

## NATURAL HEALTH PRODUCT

### FEVERFEW – *TANACETUM PARTHENIUM*

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

#### Date

July 8, 2022

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

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

Proper name(s)	Common name(s)	Source information		
		Source material(s)	Part(s)	Preparation(s)
<i>Tanacetum parthenium</i>	Feverfew	<i>Tanacetum parthenium</i>	▶ Herb top ▶ Leaf	Dry

References: Proper name: USDA 2019; Common name: McGuffin et al. 2000; Source information: Barnes et al. 2007, Bradley 1992.

#### 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.

*Digestive aid; Headache relief*

Acceptable dosage forms for oral use are indicated in the dosage form drop-down list of the web-based Product Licence Application form for Compendial applications.

*Migraine prevention; Reduction of severity, frequency and symptoms of migraines when taken as a prophylactic*

The only acceptable dosage forms are: Capsules; Tablets.

### **Use(s) or Purpose(s)**

- ▶ (Traditionally) used in Herbal Medicine to aid digestion (stomachic) (Williamson 2003; Mills and Bone 2000; Felter and Lloyd 1983).
- ▶ (Traditionally) used in Herbal Medicine to help relieve headaches (Winston and Kuhn 2008; Boon and Smith 2004; Williamson 2003; Cook 1869).
- ▶ (Used in Herbal Medicine to) help(s) prevent migraine headaches (Barnes et al. 2007; Hoffmann 2003; Bradley 1992).
- ▶ (Used in Herbal Medicine to) help(s) reduce the severity and/or frequency of migraine headaches and associated symptoms such as nausea and vomiting, when taken as a prophylactic (Palevitch et al. 1997; Murphy et al. 1988; Johnson et al. 1985).

### **Note**

Claims for traditional use must include the term “Herbal Medicine”, “Traditional Chinese Medicine”, or “Ayurveda”.

### **Dose(s)**

#### **Subpopulation(s)**

Adults 18 years and older

#### **Quantity(ies)**

*Digestive aid; Headache relief*

Methods of preparation: Dry, Powdered, Non-Standardized Ethanolic Extracts (Extract dry, Tincture)

50 - 250 milligrams of dried herb top and/or leaf, per day (Barnes et al. 2007; Sweetman 2007; Hoffmann 2003; Williamson 2003; Mills and Bone 2000; Palevitch et al. 1997; Awang 1993; Bradley 1992; Murphy et al. 1988; Johnson et al. 1985).

*Digestive aid; Headache relief; Migraine prevention; Reduction of severity, frequency and symptoms of migraines when taken as a prophylactic*

Method of preparation: Powdered standardized

50 - 250 milligrams of dried leaf per day, standardized to 0.2 - 2 % parthenolide (dry weight);

Not to exceed 4 milligrams of parthenolide, per day (Awang 2010; (Curry et al. 2004; Hoffmann 2003; Awang 1993).

### **Direction(s) for use**

#### *All products*

- ▶ Take with or after food (Barnes et al. 2007; McGuffin et al. 1997; Johnson et al. 1985).
- ▶ Reduce the dosage gradually if treatment is to be paused or discontinued (ES COP 2003; Mills and Bone 2000).

### **Duration(s) of use**

#### *All products*

Consult a health care practitioner/health care provider/health care professional/doctor/physician for use beyond 4 months (Awang 1993).

*Migraine prevention; Reduction of severity, frequency and symptoms of migraines when taken as a prophylactic*

Use for at least 4-6 weeks to see beneficial effects (Palevitch et al. 1997; Murphy et al. 1988).

### **Risk information**

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

- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician if symptoms persist or worsen.
- ▶ Consult a health care practitioner/health care provider/health care professional/doctor/physician prior to use if you are taking blood thinners (Brinker 2001; Biggs et al. 1982).
- ▶ Consult a healthcare practitioner/health care provider/health care professional/doctor/physician prior to use if you are breastfeeding (Boon 2000).

#### **Contraindication(s)**

Do not use this product if you are pregnant (Brinker 2001; McGuffin et al. 1997).

