability of ingredients for the intended application type.

Table 1 below lists the colourings (and their aluminium and calcium lakes) that:

- can be used in medicines for topical use only
- do not require evaluation of toxicology data.

Table 1 Colourings for use as excipients in medicines for topical use only

Australian approved name	Colour Index number	CAS Number	Restrictions
Acid green 25		4403-90-1	
Acid red 33	17200	3567-66-6	
Alizarin cyanine green		4403-90-1	
Basic fuchsin			
Basic red 1	45160	989-38-8	
Basic violet 11:1	45174	73398-89-7	
Brown FK		8062-14-4	
Eosine		548-26-5	
Food red 13		2150-33-6	
Malachite green			
Mordant red 11		72-48-0	Concentration not to exceed 0.05%
Pigment blue 15		147-14-8	
Pigment green 18			
Pigment green 7		1328-53-6	
Pigment red 4		2814-77-9	
Pigment red 53		2092-56-0	
Pigment red 57			
Pigment red 63		2416-46-6	
Pigment white 26		8005-37-6	
Pigment yellow 12		6358-85-6	
Ponceau SX		4548-53-2	

Australian approved name	Colour Index number	CAS Number	Restrictions
Prussian blue		14038-43-8	
Rhodamine B		81-88-9	
Solvent green 3	61565	128-80-3	
Solvent red 1		1229-55-6	
Solvent violet 13		81-48-1	
Solvent yellow 172		68427-35-0	
Solvent yellow 33		8003-22-3	
Sudan III		85-86-9	
Sulfan blue		68238-36-8	
Ultramarine blue		1317-97-1	
Vat red 1			
Vat red 5		6371-18-2	
Yellow 2G		6359-98-4	

Table 2 below lists the colourings (and their equivalents such as their aluminium and calcium lakes) that:

- can be used in medicines for oral and topical use
- do not require evaluation of toxicology data

Note

The synthetic equivalents need to be manufactured from colours that comply with the specifications in Table 2.

Table 2 Colourings for use in medicines for oral and topical use

Australian approved name	JECFA name (if different)	Colour Index number	INS number	Restrictions
Allura Red AC		16035	129	
Amaranth		16185	123	
Annatto	Annatto Extracts (Oil and Alkali-extracted) Annatto Extracts (Solvent-extracted)	75120	160b	
Anthocyanins	Grape Skin Extract	-	163(ii)	
Beet Red		-	162	
Betacarotene		40800	160a(i)	
Brilliant Black BN	Brilliant Black PN	28440	151	
Brilliant Blue FCF		42090	133	
Brilliant Scarlet 4R	Ponceau 4R	16255	124	
Calcium carbonate		77220	170	
Canthaxanthin		40850	161	
Caramel	**Caramel Colours**			
	Class I: Plain Caramel, caustic caramel		150a	
	Class II: Caustic sulfite caramel		150b	
	Class III: Ammonia caramel		150c	

Australian approved name	JECFA name (if different)	Colour Index number	INS number	Restrictions
	Class IV: Sulfite ammonia caramel		150d	
Carbon black	Vegetable carbon	77266	153	
Carmoisine	Azorubine	14720	122	
Carotenes	Carotenes (Algae) Carotenes (Vegetable)	75130	160a(ii)	
Chlorophyllins		75815	140(ii)	
Chlorophyllins – Copper Complexes Sodium and Potassium Salts (previous AAN Chlorophyllin – Copper Complex)		75810	141(ii)	
Chlorophylls		75810	140	
Chlorophylls - Copper Complexes		75810	141(i)	
Chocolate Brown HT	Brown HT	20285	155	
Cochineal		75470	120	
Curcumin		75300	100(i)	
Erythrosine		45430	127	
Fast green FCF		42053	143	
Food Orange 6	Beta-apo-8'-carotenal	40820	160e	
Food Orange 7	Beta-apo-8'-carotenoic Acid Ethyl Ether	40825	160f	

