MENODYNE®

Helps relieve primary and secondary criteria of climacteric disorders
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1 - DESCRIPTION OF THE MENOPAUSE

1.1 Physiological reminder: influence of the hypothalamic-hypophyseal axis on the menopause

The hypothalamic-hypophyseal axis is involved in controlling reproduction in humans, both men and women.

In women, the gonadotropic axis is organised as follows (diagram n°1):

- Hypothalamic neurons secrete a neuro-hormone, GnRH (*Gonadotrophin Releasing Hormone*). As in humans, this secretion has the particularity of being pulsatile: it is shown in "peaks" about every 60 to 90 minutes. GnRH is transported by the Hypothalamic-Hypophyseal Portal system (HHPS) from the hypothalamus to the anterior hypophysis (pituitary) or adenohypophysis. GnRH stimulates the secretion of two hormones by gonadotropic endocrine cells in the adenohypophysis: FSH (*Follicle Stimulating Hormone*) and LH (*Luteinising Hormone*).

- FSH and LH are transported throughout the body by the blood circulation. FSH and LH stimulate ovarian endocrine cells. These ovarian cells secrete two types of hormones: oestrogens (including oestradiol), and progesterone.

- Oestrogens and progesterone, transported by the blood circulation, act on various target organs to provide the reproductive function. Furthermore, these hormones act retroactively on the hypothalamus and pituitary.

Diagram n° 1: Simplified functional diagram of the female sexual cycle
1.2 Definition of the menopause in three stages: pre-menopause, menopause and post-menopause

The menopause is a climacteric period for women, normally occurring between the age of 50 and 55, characterised by the loss of ovarian follicular activity leading to the definitive end of menstruation.

Diagnosis is retrospective when a woman has not had a period for more than 12 months.

It is a natural, progressive and highly complex physiological process. Schematically, three stages are defined: pre-menopause, menopause and post-menopause.

The first stage, called "pre-menopause" is a phase of hormonal disorder. Indeed, the gradual disappearance of ovulation leads to the cessation of progesterone secretion; so there is a hormonal imbalance weighing on the side of oestrogens characterised by irregular menstrual cycles preceding their disappearance.

The second stage is therefore the "menopause" itself, corresponding to a lack of oestrogen, which is more or less severe, causing hypersecretion by the hypothalamus and hypophysis. Histologically, the menopause is characterised by the end of follicular function and a deficiency of oestrogen and progesterone. Biologically, the cessation of ovarian activity stops hypophyseal "feedback" of gonadotropic hormone secretion, particularly FSH (Follicle Stimulating Hormone), observed during the sexual cycle in non-menopausal women. Finally, at clinical level, the main consequence is sterility of these women.

Finally, the third and last stage is the "post-menopause" or phase of confirmed menopause with oestrogen deficiency. This stage corresponds to a restoration of balance at central nervous system level. Periods have finally stopped and the ovaries atrophy.

These hormonal changes affect all genital organs, breasts, central nervous system neuromediators and finally, hormone-sensitive tissues such as the skin, eyes, bones, vessels; this is when serious diseases such as osteoporosis or cardiovascular diseases develop.

1.3 Hypo-oestrogenism

The climacteric is the period of the menopause during which endocrine, physical and psychological changes occur. Conventionally, climacteric disorders include the following:
- Hot flushes, the intensity of which varies from simple facial flushing to a severe vasomotor hot flush disfiguring the woman.
- Night sweats Þ sleep disorders
- Fatigue
- Complexion
- Other disorders: headache, joint pain, mood swings

All these climacteric disorders are the result of hypo-oestrogenism. These symptoms are very variable from one woman to another, in their frequency, intensity, time of occurrence and duration.

The main disturbance to quality of life for menopausal women is hot flushes, observed in 3 out of 4 women.
They vary in intensity from simple facial flushing to a severe vasomotor hot flush, disfiguring the woman: the flush rises from the trunk towards the face, accompanied by profuse sweating. They can be controlled by moderate oestrogen therapy. Hot flushes probably reflect a disorder at neurotransmitter level, specifically caused by the menopausal oestrogen deficiency. They generally last several months but may continue for years.

