Health Canada Santé Canada

# NATURAL HEALTH PRODUCT

# MARIGOLD EXTRACT AND ISOLATES (LUTEIN AND ZEAXANTHIN)

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredients.

**Notes**

- Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- The solidus (/) indicates that the terms and/or statements are synonymous. Either term or statement may be selected by the applicant.
- A product may include one or more of the ingredients listed in Table 1.

**Date** February 25, 2019

## Proper name(s), Common name(s), Source material(s)

Table 1. Proper name(s), Common name(s), Source material(s)

| Proper name(s) | Common name(s) | Source material(s) | | | |
|---|---|---|---|---|---|
| | | Proper name(s) | Part(s) | Common name(s) | Preparation(s) |
| *Tagetes erecta* | ▸ Marigold (Tagetes erecta) extract<br>▸ Marigold extract | *Tagetes erecta* | Flower | N/A | Dried |
| 3R,3´R,6´R)-beta,epsilon-carotene-3,3´-diol | Lutein | *Tagetes erecta* | Herb flowering oleoresin | N/A | N/A |
| | | | | Lutein | Synthetic |
| ▸ (3R,3'R)-beta,beta-carotene-3,3'-diol<br>▸ all-trans-beta-Carotene-3,3'-diol | Zeaxanthin | *Tagetes erecta* | Herb flowering oleoresin | N/A | N/A |
| | | | | Zeaxanthin | Synthetic |
| Lutein esters | Lutein esters | *Tagetes erecta* | Herb flowering oleoresin | N/A | N/A |
| | | | | Lutein ester | Synthetic |

| | | | | | |
|---|---|---|---|---|---|
| Zeaxanthin esters | Zeaxanthin esters | *Tagetes erecta* | Herb flowering oleoresin | N/A | N/A |
| | | | | Zeaxanthin esters | Synthetic |

References: Proper names: ChemIDplus 2018, USDA 2018, US FDA 2016, FAO/WHO 2014, USP 34 2011; Common names: ChemIDplus 2018, US FDA 2016, FAO/WHO 2014, USP 34 2011, WHO 2005; Source materials: FAO/WHO 2014, USP 34 2011, WHO 2005.

## Route of administration

Oral

## Dosage form(s)

This monograph excludes foods or food-like dosage forms as indicated in the Compendium of Monographs Guidance Document.

Acceptable dosage forms for the age category listed in this monograph and specified route of administration are indicated in the Compendium of Monographs Guidance Document.

## Use(s) or Purpose(s)

- Source of/Provides antioxidants (for the maintenance of good health) (Miranda et al. 2006; Blakely et al. 2003; Dwyer et al. 2001).
- Source of/Provides antioxidants for the maintenance of eye health (Miranda et al. 2006; Blakely et al. 2003; Dwyer et al. 2001).
- Helps to maintain eyesight/support eye health in conditions (associated with sunlight damage), such as cataracts and age-related macular degeneration (Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008; Alves-Rodrigues and Shao 2004; Richer et al. 2004; Olmedilla et al. 2003; Brown et al. 1999).
- Helps to reduce the risk of developing cataracts (Christen et al. 2008; Moeller et al. 2008; Brown et al. 1999; Chasan-Taber et al. 1999).
- Helps to improve macular pigment optical density (Johnson et al. 2008; Richer et al. 2004; Berendschot et al. 2000).

## Dose(s)

### Subpopulation(s)

Adults 18 years and older

**Quantity(ies)**

LUTEIN AND ZEAXANTHIN

Method of preparation: Isolate

*Antioxidant*

Lutein
Not to exceed 20 milligrams of lutein, per day (Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

Zeaxanthin (Optional)
Not to exceed 2.5 milligrams of zeaxanthin, per day (Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

*Eyesight*

Lutein
6 - 20 milligrams of lutein, per day (Shao and Hathcock 2006; WHO 2005; Alves-Rodrigues and Shao 2004; Richer et al. 2004; Olmedilla et al. 2003; Brown et al. 1999).

Zeaxanthin (Optional)
0.7 - 2.5 milligrams of zeaxanthin, per day (Shao and Hathcock 2006; WHO 2005; Alves-Rodrigues and Shao 2004; Richer et al. 2004; Olmedilla et al. 2003; Brown et al. 1999).

LUTEIN AND ZEAXANTHIN ESTERS

Method of preparation: Isolate

*Antioxidant*

Lutein esters
Not to exceed 40 milligrams of lutein esters, per day (Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

Zeaxanthin esters (Optional)
Not to exceed 5 milligrams of zeaxanthin esters, per day (FAO/WHO 2014; USP 34 2011; Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

*Eyesight*

Lutein esters
12 - 40 milligrams of lutein esters, per day (Bone and Landrum 2010; Shao and Hathcock 2006; WHO 2005; Alves-Rodrigues and Shao 2004; Richer et al. 2004; Olmedilla et al. 2003; Brown et

al. 1999).

