FLORDIS™
Simply Different.

Femular® & Femular® Forte

For menopause

The Femular® range difference

- Uses a clinically trialled extract of *Actaea racemosa* - Ze 450.
- Non-hormonal extract specifically researched in over 1000 women for menopausal symptoms.
- Dose-dependent (including placebo controlled) studies confirm effective once a day dose for varying degrees of symptoms.
- Available in two evidence-based dosage strengths, supporting its use for all stages of menopause.
- Conforms to well established use by the European Medicines Agency (EMA) herbal preparation guidelines for menopausal symptom relief.
- Produced from the world's first controlled black cohosh cultivation for sustainability and quality control.
- Well established tolerability, with no known reported drug interactions, and annual global safety and efficacy reports completed.

The Femular® range contains the scientifically researched extract of *Actaea racemosa* Ze 450

The Femular® range therapeutic indications

In perimenopause, menopause and post menopause, Femular® and Femular® Forte may:

- Relieve feelings of general malaise and general debility, weariness and fatigue
- Decrease excessive or spontaneous sweating
- Relieve irritability and reduce symptoms of mild anxiety
- Support healthy emotional and mood balance
- Decrease headache symptoms and occurrence of symptoms
- Support neuroendocrine function
- Reduce mild joint aches and pains (Femular® Forte only)

During menopause, Femular® and Femular® Forte may also:

- Support a healthy female hormonal balance
- Help decrease symptoms of menopause, including night sweats and hot flushes, irritability and mood swings

Ze 450 - the black cohosh extract clinically proven for menopause symptom relief

SFI™

Multiple clinical trials and history of use show efficacy and tolerability

The Femular® range has a long history of use and high levels of tolerability:

- International birth date of Femular®: 4 August 2005 - when first released to the global market
- Patient exposure: Millions of doses have been estimated to be taken since global release
- Periodic Safety Update Reports (PSURs) are conducted yearly to evaluate and summarise safety data on Ze 450

The Femular® range research summary

The Femular® range, and the specialised extact Ze 450, have been researched for efficacy and dose-finding (dependent) studies in hundreds of women. This research shows a clinically proven use of the Femular® range for the relief of menopausal symptoms.

Lead author/year	Study design	Subjects/Dose	Outcome Summary
Schellenberg, et al. 2012[1]	Randomised, double-blind, placebo controlled, 3-armed study	180 women with menopausal symptoms 6.5mg and 13mg for 3 months	**Menopause efficacy and dose-dependent (dose-finding) study** This placebo controlled trial showed significant dose dependent reductions in menopausal symptoms and improved quality of life. The 6.5mg dose supported mild to moderate symptoms, while the 13mg dose was effective at all stages but superior to the low dose in severe menopausal symptoms. Ze 450 was well tolerated.
Drewe et al. 2013[2]	Open prospective observational study	442 women with menopausal symptoms 13mg for 3 months; 6.5mg or 13mg for further 6 months	**Menopause efficacy and dose-dependent (dose-finding) study** Supporting the results of Schellenberg 2012 over a 3 month period, this observational study extended treatment for another 6 months, with significant improvements in menopausal symptoms. This showed long term treatment over 9 months effective, especially with the 13mg dose. Ze 450 was well tolerated.
Lopatka et al. 2007[3]	Multicentre, open observational study	541 women in all stages of menopause 6.5mg for 4 months	**Menopause symptom improvement study** This large study showed steady and significant improvements in menopausal symptoms over the treatment period, especially in hot flushes and sweating. Ze 450 was well tolerated.