A summary of scientific work (1; 2; 3; 4) carried out during the 1980s was produced to explain this climacteric problem of hot flushes.

This work on hot flushes expresses the sudden activation of autonomous and behavioural thermolytic mechanisms. Body temperature is controlled by centres, the most important of which is in the hypothalamus. These centres adjust the internal temperature through neurovegetative effectors and behavioural reactions. The adjustments of body temperature by the hypothalamic centre are based on a fixed value called the body temperature set point, normally 37°C. Unlike a fever, a hot flush causes a sudden fall in this set-point temperature, activating thermolytic mechanisms leading to a very discrete fall in body temperature. Perspiration, vasodilation, erythema and elevation of skin temperature are due to the sympathetic autonomous effector whereas the subjective unpleasant feeling of heat is a behavioural reaction.

Several in vivo (5) studies have highlighted the influence of hormonal imbalance observed during the menopause, itself influenced by the hypothalamic-hypophyseal axis. Indeed, it has been noted that a hot flush is followed by a steep, transient elevation in LH (Luteinising hormone); itself secondary to a pulsatile release of GnRH, a neurohormone secreted by the hypothalamus. GnRH secretion is regulated by plasma concentration of oestrogen, as well as neuromediators such as dopamine (6;7).

Hypo-oestrogenism or oestrogen deficiency observed during the menopause leads to the disappearance of hormonal feedback which would have the effect of lowering the temperature set point of the hypothalamic thermostat.

A hot flush is therefore seen to be a dual autonomous vegetative adaptation reaction, activating thermolytic mechanisms and reflecting the imbalance between ovarian hormones and neuromediators.
1.4 Coronary Atherosclerosis: one of the long-term risks during post-menopause

Before the menopause, coronary disease is much more common in men than in women. After the menopause, the frequency of female coronary pathologies gradually increases to match that of men. The respective roles of age and oestrogen deficiency are a subject of controversy.

The other factors are:
- modifications in lipid metabolism (Total cholesterol, LDL-Cholesterol)
- changes in certain coagulation factors (factor VII, fibrinogen); blood glucose does not vary physiologically during this period.

The frequency of coronary accidents doubles after the menopause.
2 - PRESENTATION OF A FOOD SUPPLEMENT - MENODYNE®

**Ingredients:**
Capsule (gelatin, stabilisers: glycerol, sorbitol, colouring agent: caramel, flavour: ethylvanilline); citrus extract (*Citrus sinensis*, maltodextrin); borage oil (*Borago officinalis*); fish oil; mineral: ferrous gluconate; marine origin phospholipids (fish, crustaceans, molluscs); mineral: zinc gluconate; emulsifier: fatty acid mono and diglycerids; thickener: yellow beeswax; natural vitamin E; natural beta-carotene (*Dunaliella salina*); sunflower oil; vitamin B9

This product contains traces of sulfites

**Major allergens:** FISH, SULFITES + CRUSTACEANS, MOLLUSCS according to current European regulation

**Net weight:**
- 1 soft capsule: 865 mg
- 1 case of 30 soft capsules: 25,95 g
- 1 case of 60 soft capsules: 51,9 g

**Directions for use:**
1 capsule daily

**Claims:**

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*AJR = Apports Journaliers Recommandés / Recommended daily supplies - OK directive 2008/100/CE
3 - SCIENTIFIC EVIDENCE OF EFFICACY

Current knowledge of the mechanisms of action of substances and their metabolic impact largely explains the activity of MENODYNE® which is based on:

- regulating inflammation by providing direct prostaglandin precursors (gamma-linolenic acid or GLA, and eicosapentaenoic acid or EPA)
- acting on the composition of nerve cell membranes and climacteric disorders through an exogenous provision of long-chain phospholipids (or LC-phospholipids)
- antioxidant activity and improved microcirculation through a combination of vitamins and minerals: zinc, vitamin E, β-carotene and citrus flavonoids.

