

NATURAL HEALTH PRODUCT

SOYBEAN EXTRACTS AND ISOLATES

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 ingredient.

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 synonyms. Either term or statement may be selected by the applicant.

Date

July 1, 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 ingredient(s)	Source material(s)		Preparation(s)
		Common name(s)	Proper name(s)	Part(s)	
<ul style="list-style-type: none"> ▶ 4',5,7-Trihydroxyisoflavone ▶ 5,7-Dihydroxy-3-(4-hydroxyphenyl)-4H-1-benzopyran-4-one 	Genistein	<ul style="list-style-type: none"> ▶ Genistein ▶ Soy isoflavone extract ▶ Soy protein extract ▶ Soy protein isolate 	<i>Glycine max</i>	Seed	Isolate
7-(beta-D-glucopyranosyloxy)-3-(4-hydroxyphenyl)-4H-1-Benzopyran-4-one	<ul style="list-style-type: none"> ▶ 7-O-beta-D-Glucopyranoside ▶ Genistein 7-glucoside ▶ Genistin 	<ul style="list-style-type: none"> ▶ Genistin ▶ Soy isoflavone extract ▶ Soy protein extract ▶ Soy protein isolate 	<i>Glycine max</i>	Seed	Isolate
<i>Glycine max</i>	<ul style="list-style-type: none"> ▶ Black soya bean ▶ Da dou ▶ Soy ▶ Soya ▶ Soyabean ▶ Soybean 	N/A	<i>Glycine max</i>	Seed	N/A
Soy isoflavone extract	Soy isoflavone extract	N/A	<i>Glycine max</i>	Seed	N/A

Soy protein extract	Soy protein extract	N/A	<i>Glycine max</i>	Seed	N/A
Soy protein isolate	Soy protein isolate	N/A	<i>Glycine max</i>	Seed	N/A

References: Proper names: NHPID 2019, USDA 2019, Evans et al. 2007, Newton et al. 2006, Roudsari et al. 2005, Arjamandi et al. 2003, Yamori et al. 2002, Alekel et al. 2000, Scambia et al. 2000, Upmalis et al. 2000 Wangen et al. 2000, Potter et al. 1998; Common names: NHPID 2019, Evans et al. 2007, Newton et al. 2006, Roudsari et al. 2005, Arjamandi et al. 2003, Yamori et al. 2002, Alekel et al. 2000, Wangen et al. 2000, Potter et al. 1998; Source information: NHPID 2019, USDA 2019, D’Anna et al. 2007, Evans et al. 2007, Nahas et al. 2007, Newton et al. 2006, Ye et al. 2006, Roudsari et al. 2005, Crisafulli et al. 2004, Harkness et al. 2004, Kreijkamp-Kaspers et al. 2004, Arjamandi et al. 2003, Uesugi et al. 2003, Han et al. 2002, Albert et al. 2002, Faure et al. 2002, Yamori et al. 2002, Alekel et al. 2000, Wangen et al. 2000, Albertazzi et al. 1998, Potter et al. 1998.

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)

- ▶ Helps to attenuate/reduce bone mineral density (BMD) loss in post-menopausal women when used in conjunction with adequate amounts of calcium and vitamin D (Marini et al. 2007; Newton et al. 2006; Ye et al. 2006; Chen et al. 2004; Kreijkamp-Kaspers et al. 2004; Lydeking et al. 2004; Uesugi et al. 2003; Alekel et al. 2000; Potter et al. 1998).
- ▶ May reduce severe and frequent menopausal symptoms (such as hot flashes and/or night sweats) (D’Anna et al. 2007; Nahas et al. 2007; Williamson-Hughes et al. 2006; Crisafulli et al. 2004; Albert et al. 2002; Han et al. 2002; Scambia et al. 2000; Upmalis et al. 2000; Albertazzi et al. 1998).

The following combined use(s) or purpose(s) is/are also acceptable:

May reduce severe and frequent menopausal symptoms (such as hot flashes and/or night sweats) and help reduce loss of bone mineral density in post-menopausal women when used in conjunction with adequate amounts of calcium and vitamin D (D’Anna et al. 2007; Marini et al. 2007; Nahas et al. 2007; Newton et al. 2006; Williamson-Hughes et al. 2006; Ye et al. 2006; Chen et al. 2004; Crisafulli et al. 2004; Kreijkamp-Kaspers et al. 2004; Lydeking et al. 2004; Uesugi et al. 2003; Albert et al. 2002; Han et al. 2002; Alekel et al. 2000; Scambia et al. 2000; Upmalis et al. 2000;



Albertazzi et al. 1998; Potter et al. 1998).