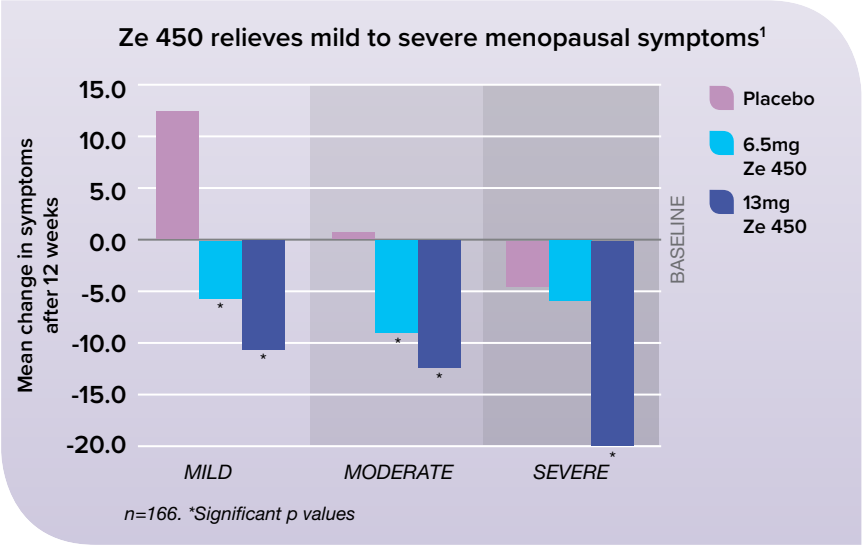
Ze 450 conforms to EMA standards

The highly regarded European Medicines Agency (EMA) Committee on Herbal Medicinal Products (HPMC) reported in 2018 that the Ze 450 extract conforms to the requirements for the well-established use in menopausal symptom relief.[5]

Dose-dependent and efficacy study

Researchers reported efficacy for both 6.5mg and 13mg daily doses, in the first dose-dependent study. Over 3 months, symptoms recorded with the Kupperman Index were significantly improved in both doses, compared to placebo. The higher dose was the most effective in reducing severe menopausal symptoms, especially in hot flushes and sweating.[1]

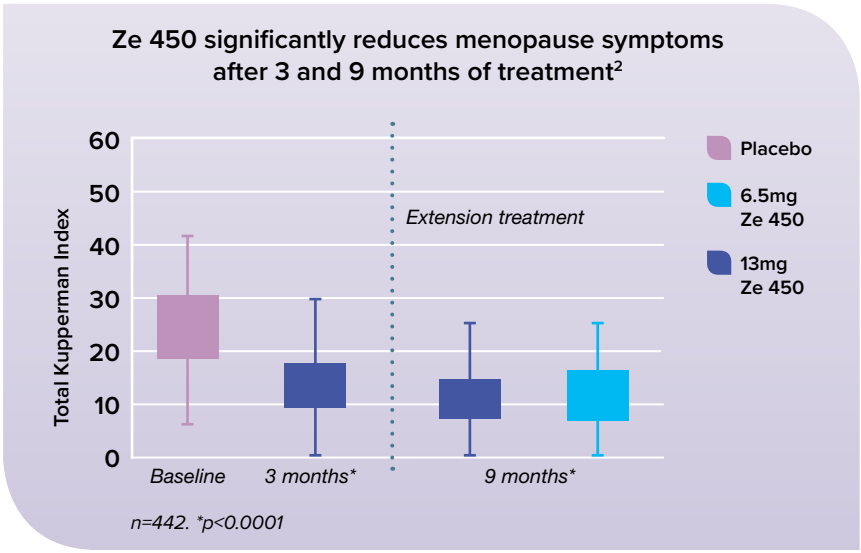
Schellenberg R, et al. Dose-dependent effects of the Cimicifuga racemosa extract Ze 450 in the treatment of climacteric complaints: a randomized, placebo-controlled study. Evid Based Complement Alternat Med. 2012;(1): article ID 2603101.