3.1 Long-Chain polyunsaturated fatty acids: LC-PUFA

3.1.1 Fatty acid metabolism (diagram n°2)

Fatty acids belong to the lipid family; there are three main categories of fatty acids: saturated, monounsaturated and polyunsaturated fatty acids.

Compounds in the Polyunsaturated Fatty Acid (PUFA) family have at least two double bonds; the PUFAs include the omega-3 (n-3) and omega-6 (n-6) families.

Their lead components, alpha-linolenic acid (omega 3) and linoleic acid (omega 6) respectively, are said to be "essential" because the body cannot synthesise them itself. Therefore, dietary intake is required. These leading components, also called "precursors" produce the higher derivatives of each omega family. These higher derivatives contain more than twenty carbon atoms, so they are called "long-chain" derivatives. Finally, Long-chain PUFA (LC PUFA) are:
- Arachidonic acid for omega 6
- Eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids for omega 3

However, this metabolism which transforms precursors into Long-Chain derivatives is limited. Indeed, it depends on the activity of two types of enzymes: elongases and desaturases. These enzymes are involved in the metabolism of both omega 3 and omega 6. There is said to be competition between these two families of PUFAs. This competition increases according to the imbalance in the equilibrium between omega 6 and omega 3.
Diagram n°2: Polyunsaturated fatty acid metabolism

Série n-6
Acide linoléique C18:2 n-6
↓
GLA C18:3 n-6
↓
DIGLA C 20:3 n-6
↓
Acide arachidonique C20:4 n-6
↓
Acide eicosapentanoïque EPA C22:6 n-3

Thrombosis, inflammation

Série n-3
Acide alpha linolénique C18:3 n-3
Δ 6 désaturase
↓
C18:4 n-3
Δ 5 désaturase
↓
C20:4 n-3
↓
C20:5 n-3
↓
Acide docosahexanoïque DHA C22:6 n-3

Borage oil

Sunflower, olive and corn oil

Rapeseed, soybean oil, wheatgerm

Fish oil

Diagram:
- Sunflower, olive and corn oil
- Borage oil
- Rapeseed, soybean oil, wheatgerm
- Fish oil

Thrombosis, inflammation
3.1.2 Consequences of ageing

Ageing alters fatty acid metabolism. The enzyme systems grow weaker: It has been shown that body ageing leads to a reduction in activity of Δ-5 and Δ-6 desaturases. Long-chain derivatives are less well synthesised, which raises the problem of providing fatty acids such as arachidonic acid, GLA, EPA and DHA in subjects aged over 50.

Under these conditions of ageing, Long-Chain PUFAs (EPA/DHA) become essential and must be provided by sources outside the body.

3.2 Functional roles of polyunsaturated fatty acids (PUFA)

3.2.1 Regulation of eicosanoids

The efficacy of MENODYNE® is attributed to the activity of two particular PUFAs which act as prostaglandin precursors (8). These are gamma linoleic acid (GLA) for omega 6 and EPA for omega 3.

The fatty acids we ingest are incorporated into our cell membranes. Then, via phospholipases, cyclo-oxygenases and lipoxygenases, they give rise to lipid mediators: eicosanoids (prostaglandins and leukotrienes in particular). These mediators are involved in many bodily processes, notably the regulation of inflammatory and vascular reactions which are modulated by the omega 6/omega 3 ratio (diagram n°3).
Oral intake of long-chain omega 3 fatty acids reduces their membrane concentration of arachidonic acid (omega 6) and hence its availability for synthesising eicosanoids (12;13).

Moreover, the mediators resulting from the n-3 series (prostaglandin 3 or PGE3 and leukotriene 5) and DIGLA (PGE1 and leukotriene 3) have less inflammatory and less aggregating activity (limiting the thrombotic process) than those from arachidonic acid (PGE2, TXA2 and leukotriene 4).

- **Gamma-linolenic acid** or GLA has anti-inflammatory activity and gives rise to dihomo-gamma-linolenic acid, a precursor of series 1 eicosanoids.