#### **Known adverse reaction(s)**

- ▶ Stop use if hypersensitivity/allergy occurs (Paulsen et al. 2001; Hausen 1996).
- ▶ Some people may experience sore mouth, mouth ulcers and/or gastrointestinal discomfort (McGuffin et al. 1997; Murphy et al. 1988; Johnson et al. 1985).

## 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

Must be established in accordance with the requirements described in the *Natural Health Products Regulations* (NHPR).

## 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 migraine prevention and Reduction of severity, frequency and symptoms of migraines when taken as a prophylactic: Products must contain a minimum of 90% dried leaf (Awang 1993).

## References cited

Awang DVC. Feverfew. In: Coates PM, Betz JM, Blackman MR, Cragg GM, Levine M, Moss J, White JD, editors. *Encyclopedia of Dietary Supplements*. Second Edition. New York (NY): Informa Healthcare; 2010. p. 267-273.

Awang DVC. 1993. Feverfew Fever: A Headache for the Consumer. *Herbalgram* 29:34-36.

Barnes J, Anderson LA, Philipson JD. 2007. *Herbal Medicines*, 3<sup>rd</sup> edition. London (GB): The Pharmaceutical Press.

Biggs MJ, Johnson ES, Persaud NP, Ratcliffe DM. 1982. Platelet aggregation in patients using feverfew for migraine. *Lancet* 2(8301):776.

Boon H. 2000. Feverfew. In: Chandler F, editor. *Herbs: Everyday Reference for Health Professionals*. Ottawa (ON): Canadian Pharmacists Association and the Canadian Medical Association.

Boon H, Smith MJ. 2004. *The Complete Natural Medicine Guide to the 50 Most Common Medicinal Herbs*, 2nd edition. Toronto (ON): Robert Rose Inc.

Bradley PR, editor. 1992. *British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plant Drugs*, Volume 1. Bournemouth (GB): British Herbal Medicine Association.



Brinker F. 2001. Herb Contraindications and Drug Interactions, 3<sup>rd</sup> edition. Sandy (OR): Eclectic Medical Publications.

Cook WH. 1869. The Physio-Medical Dispensatory: A Treatise on Therapeutics, Materia Medica, and Pharmacy, in Accordance with the Principles of Physiological Medication. Cincinnati (OH): WH Cook. Reprint version by Medical Herbalism: Journal for the Clinical Practitioner. [Accessed 2019 June 28]. Available from: <http://medherb.com/cook/home.htm>

Curry EA, Murry DJ, Yoder C, Fife K, Armstrong V, Nakshatri H, O'Connell M, Sweeney CJ. 2004. Phase I dose escalation trial of feverfew with standardized doses of parthenolide in patients with cancer. *Investigational New Drugs* 22:299-305.

ESCOP 2003: ESCOP Monographs: The Scientific Foundation for Herbal Medicinal Products, 2<sup>nd</sup> edition. Exeter (GB): European Scientific Cooperative on Phytotherapy and Thieme.

Felter HW, Lloyd JU. 1983. King's American Dispensatory, Volume 1, 18<sup>th</sup> edition. Sandy (OR): Eclectic Medical Publications [Reprint of 1898 original].

Hausen BM. 1996. A 6-year experience with compositae mix. *American Journal of Contact Dermatitis* 7(2):94-99.

Hoffmann D. 2003. Medical Herbalism: The Science and Practice of Herbal Medicine. Rochester (VT): Healing Arts Press.

Johnson ES, Kadam NP, Hylands DM, Hylands PJ. 1985. Efficacy of feverfew as prophylactic treatment of migraine. *British Medical Journal* 291(6495):569-573.

McGuffin M, Hobbs C, Upton R, Goldberg A, editors. 1997. American Herbal Products Association's Botanical Safety Handbook. Boca Raton (FL): CRC Press.

McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. 2000. Herbs of Commerce, 2<sup>nd</sup> edition. Silver Spring (MD): American Herbal Products Association.

Mills S, Bone K. 2000. Principles and Practice of Phytotherapy. Toronto (ON): Churchill Livingstone.

Murphy JJ, Heptinstall S, Mitchell JR. 1988. Randomized double-blind placebo-controlled trial of feverfew in migraine prevention. *Lancet* 2(8604):189-192.