Long term dose-dependent and efficacy study

This observational study found a significant reduction in menopausal symptoms measured by the Kupperman Index at 3 months and 9 months, with increased efficacy at the trial completion for the higher dose group.[2]

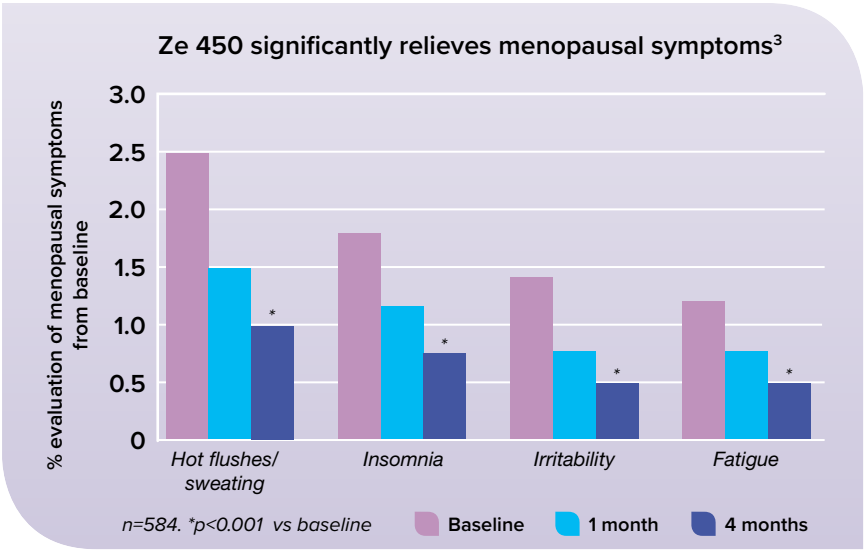
Drewe J, et al. The effect of a Cimicifuga racemosa extract Ze 450 in the treatment of climacteric complaints – an observational study. Phytomedicine. 2013;15 (20):659– 666.



Menopause symptom reduction in large clinical trial

This observational study showed 6.5mg of Ze 450 had a significant effect on multiple menopausal symptoms, with a 59% reduction of hot flushes and sweating after 4 months treatment.[3]

Lopatka L, et al. Black cohosh in the treatment of menopausal symptoms-results of an observational study with Cimifemin® uno (English translation) J für Menopause. 2007;2:3-7.



The Femular® range potential modes of action

The modes of action for *Actaea racemosa* have not been confirmed; however, research suggests it does not alleviate menopausal symptoms through an oestrogenic effect, but by modulating serotonin, dopamine, GABA and μ-opioid brain receptor activity and signalling pathways in the brain. This may increase neuronal sensitivity to temperature changes; thereby, reducing hot flushes. Black cohosh may also work by counteracting inflammation and oxidation caused by oestrogen fluctuations, through its anti-inflammatory and antioxidant actions.[12,13]

Active ingredients

Each Femular® tablet contains:

- *Actaea racemosa* (Black cohosh) specific extract Ze 450 6.5mg*, equivalent to dry rhizome and root 42.25mg

Each Femular® Forte tablet contains:

- *Actaea racemosa* (Black cohosh) specific extract Ze 450 13mg*, equivalent to dry rhizome and root 84.5mg.

Dosage and administration

Adults: *For mild symptoms:* Take 1 Femular® tablet daily, in the morning, with or after a meal.

For moderate to severe symptoms: Take 1 Femular® Forte tablet daily, in the morning, with or after a meal.

*Ze 450 is a scientifically researched extract of *Actaea racemosa*. Each batch is tested for consistency and uniform quality using the triterpenoid glycosides (minimum of 6% (m/m) - expressed as 27-deoxyactein) as the analytical marker. Triterpenoid glycosides are thought to be the most important biologically active constituents.[9]

Presentation

Femular®:
30 round biconvex yellow beige tablets (~8mm)

Femular® Forte:
30 and 90 round biconvex yellow beige tablets (~8mm)

Storage conditions

Store below 25°C.

Contraindications and precautions

Do not recommend if there is a history of hypersensitivity to *Actaea racemosa* (also known as *Cimicifuga racemosa*).

Femular® and Femular® Forte contain 44 milligrams lactose. According to a systematic review, up to 12-15 grams may be tolerated by those with lactose intolerance or malabsorption, with a minimum of 15 grams required for diagnosis.[6] Therefore, 44mg is a very low amount of lactose. However, those with the rare hereditary conditions of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take lactose containing medications.