- **EPA** competitively inhibits the oxygenation of arachidonic acid by cyclo-oxygenase, slowing the formation of pro-inflammatory mediators (14; 15). Moreover, EPA is a substrate of this enzyme, but it promotes the formation of prostaglandin E3 and leukotriene B5 which has less effect on inflammation than that of the corresponding derivatives, of which omega-6 compounds are precursors. EPA is the series 3 eicosanoid which exerts beneficial action on the cardiovascular system (anti-atherogenic, hypotriglyceridaemic and anti-inflammatory).

Other mediators, such as cytokines, interleukins and TNF (tumour necrosis factor) have pro-inflammatory cellular action. EPA and DHA inhibit the production of the cytokines IL-1α and TNF-α via a mechanism that has not been elucidated to date.

We can now see the benefit of providing PUFA precursors of eicosanoids, the provision of which modulates the inflammatory reaction by inhibiting the metabolism of arachidonic acid and promoting the production of mediators which are much less inflammatory.

### 3.2.2 Role of GLA and EPA in premenstrual syndrome

During the perimenopause, luteal insufficiency leads to the development of signs and symptoms which demonstrate the permanent influence of oestrogens on target organs. This is why premenstrual syndrome may be accentuated during this period.

A lack of prostaglandin E1 has been suggested as the source of most of the symptoms of premenstrual syndrome (9, 10) particularly in benign mastopathy with mastodynia (11).

The omega 3 fatty acids in fish oils have been studied for their ability to soothe dysmenorrhoea by affecting the metabolism of prostaglandins and other factors involved in pain and inflammation. Some experts confirm that an omega 3 supplement helps reduce menstrual pain because of its anti-inflammatory activity (16; 17)

According to an epidemiological survey carried out in Denmark on 181 women aged 20 to 45, the women who suffered least from dysmenorrhoea were those who consumed more omega 3 fatty acids of marine origin (10; 18; 19)
3.2.3 Other physiological activities: bone density and cardiovascular system

A study involving 65 elderly women (79 on average) concluded that a gamma-linolenic acid supplement (in the form of borage oil) and fish oil had helped increase their bone mass (20; 21).

Finally, the protective effects of omega 3s on the cardiovascular system go without saying. Because of the oestrogen deficiency, we know that the incidence of cardiovascular diseases increases significantly after the menopause. All subject intervention and observation studies have been collected in a guide produced by the AFSSA (French food safety agency) (22).

3.3 Long-chain phospholipids: specific neuronal membrane nutrients

The menopause can be characterised by mood swings, irritability, anxiety, sometimes even loss of memory and concentration problems.

Neurotransmitters are involved in these emotional and cognitive imbalances. Acetylcholine is particularly involved in the memorisation process, melatonin and quality of sleep and dopamine in desire, pleasure and movement.

3.3.1 Structural role of phospholipids constituting neuronal membranes

Neurotransmitters are released into the synaptic cleft by exocytosis, owing to the fluidity of the membrane.

However, it has been demonstrated that membrane properties are closely linked to their phospholipid composition. Indeed, neuronal membranes, like any other cell membrane, consist of a phospholipid bilayer (diagram n°4). These neuronal membranes have the particularity of being rich in phospholipids with long polyunsaturated chains (ARA/EPA/DHA). Phospholipids (diagram n°5) represent 25% of the weight of the brain.

Diagram n°4: Structure of the cell membrane
At this level, polyunsaturated fatty acids, in the form of phospholipids, play an essential role in membrane fluidity.

![Diagram n°5: Structure of a phospholipid.](image)

DHA is particularly represented because it constitutes 35 to 56% of phospholipid fatty acids in nerve tissue.

The composition of phospholipids exerts a direct influence on membrane properties. The more unsaturated the phospholipid chains, the more fluid they are and the more effective intercellular exchanges are.