Dose(s)

Subpopulation(s)

Menopausal and postmenopausal women (D'Anna et al. 2007; Nahas et al. 2007; Crisafulli et al. 2004; Albert et al. 2002; Faure et al. 2002; Han et al. 2002; Scambia et al. 2000; Upmalis et al. 2000; Albertazzi et al. 1998).

Quantity(ies)

Reduction of BMD loss

Glycine max, Soy isoflavone extract, Soy protein extract and Soy protein isolate

Methods of preparation: Standardized extracts

75 - 125 milligrams of total Aglycone Isoflavone Equivalents (AIE), per day; not to exceed 35 grams of soy protein extract and/or isolate, per day (CNF 2015; Marini et al. 2007; Newton et al. 2006; Ye et al. 2006; Chen et al. 2004; CPS 2004; Kreijkamp-Kaspers et al. 2004; Lydeking et al. 2004; Uesugi et al. 2003; Alekel et al. 2000; Potter et al. 1998).

Genistein, Genistin

Methods of preparation: Isolates

75 - 125 milligrams of total Aglycone Isoflavone Equivalents (AIE), per day (Marini et al. 2007; Newton et al. 2006; Ye et al. 2006; Chen et al. 2004; Kreijkamp-Kaspers et al. 2004; Lydeking et al. 2004; Uesugi et al. 2003; Alekel et al. 2000; Potter et al. 1998).

Reduction of menopausal symptoms

Glycine max, Soy isoflavone extract, Soy protein extract and Soy protein isolate

Methods of preparation: Standardized extracts

30 - 125 milligrams of total AIE with a minimum of 15 milligrams of AIE from genistein and/or genistin, per day; not to exceed 35 grams of soy protein extract and/or isolate, per day (CNF 2015; D'Anna et al. 2007; Nahas et al. 2007; Williamson-Hughes et al. 2006; CPS 2004; Crisafulli et al. 2004; Albert et al. 2002; Han et al. 2002; Scambia et al. 2000; Upmalis et al. 2000; Albertazzi et al. 1998).



Genistein, Genistin

Methods of preparation: Isolates

15 - 125 milligrams of total AIE, per day (D'Anna et al. 2007; Nahas et al. 2007; Williamson-Hughes et al. 2006; Crisafulli et al. 2004; Albert et al. 2002; Han et al. 2002; Scambia et al. 2000; Upmalis et al. 2000; Albertazzi et al. 1998).

Direction(s) for use

Take a few hours before or after taking other medications or health care products (Sweetman 2007; ASHP 2005).

Duration(s) of use

Reduction of BMD loss

Use for at least 6 months to see beneficial effects (Ye et al. 2006; Harkness et al. 2004; Alekel et al. 2000; Potter et al. 1998).

Reduction of menopausal symptoms

Use for at least 2 weeks to see beneficial effects (D'Anna et al. 2007; Nahas et al. 2007; Crisafulli et al. 2004; Han et al. 2002; Scambia et al. 2000; Upmalis et al. 2000; Albertazzi et al. 1998).

All uses

Consult a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 1 year (Tomar and Shiao 2008; BfR 2007; Duffy et al. 2007; Palacios et al. 2007; Unfer et al. 2004; Petrakis et al. 1996).

Risk information

Caution(s) and warning(s)

All products

- ▶ Ensure you are up-to-date on mammograms and gynaecological evaluations prior to use (Tomar and Shiao 2008; BfR 2007; Duffy et al. 2007; Palacios et al. 2007; Unfer et al. 2004; Petrakis et al. 1996).
- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician if symptoms worsen.
- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are taking blood thinners or hormone replacement therapy (HRT), including



thyroid hormone replacement therapy (Rios et al. 2008; BfR 2007; Messina and Redmond 2006; ASHP 2005; Izzo et al. 2005; Mills and Bone 2005; Franco et al. 2004; Mazer 2004; Murray et al. 2003; Cambria-Keily 2002; Bell and Ovalle 2001; IOM 2001; Hansten et al. 1997; Petrakis et al. 1996).

- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you have a liver disorder, develop liver-related symptoms (e.g. abdominal pain, jaundice, dark urine) or have a history of hormonal or gynaecological disease, including ovarian cancer, endometriosis, and/or uterine fibroids (Cecchi et al. 2009; NIH 2009; Chandrareddy et al. 2008; Gasteyger et al. 2008; Tomar and Shiao 2008; Jefferson et al. 2007; Palacios et al. 2007; Kaari et al. 2006; Noel et al. 2006; Maskarinec et al. 2004a; Maskarinec et al. 2004b; Unfer et al. 2004; Borghi-Scoazec et al. 2002; Wu et al. 2000; Duncan et al. 1999b; Hargreaves et al. 1999; McMichael-Phillips et al. 1998; Petrakis et al. 1996).
- ▶ Stop use and consult a health care practitioner/health care provider/health care professional/doctor/physician if you experience breast pain, discomfort and/or tenderness, or if you experience a recurrence of menstruation and/or uterine spotting (Chandrareddy et al. 2008; Martinez and Lewi 2008; Palacios et al. 2007; Olawaiye et al. 2005; Albert et al. 2002; Han et al. 2002; Hargreaves et al. 1999; McMichael-Phillips et al. 1998; Petrakis et al. 1996).