There are no known reported drug interactions; however, concomitant use with hormone replacement therapy or menopause hormone therapy is not recommended. Numerous studies have not found an oestrogenic effect of black cohosh and current research does not support an association between black cohosh and increased risk of breast cancer.[7,8] However, as the modes of action are not clarified, care may be required when prescribing Femular® and Femular® Forte in those with a breast cancer history or undergoing treatment for breast cancer or other hormone-dependent tumours.[4,5]

In very rare cases, black cohosh has been reported to be associated with liver toxicity; however, a true causal relationship is yet to be confirmed.[10] Some of the reports were confounded by multiple ingredients, by more than one medication, possible adulteration, use of incorrect Actaea species or other medical conditions.[11] Liver function monitoring may be advised, especially in those with liver disease or a history of liver damage.[4]

Pregnancy and lactation: There are no published studies to establish safety or rationale for the use of the Femular® range during pregnancy, or while breastfeeding, so use is not recommended. Extra contraceptive precautions may be required when prescribing Femular® and Femular® Forte to women of childbearing potential.[4]

FAQ

Does the Femular® range contain hormones?

The Femular® products only contain the herb, black cohosh, and do not contain any hormones. Although the mode of action is still not fully elucidated, research to date suggests that black cohosh does not have an oestrogenic effect.[12,13]

Vegetarian friendly formula. No added:

- Gluten
- Wheat
- Corn
- Egg
- Soy
- Yeast
- Sesame
- Peanuts or tree nuts
- Genetically modified ingredients
- Artificial or nature identical flavours, colours or sweeteners

References

1.Schellenberg R, et al. Dose-dependent effects of the Cimicifuga racemosa extract Ze 450 in the treatment of climacteric complaints: a randomized, placebo-controlled study. Evid Based Complement Alternat Med. 2012;(1): article ID 2603101. **2. Drewe J,** et al. The effect of a Cimicifuga racemosa extract Ze 450 in the treatment of climacteric complaints – an observational study. Phytomedicine. 2013;15 (20):659– 666. **3. Lopatka L,** et al. Black cohosh in the treatment of menopausal symptoms-results of an observational study with Cimifemin® uno (English translation) J für Menopause. 2007;2:3-7. **4. European Medicines Agency.** Assessment report on Cimicifuga racemosa (L.) Nutt., rhizoma. Final. Committee on Herbal Medicinal Products (HMPC) EMA/ HPMC/ 48744/2017. https://www.ema.europa.eu/en/documents/herbal-report/final-assessment-report-cimicifuga-racemosa-l-nutt-rhizome-revision-1_en.pdf **5. Periodic Safety Update Report** for active substance: Black Cohosh dry extract Ze 450. Max Zeller SÖhne AG, CH-8590 Romanshorn. 2019. **6. Shaukat A,** et al. Systematic review: effective management strategies for lactose intolerance. Annals of internal medicine. 2010 Jun 15;152(12):797-803. **7. Fritz H,** et al. Black cohosh and breast cancer: a systematic review. Integr Cancer Ther. 2014;13(1):12-29. **8. Garcia de Arriba S,** et al. Cimicifuga racemosa (CR) safety: Pre-and clinical evidence for lack of widespread estrogenic risk. Maturitas. 2015;82(3):316. **9. Lopes CM,** et al. Phytotherapy and nutritional supplements on breast cancer. BioMed research international. 2017. Article ID 7207983. DOI: 10.1155/2017/7207983. **10. Henneicke-von Zepelin HH.** 60 years of Cimicifuga racemosa medicinal products. Wiener medizinische wochenschrift. 2017;167(7-8):147-59 **11. National Institutes of Health.** Office of Dietary Supplements. Black Cohosh Monograph. 2018. https://ods.od.nih.gov/factsheets/BlackCohosh-HealthProfessional/. **12. Nicken P,** et al. Cimicifuga racemosa for treatment of vasomotor symptoms: Mode of action. Maturitas. 2017 Jun 1;100:152. **13. Friederichsen L,** et al. Effect of CIMicifuga racemosa on metaBOLIC parameters in women with menopausal symptoms: a retrospective observational study (CIMBOLIC). Arch Gynecol Obstet. 2019 Nov 16:1-7.

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