### 3.3.2 Functional role of phospholipids: Neurotransmission

#### 3.3.2.1 Role of phospholipids in the regeneration of cell membranes and ageing (23; 24; 25)

It has been shown that ageing is characterised by modifications in the function and fatty acid composition of membrane phospholipids. We know that this change of composition leads to the modification of neurotransmission.

In animals deficient in PUFA, the DHA concentration falls in the brain. Dopaminergic transmission is modified. On the other hand, supplementation with phospholipids rich in DHA corrects the cerebral DHA level and behavioural disturbances induced by the deficit (26). Furthermore, this supplementation increases the secretion of melatonin, a hormone involved in regulating wake/sleep rhythms and the secretion of acetylcholine, mainly involved in memarisation and learning processes, but also in attention processes and behavioural flexibility levels, motivation, reactivity to new things, and sleep.

#### 3.3.2.2 Role of Phospholipids in cognitive and menopausal disorders

Long-chain phospholipids are complex lipids which play important roles in dopaminergic and serotonergic neurotransmission (24).

Several studies have demonstrated that a deficiency in omega 3 in the diet can lead to a reduction in concentration of these essential fatty acids in the brain (26; 27; 55)
It has been shown in animal and human models, that there is a reduction in acetylcholine release in the brain during ageing. This is a major causal factor in both Alzheimer’s disease and less serious age-related mnesic conditions.

The EVA Study (Etude du Vieillissement Artériel) performed over 4 years on subjects aged from 63 to 74, showed the link between membrane concentrations of phospholipid polyunsaturated fatty acids in erythrocytes and cognitive decline in the 246 subjects examined. An increase in the concentration of stearic acid (saturated) and total omega 6 is linked to a greater risk of cognitive decline. On the other hand, an increased phospholipid concentration of omega 3s is linked to a lower risk of cognitive decline17.

Several studies have revealed a plasma and/or erythrocyte deficit in PUFAs during depression (HIBBELN J.R. et al. 1995; ADAMS P.B. et al. 1996). Significant reductions in PUFA levels of omega 6, and above all, omega 3, were measured in red cell membrane phospholipids in depressed patients, thus leading to an overall increase in the omega 6/omega 3 ratio.

At the menopause, profound modifications alter brain function. This reorganisation takes several years and towards the age of sixty, the brain achieves a steady post-menopausal state. From a clinical point of view, a dietary supplement versus placebo in 494 subjects aged 65 to 93 with animal phospholipids obtained improvements in certain age-related cognitive disorders (28). It has also been shown that adequate intake of phospholipids was likely to prevent the memory from declining too quickly (29).

The efficacy of long-chain phospholipids on hot flushes has also been demonstrated; (30; 31; 32; 33, 34; 56). Phospholipids are thought to act as dopamine receptor stimulators (dopamine is a neuromediator in the autonomous nervous system which regulates body temperature) (35; 36; 37; 38; 39).

### 3.4 Antioxidant complex: zinc, beta-carotene, vitamin E

#### 3.4.1 Antioxidant effect

The formula of the food supplement MENODYNE® combines three antioxidants which act in a complementary way to combat oxidative stress, partly responsible for cell ageing: vitamin E, zinc and β-carotene.

Oxidative attack is generated by reactive oxygen species which attack cell structures: proteins, DNA and cell membrane lipids. These attackers are generated both by the body itself because of oxygen metabolism waste, and by external sources: UV radiation, pollution, smoking, etc.

Studies of antioxidants show the complementary effect of antioxidants. Indeed, these substances act by becoming the target of reactive oxygen species, thus protecting the cell from oxidative stress.