Zeaxanthin esters (Optional)

1.5 - 5 milligrams of zeaxanthin esters, per day (FAO/WHO 2014; USP 34 2011; Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

MARIGOLD EXTRACT

Methods of preparation: Standardized extracts

*Antioxidant*

Extract containing 60% or less lutein esters and providing 40 milligrams or less of lutein esters, per day (Bone and Landrum 2010; Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

Optional potency
Not to exceed 5 milligrams of zeaxanthin esters, per day (FAO/WHO 2014; USP 34 2011; Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

*Eyesight*

Extract containing 60% or less lutein esters and providing 12-40 milligrams of lutein esters, per day (Bone and Landrum 2010; Shao and Hathcock 2006; WHO 2005; Alves-Rodrigues and Shao 2004; Richer et al. 2004; Olmedilla et al. 2003; Brown et al. 1999).

Optional potency
1.5 - 5 milligrams of zeaxanthin esters, per day (FAO/WHO 2014; USP 34 2011; Christen et al. 2008; Fletcher et al. 2008; Johnson et al. 2008; Moeller et al. 2008).

**Notes**

- The quantity of the marigold extract must be indicated on the PLA form and label.
- Lutein and zeaxanthin esters are potencies of marigold extract and must be indicated as such on the PLA form and label. The amounts of the esters must be expressed as the quantity (mg) and/or percent (%) of the total quantity of the marigold extract.
- The maximum daily amount indicated for lutein and zeaxanthin esters should not be exceeded when lutein esters and/or zeaxanthin esters are combined with marigold extract.
- Disclosing the amount of zeaxanthin ester in a product is optional.

**Direction(s) for use**

*Lutein and zeaxanthin esters, and marigold extract*

Take with a meal containing oil/fat (Chung et al. 2004; Roodenburg et al. 2000).

## Duration(s) of use

No statement required.

## Risk information

### Caution(s) and warning(s)

No statement required.

### Contraindication(s)

No statement required.

### Known adverse reaction(s)

No statement required.

## Non-medicinal ingredients

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in the database.

## Storage conditions

Store in tightly sealed, light- and oxygen-resistant container in a cool, dry place (USP 34 2011).

## Specifications

- The finished product specifications must be established in accordance with the requirements describes in the Natural and Non-prescription Health Products Directorate (NNHPD) Quality of Natural Health Products Guide.
- The medicinal ingredient must comply with the requirements outlined in the NHPID.
- Some commercial lutein preparations are sold as "5% or 10% lutein". These preparations are actually purified lutein (esterified or free) typically added at 5-15% to an inert stabilizing medium (e.g. USP 34 2011: Lutein Preparation).
- When using these preparations, the applicant must specify whether lutein is esterified or free and use the appropriate dose information. For these preparations, the stabilizing medium must be listed as a non- medicinal ingredient in the PLA and label and identified as "stabilizing agent" in the PLA.
- In all cases where lutein and zeaxanthin (free or esterified) are listed on the PLA form, potency testing at the finished product stage is required to verify the quantity as different

preparations may provide different amounts of lutein and zeaxanthin
OR
The manufacturer of the finished product should ensure that there are sufficient controls on the raw materials so that the quantity of lutein and zeaxanthin (esterified or free) is the actual amount of lutein and zeaxanthin and not the amount of the lutein and zeaxanthin with the stabilizing excipient.

**LUTEIN AND ZEAXANTHIN**

The medicinal ingredient must comply with the specifications outlined in either of the following references:

- FAO/WHO 2014: LUTEIN from *TAGETES ERECTA*: Lutein
- USP 34 2011: Lutein, Lutein preparation

Lutein and zeaxanthin are preparations from the oleoresin of marigold (*Tagetes erecta*) petals obtained by hexane extraction and purified by saponification and crystallisation.

**LUTEIN AND ZEAXANTHIN ESTERS**

Lutein and zeaxanthin esters are preparations of oleoresin of marigold (*Tagetes erecta*) petals obtained by hexane extraction and then purified and concentrated.

**MARIGOLD EXTRACT**

- Marigold extract is a hexane extraction of the oleoresin of marigold (*Tagetes erecta*) petals which provides less than 60% lutein.
- The medicinal ingredient may comply with the specifications outlined in the FAO/WHO 2014: LUTEIN from *TAGETES ERECTA*.

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