Palevitch D, Earon G, Carasso R. 1997. Feverfew (*Tanacetum parthenium*) as a prophylactic treatment for migraine: a double-blind placebo-controlled study. *Phytotherapy Research* 11:508-511.

Paulsen E, Anderson KE and Hausen BM. 2001. Sensitization and cross-reaction patterns in Danish Compositae-allergic patients. *Contact Dermatitis* 45(4):197-204.

Pittler MH, Ernst E. 2004. Feverfew for preventing migraine (Review). The Cochrane Database of Systematic Reviews, Issue 1. Art. No.: CD002286.pub2. DOI: 10.1002/14651858.CD002286.pub2.

Sweetman SC, editor. 2007. Martindale: The Complete Drug Reference, 35<sup>th</sup> edition. London (GB): Pharmaceutical Press.

USDA 2019: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. *Tanacetum parthenium* (L.) Sch. Bip. Beltsville (MD): National Germplasm Resources Laboratory. [Accessed 2019 June 28] Available from: <https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx>

Williamson EM. 2003. Potter's Herbal Cyclopaedia: The Authoritative Reference work on Plants with a Known Medical Use. Saffron Walden (GB): The C.W. Daniel Company Limited.

Winston D, Kuhn MA. 2008. Winston and Kuhn's Herbal Therapy and Supplements: A Scientific and Traditional Approach, 2<sup>nd</sup> edition. Philadelphia (PA): Lippincott Williams and Wilkins.

## References reviewed

Abebe W. 2002. Herbal medication: potential for adverse interactions with analgesic drugs. *Journal of Clinical Pharmacy and Therapeutics* 27(6):391-401.

Anderson D, Jenkinson PC, Dewdney RS, Blowers SD, Johnson ES, Kadam NP. 1988. Chromosomal aberrations and sister chromatid exchanges in lymphocytes and urine mutagenicity of migraine patients: a comparison of chronic feverfew users and matched non-users. *Human Toxicology* 7(2):145-152.

Awang DVC, Dawson BA, Kindack DG. 1991. Parthenolide content of feverfew (*Tanacetum parthenium*) assessed by HPLC and <sup>1</sup>H-NMR spectroscopy. *Journal of Natural Products* 54(6):1516-1521.

Bedard M. 2002. Feverfew and migraine prophylaxis. *Canadian Pharmaceutical Journal/La Revue Pharmaceutique Canadienne* 4:24-25.

Berry MI. 1984. Feverfew faces the future. *Pharmaceutical Journal* 232:611-614.

BHP 1996: British Herbal Pharmacopoeia. Bournemouth (GB): The British Herbal Medicine Association.

Blumenthal M. 2003. ABC Clinical Guide to Herbs. New York (NY): Theime.



Brinker F. 2008. Online Updates and Additions to Herb Contraindications and Drug Interactions, 3<sup>rd</sup> edition. Sandy (OR): Eclectic Medical Publications. Available from: <http://www.eclecticherb.com/emp/updatesHCDI.html> [Accessed 05 September 2008].

Brown AM, Edwards CM, Davey MR, Power JB, Lowe KC. 1997. Pharmacological activity of feverfew (*Tanacetum parthenium* (L.) Schultz-Bip.): assessment by inhibition of human polymorphonuclear leukocyte chemiluminescence in-vitro. *Journal of Pharmacy and Pharmacology* 49(5):558-561.

Brown D, Gaby A, Reichert R. 1997. Clinical applications of natural medicine: migraine. *American Journal of Natural Medicine* 4(9):18-20.

Colodny L, Bryan N, Luong S, Rooney J. 2003. Magnesium, feverfew, and riboflavin: therapeutic use in migraine prevention. *Journal of American Nutraceutical Association* 6(4):35-48.

De Weerd CJ, Bootsma HPR, Hendricks H. 1996. Herbal medicines in migraine prevention: Randomized double-blind placebo-controlled crossover trial of a feverfew preparation. *Phytomedicine* 3(3):225-230.

Diener HC, Pfaffenrath V, Schnitker J, Friede M, Henneicke-von Zepelin HH. 2005. Efficacy and safety of 6.25 mg t.i.d. feverfew CO<sub>2</sub>-extract (MIG-99) in migraine prevention -- a randomized, double-blind, multicentre, placebo-controlled study. *Cephalgia: An International Journal of Headache* 25(11):1031-1041.