This "neutralisation" reaction of oxygen species has the effect of inactivating antioxidant molecules. They must then be regenerated in order to counter a new oxygen species once again.
β-carotene and vitamin E are both part of the body's non-enzymatic antiradical defence systems. Antioxidants are capable of mutual regeneration, as is the case of vitamin E, for example, which regenerates carotenoids, of which β-carotene is the main representative (Diagram n°6).
1.1 Normal metabolic

Reactive oxygen species (ROS) + PUFAs → RO* + RO2*

Beta-carotene

carotenoid

tocopherol*

tocopherol*

Vitamin E

Vitamin C

GSH → GSSG

GSH-Px

Se → GSSG

? → GS

NAD → NADH

ADP → ATP

NADP → NAD

Diagram n°6: The body’s antioxidant systems


Antioxidant vitamin intake has been reviewed in autonomous elderly subjects. Indeed, the results of most vitamin E supplementation studies are in favour of increasing intake (benefit on immunity, cardiovascular risk). The current consensus is to suggest a daily intake of 20 to 50 mg per day in mature subjects.

3.4.2 Zinc

In France, 30% of women aged over 50 are short of zinc, with levels at the lower limit of the normal value and 10% are close to deficient (40; 41).

Zinc is a trace element necessary for the activity of more than 200 enzyme reactions. It is involved in the metabolism of unsaturated fatty acids and is involved in haemoglobin, prostaglandin and collagen synthesis. The antioxidant activity of zinc involves different mechanisms, particularly enzyme mechanisms. Zinc is part of the structure of SOD (superoxide dismutase) which is part of the body's enzyme defence system against oxidative stress.

3.4.3 Beta-carotene or provitamin A and vitamin E

Beta-carotene is a vitamin A precursor, meaning that the beta-carotene molecule is split in the body, according to need, giving rise to vitamin A.

According to the national centre for studies and research into nutrition and food, beta-carotene should represent 60% of vitamin A activity in the diet. A certain proportion of this vitamin should be maintained due to individual variability in converting beta-carotene to vitamin A. Needs are increased, particularly in elderly people: the metabolism leading to the use of vitamin A is less effective after the age of 60 (42).

Carotenoids and vitamin A stored in the liver are distributed to many extra-hepatic organs. Some provide secondary storage sites, such as the retina and the skin. Indeed, it is known that vitamin A is essential to maintain the epithelium and particularly acts against skin dryness.

Several clinical studies performed versus placebo have shown that vitamin E, at daily doses of 50 to 400 IU, helps reduce hot flushes and other symptoms linked to the menopause (irritability, fatigue, dizziness). The results were only observed after consumption of vitamin E for at least four weeks (43).

3.5 Vitamin B9 and the cardiovascular system

Combined with LC-PUFAs provided by fish oil and phospholipids, vitamin B9 helps improve cardiovascular function. Indeed, vitamin B9 helps reduce the formation of homocysteine, an amino acid found in the blood, which is linked to a higher risk of cardiovascular disease when present in high concentrations (44; 45).
3.6 Iron and the immune system

The immune system weakens with age. Iron plays a part in the body's defence system (46). An iron supplement has a beneficial effect on bone density in post-menopausal women taking HRT (47).

3.7 Citrus flavonoids

Citrus flavonoids help reinforce the strength of blood vessel and capillary walls and reduce vessel permeability (48). They are used for their action on venous-lymphatic insufficiency (49; 50).

Citrus flavonoids have also been the subject of many studies which have demonstrated their antioxidant properties and highlight their anti-atherogenic action as well as their benefits in maintaining bone structure (51; 52; 53; 54).
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5 - EFFICACY STUDIES: ABSTRACT, PROTOCOL, RESULTS

5.1 Preliminary study, coordinated by Dr FRIDERICH and Dr HAMZAOUl, 1991

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<th>Objectives:</th>
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<td>Populations:</td>
<td>47 women of average age 55, presenting clinical symptoms of the menopause.</td>
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<td>Method:</td>
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<tr>
<td>Exclusion criteria:</td>
<td>women treated with hormone replacement therapy, anxiolytics, hypnotics or beta-blockers</td>
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<td>Recommendations for use:</td>
<td>1 capsule per day for 2 months</td>
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**Results:**

High level of efficacy in 87% of patients.
Improvement of the main clinical symptoms of the climacteric such as hot flushes, night sweats, palpitation and withdrawal.
5.2 Multi-centre study of efficacy on climacteric disorders, coordinated by Dr NGUYEN, 2005