Contraindication(s)

Do not use this product if you currently have or previously had breast cancer and/or breast tumours or if you have a predisposition to breast cancer, as indicated by an abnormal mammogram and/or biopsy, or a family member with breast cancer (Helferich et al. 2008; Tomar and Shiao 2008; BfR 2007; Duffy et al. 2007; Kaari et al. 2006; Nikander et al. 2005; Hargreaves et al. 1999; McMichael-Phillips et al. 1998; Petrakis et al. 1996).

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

No statement required.

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described 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.
- ▶ For an accurate measure of specific isoflavones in AIE, follow the methods outlined in AOAC 2008.03 (Collison 2008).

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Appendix 1: Definitions and Conversion

Factors Definitions:

Aglycone Isoflavone Equivalent (AIE): The maximum amount of bioavailable isoflavone upon ingestion. The glycoside forms of the isoflavones must first be cleaved to the aglycone form before they can be absorbed. As such, simple addition of aglycone and glycoside forms of isoflavone quantities, without taking into consideration the biochemical transformation of the isoflavones, will overestimate bioavailable quantities by almost a factor of two (Wang and Murphy 1996).

Conversion factors:

The quantity of isoflavones must always be determined in terms of AIE quantities (i.e. in terms of genistein, daidzein, and/or glycitein) for each of the glycoside, acetyl glycoside, malonyl glycoside and/or aglycone forms present in the product.

Table 2: Conversion of specific isoflavone quantities into aglycone isoflavone equivalent (AIE) quantities (Collison 2008)

Isoflavone (1 mg)	Aglycone Isoflavone Equivalent (mg AIE) quantity
Genistein	1.0
Genistin	0.625
Malonyl genistin	0.521
Acetyl genistin	0.570
Daidzein	1.0
Daidzin	0.611
Malonyl daidzin	0.506
Acetyl daidzin	0.555
Glycitein	1.0
Glycitin	0.637
Malonyl glycitin	0.534
Acetyl glycitin	0.582

Example of using the Aglycone Isoflavone Equivalent (AIE) conversion factors: Converting glycoside quantity into quantity of AIE (mg):

Convert 20 mg of genistin into mg AIE:

= 20 mg x 0.625 mg AIE/mg genistin

= 12.5 mg AIE genistin

Appendix 2: Calculating Total Isoflavones and Reporting Amounts on the PLA Form

1) Example of a 30 g/day soy protein extract product:

For a product with a claim for the reduction of menopausal symptoms, the amount of protein, total isoflavones, and genistein/genistin compounds must be reported on the PLA form.

a) Calculating total isoflavones (mg AIE)

Convert genistin, genistein, malonyl genistin, acetyl genistin, daidzein, and daidzin AIE quantities into quantities of total isoflavones in AIE (mg):
= 12.5 mg AIE genistin + 10 mg AIE genistein + 1 mg AIE malonyl genistin + 1 mg AIE acetyl genistin + 6.1 mg AIE daidzin + 5 mg AIE daidzein
= 35.6 mg AIE total isoflavones

b) Calculating genistein/genistin compounds (mg AIE)

Convert genistein, genistin, malonyl genistin, and acetyl genistin AIE quantities into quantities of total isoflavones in AIE (mg):
= 12.5 mg AIE genistin + 10 mg AIE genistein + 1 mg AIE malonyl genistin + 1 mg AIE acetyl genistin
= 24.5 mg AIE genistein/genistin compounds

c) Reporting on the PLA form should be as follows:

Proper Name: Soy protein extract
Common Name: Soy protein extract
Quantity per dosage unit: 30 g
Source Material: *Glycine max* - Seed
Potencies:
Total isoflavones: 35.6 mg AIE
Genistein/genistin: 24.5 mg AIE

2) Example of a 30 mg/day genistein/genistin isolate product:

For a product with a claim for the reduction of menopausal symptoms, the amount of genistein/genistin must be reported on the PLA form.

Reporting on the PLA form should be as follows:

Proper Name: Genistein / Genistin
Common Name: Genistein / Genistin
Quantity per dosage unit: 30 mg AIE



Source Ingredient: Soy isoflavone extract or Soy protein extract or Soy protein isolate or None

Source Material: *Glycine max* - Seed

Potencies: None