Australian approved name	JECFA name (if different)	Colour Index number	INS number	Restrictions
Green S		44090	142	
Indigo Carmine	Indigotine	73015	132	
Iron Oxide Black		77499	172(i)	In divided preparations for oral use: concentration not exceed 10mg per dosage unit. In undivided preparations for oral use: the concentration is part of the iron content if it exceeds 1%.
Iron Oxide Red		77491	172(ii)	
Iron Oxide Yellow		77492	172(iii)	
Patent Blue V		42051	131	
Phloxine B	(none allocated)	45410	-	Phloxine to comply with the specifications in the US Code of Federal Regulations (Volume 21) for D&C Red 28 – Part (b) of Section 74.1328
Quinoline Yellow		47005	104	
Red 27		45410	-	
Riboflavin		-	101(i)	
Riboflavin-5-phosphate			101(ii)	
Saffron		75100	-	
Sunset Yellow FCF		15985	110	

Australian approved name	JECFA name (if different)	Colour Index number	INS number	Restrictions
Tartrazine		19140	102	The presence of tartrazine must be declared on the label.
Titanium Dioxide		77891	171	

Compliance with monographs and other standards for colourings

For colourings that are covered by a default standard monograph

- The colourings are required to comply with the monograph specifications, unless an exemption is granted under section 14 of *Therapeutic Goods Act 1989* (the Act).
- Apply to the TGA in writing, seeking an exemption under section 14 of the Act.

For colourings that do not have a default standard monograph

- The colourings need to conform to either:
  - the Food and Agriculture Organization (FAO)/World Health Organization (WHO) Combined compendium of food additive specifications
  - the European Union regulations - Laying down specifications for food additivies No. 231/2012

Data requirements for new colourings

Using colourings in topical or orally administered medicines that are not in the published list

- Provide data to the TGA for evaluation and approval.
- Follow the data requirements for applications of this type detailed below.

All applications

Provide a complete and unambiguous identification of the colouring including:

- the chemical name
- any common names by which the chemical is known or identified in the technical literature
- any names under which the colouring has been or will be marketed (including trade names)
- the Colouring Index (CI) number
- the INS Food Additives number
- the Chemical Abstract Service (CAS) number.

Applications where Food Standards Australia New Zealand has evaluated data

For quality data (CTD Module 3)

Ensure the Quality data (consistent with Module 3 of the Common Technical Document [CTD]) includes:

- details of the test methods used during quality control of each batch, and the limits for results
- evidence of compliance with the standard approved by Food Standards Australia New Zealand (FSANZ) (i.e. test results from at least two batches of the colouring).

For nonclinical data (CTD Module 4)

Include:

- FSANZ reports
- reports of all toxicology studies completed after the FSANZ evaluation that are relevant to the assessment of the colouring.

For clinical data (CTD Module 5 if relevant)

Include reports of all human studies (if any) completed after the FSANZ evaluation that are relevant to the assessment of the chemical.

Applications where Food Standards Australia New Zealand has not evaluated data

For quality data (CTD Module 3)

Include:

- for colours included in the European Union regulations - Laying down specifications for food additives No. 231/2012; evidence of compliance with the directive
- for other new colourings, quality data requirements as outlined in 2.2.2 of the European Union Guideline on excipients in the dossier for application for marketing authorisation of a medicinal product (EMEA/CHMP/QWP/396951/2006).

For nonclinical data (CTD Module 4)

For a colouring that has not been used previously in a topical and/or oral medicine, include:

- toxicology, pharmacology and pharmacokinetics data as required for a new drug substance
- any existing data to support the use of the new colouring in a topical and/or oral medicine - for example, toxicological data based on other uses (e.g. veterinary, agricultural and industrial chemicals), or animal toxicological and human safety data arising from its use as a food or food additive.

For clinical data (CTD Module 5)

- Include reports of all human clinical studies of the colouring.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication (previously ARGPM Appendix 22: Colourings used in medicines for oral use)	Office of Medicines Authorisation	01/07/2013
V2.0	Updated to include: · colourings permitted in medicines for topical use (extracted from Substances that may be used in listed medicines in Australia, December 2007), · the following colourings for use in oral medicines – Calcium carbonate – Lutein – Chlorophyllins – Riboflavin-5-phosphate – Tartrazine Refer to the updated EU regulations – laying down specifications for food additives - No. 231/2012	Office of Medicines Authorisation	30/05/2014
V2.1	Updated 'Colourings for use as excipients in medicines for topical use only' table to include: Basic red 1 Basic violet 11:1	Scientific Evaluation Branch	26/05/2016
V2.2	Updated 'Colourings that do not require evaluation' to allow general excipients to be used as colours.	Scientific Evaluation Branch	28/08/2018

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