**Objective:** Multi-centre study designed to measure the efficacy of MENODYNE ® on climacteric disorders.

**Population:** 101 menopausal women, not taking HRT

**Method:** Clinical evaluation by a gynaecologist of 15 menopausal disorders using a visual analog scale.

**Recommendations for use:** 1 capsule per day for 1 month

**Results:**

Significant improvement of 14 menopausal disorders after 1 month of use:

MENODYNE® helps relieve primary and secondary criteria of climacteric disorders.
5.3 Multi-centre study of efficacy on climacteric disorders in menopausal women taking Hormone Replacement Therapy (HRT) \textit{versus} women not taking HRT, coordinated by Dr NGUYEN, 2007

\begin{tabular}{|l|l|}
\hline
\textbf{Critères} & \textbf{\% amélioration} \\
\hline
réveil nocturne & 72,88\% \\
tristesse, anxiosité & 62,71\% \\
prise de poids & 62,71\% \\
maux de tête & 62,71\% \\
fatigue & 79,66\% \\
sensation lourdeur des jambes & 61,02\% \\
vertige & 45,76\% (NS) \\
seins sensibles, douloureux & 55,17\% \\
bouffées de chaleur & 71,19\% \\
bien être, image de soi & 54,24\% \\
sueurs nocturnes & 69,49\% \\
ventre gonflé & 57,63\% \\
éclat de la peau & 55,17\% \\
rapports sexuels (sécheresse vaginale) & 64,15\% \\
belle, image de soi & 46,55\% \\
troubles urinaires & 47,46\% (NS) \\
Douleurs articulaires & 57,63\% \\
\hline
\end{tabular}
Group 2: MENODYNE ® only

<table>
<thead>
<tr>
<th>Critères</th>
<th>% amélioration</th>
</tr>
</thead>
<tbody>
<tr>
<td>réveil nocturne</td>
<td>73,81%</td>
</tr>
<tr>
<td>tristesse, anxiosité</td>
<td>63,41%</td>
</tr>
<tr>
<td>prise de poids</td>
<td>65,85%</td>
</tr>
<tr>
<td>maux de tête</td>
<td>62,71%</td>
</tr>
<tr>
<td>fatigue</td>
<td>85%</td>
</tr>
<tr>
<td>sensation lourdeur des jambes</td>
<td>64,29%</td>
</tr>
<tr>
<td>vertige</td>
<td>50%</td>
</tr>
<tr>
<td>seins sensibles, douloureux</td>
<td>45,24%</td>
</tr>
<tr>
<td>bouffées de chaleur</td>
<td>83,33%</td>
</tr>
<tr>
<td>bien être, image de soi</td>
<td>61,90%</td>
</tr>
<tr>
<td>sueurs nocturnes</td>
<td>80,95%</td>
</tr>
<tr>
<td>ventre gonflé</td>
<td>66,67%</td>
</tr>
<tr>
<td>éclat de la peau</td>
<td>69,05%</td>
</tr>
<tr>
<td>rapports sexuels (sécheresse vaginale)</td>
<td>60,98%</td>
</tr>
<tr>
<td>belle, image de soi</td>
<td>42,86% (NS)</td>
</tr>
<tr>
<td>troubles urinaires</td>
<td>38,10%</td>
</tr>
<tr>
<td>douleurs articulaires</td>
<td>57,14%</td>
</tr>
</tbody>
</table>

The four main menopausal symptoms improved in groups 1 and 2 were:
- fatigue
- hot flushes
- waking at night
- night sweats
Conclusion

MENODYNE® provides a non-hormonal approach to treating most climacteric disorders linked to the menopause and perimenopause. It can be used very early (from the age of 40) for women not yet presenting any irregularity in their cycle but already complaining of this type of symptom.

The clinical studies performed on MENODYNE® have shown the benefit of this food supplement in women suffering from climacteric signs linked to the menopause.

The conclusions of this report on routine treatment of the menopause fully justify the use of products such as MENODYNE to complete or create an alternative to the usual treatments.