Draves AH, Walker SE. 2003. Parthenolide content of Canadian commercial feverfew preparations: label claims are misleading in most cases. *Canadian Pharmaceutical Journal/La Revue Pharmaceutique Canadienne* 136(10):23-30.

Ernst E, Pittler MH. 2000. The efficacy and safety of feverfew (*Tanacetum parthenium* L.): an update of a systematic review. *Public Health Nutrition* 3(4A):509-514.

Farnsworth NR, Bingel AS, Cordell GA, Crane FA, Fong HH. 1975. Potential value of plants as sources of new antifertility agents I. *Journal of Pharmaceutical Sciences* 64(4):535-598.

Gawel MJ. 1995. The use of feverfew in the prophylaxis of migraine attacks. *Today's Therapeutic Trends* 13(2):79-86.

Grieve M. 1971. *A Modern Herbal, Volume 1*. New York (NY): Dover Publications [Reprint of 1931 Harcourt, Brace & Company publication].

Hausen BM, Osmundsen PE. 1983. Contact allergy to parthenolide in *Tanacetum parthenium* (L.) Schulz-Bip. (feverfew, Asteraceae) and cross-reactions to related sesquiterpene lactone containing Compositae species. *Acta Dermato-Venereologica* 63(4):308-314.

Heptinstall S. 1988. Feverfew-an ancient remedy for modern times? *Journal of the Royal Society*





of Medicine 81(7):373-374.

Heptinstall S, Awang DV, Dawson BA, Kindack D, Knight DW, May J. 1992. Parthenolide content and bioactivity of feverfew (*Tanacetum parthenium* (L.) Schultz-Bip.). Estimation of commercial and authenticated feverfew products. *Journal of Pharmacy and Pharmacology* 44(5):391-395.

Klepser TB, Klepser ME. 1999. Unsafe and potentially safe herbal therapies. *American Journal of Health-System Pharmacy* 56(2):125-138.

Kwok BH, Koh B, Ndubuisi MI, Eloffsson M, Crews CM. 2001. The anti-inflammatory natural product parthenolide from the medicinal herb Feverfew directly binds to and inhibits IkappaB kinase. *Chemistry & Biology* 8(8):759-766.

Jain NK, Kulkarni SK. 1999. Antinociceptive and anti-inflammatory effects of *Tanacetum parthenium* L. extract in mice and rats. *Journal of Ethnopharmacology* 68(1-3):251-259.

Makheja AN, Bailey JM. 1982. A platelet phospholipase inhibitor from the medicinal herb feverfew (*Tanacetum parthenium*). *Prostaglandins, Leukotrienes, and Medicine* 8(6):653-660.

Meyer JE. 1993. *The Herbalist*. Glenwood (IL): Meyerbooks.

Miller LG. 1998. Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions. *Archives of Internal Medicine* 158(20):2200-2211.

Mills S. 1985. *The Dictionary of Modern Herbalism*. Wellingborough (GB): Thorsons Publishers Ltd;

Nelson MH, Cobb SE, Shelton J. 2002. Variations in parthenolide content and daily dose of feverfew products. *American Journal of Health-System Pharmacy* 59(16):1527-1531.

Patrick M, Heptinstall S, Doherty M. 1989. Feverfew in rheumatoid arthritis: a double blind, placebo controlled study. *Annals of the Rheumatic Diseases* 48(7):547-549.

Paulsen E, Andersen KE, Hausen BM. 1993. Compositae dermatitis in a Danish dermatology department in one year (I). Results of routine patch testing with the sesquiterpene lactone mix supplemented with aimed patch testing with extracts and sesquiterpene lactones of Compositae plants. *Contact Dermatitis* 29(1):6-10.

Tilgner S. 1999. *Herbal Medicine from the Heart of the Earth*. Creswell (OR): Wise Acre Press.

Williamson EM, Evans FJ, Wren RC. 1988. *Potter's New Cyclopaedia of Botanical Drugs and Preparations*. Saffron Walden (GB): C.W. Daniel Company Limited.

Wren RC. 1907. *Potter's Cyclopaedia of Botanical Drugs and Preparations*. London (GB): Potter and Clark.