

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. NAME OF THE MEDICINAL PRODUCT**

GERISO<sup>®</sup> 120 mg / 1000 U.I. / 2 mg / 0,5 mg / 20 mg Soft Capsules

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each GERISO<sup>®</sup> Soft Capsule contains, as active substances, the following:

Triglyceride of the linoleic acid	120 mg
Retinol, palmitate (Vitamin A, palmitate)	1000 U.I.
Alpha-tocopherol, acetate (Vitamin E, acetate)	2 mg
Pyridoxine, hydrochloride (Vitamina B6, hydrochloride)	0,5 mg
Lecithin	20 mg

Excipients:

Ethyl para-hydroxybenzoate (ethylparaben): 0,4 mg

Propyl p-hydroxybenzoate; (propylparaben): 0,2 mg

Red Ponceau 4R (E124): 0,54 mg

For full list of excipients, see section 6.1.

### **3. PHARMACEUTICAL FORM**

Capsule, soft.

### **4. CLINICAL PARTICULARS**

#### **4.1 Therapeutical Indications**

GERISO<sup>®</sup> is indicated for the prevention of avitaminosis (A, E and B6).

#### 4.2 Posology and method of administration

The recommended dose of GERISO<sup>®</sup> is 1 to 2 capsules, three times a day, after meals.

These capsules may be taken with water, milk, liquid yogurt or fruit juice.

#### 4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients.

Vitamin A is contraindicated in subjects with hypervitaminosis A.

#### 4.4 Special warnings and precautions for use

An extended administration of a high dose may cause Vitamin A hypervitaminosis. Vitamin A, when taken in a high dose, during pregnancy, especially in the first three months, may harm the embryonic and foetal development. Full ingestion of vitamin A, food intake included, must not exceed the 5000 U.I. a day during pregnancy, given the risk of possible congenital anomalies in the Central Nervous System of the foetus. Vitamin E intensifies the response of oral anticoagulants, when concomitantly administered.

GERISO<sup>®</sup> contains parabens which may probably cause later allergic reactions.

GERISO<sup>®</sup> contains Ponceau Red 4R (E124) which may cause allergic reactions.

#### 4.5 Interaction with other medicinal products and other forms of interaction

Vitamin A may interact with some other drugs such as colestyramine, colestipol, neomycin, calcium supplements, oral anticoagulants, etretinate and isotretinoin.

Pyridoxine (vitamin B<sub>6</sub>) neutralizes the activity of levodopa in patients with Parkinson. This being so, soft capsules GERISO<sup>®</sup> must not be administered to patients in these circumstances. This antagonism will not occur if levodopa is associated with a dopa decarboxylase inhibitor. Pyridoxine may reduce the activity of altretamine and diminish the plasmatic concentrations of phenobarbital and fenitoin.

Vitamin E intensifies the response of oral anticoagulants, when concomitantly administered. Patients on vitamin E together with oral anticoagulants must be supervised and monitored. Some drugs may interfere with the absorption of vitamin A as well as cholestyramine, colestipol, orlistat, iron and dicumarol.

#### 4.6 Pregnancy and Lactation

Vitamin A taken in a high dose during pregnancy, especially in the first three months, may harm the embryonic and foetal development. Full ingestion of vitamin A, food intake included, must not exceed the 5000 U.I. a day during pregnancy, given the risk of possible congenital anomalies in the Central Nervous System of the foetus. Vitamin A is excreted in breast milk.

There is no scientific evidence regarding the safety of the use of lecithin during pregnancy.

#### 4.7 Effects on ability to drive and use machines

There are no known effects on the ability to drive and use machines.

#### 4.8 Undesirable effects

This medicinal product is generally well tolerated. No adverse reactions have been observed.

Nevertheless, as described in the bibliographic references, lecithin may possibly cause a slight increase in the abdominal volume, nausea and diarrhoea, when administered orally. Some cases of peripheral sensory neuropathy may be found in bibliographic references whenever there is an extended administration of pyridoxine (vitamin B6) even in relatively low dosages (more or less 50mg per day).

Gastrointestinal effects may also be found in these bibliographic references because of the ingestion of linoleic acid. The same happens with vitamins A and E.

#### 4.9 Overdose

No cases of overdose have been observed with GERISO®.

The symptoms of overdose correspond to those of a hypervitaminosis or intoxication. Hypervitaminosis A (acute ingestion, superior to 1 500 000 U.I. in adults, or chronic ingestion, superior to 25 000 U.I./per day during 8 months) may result in severe toxicity and death.

Hypervitaminosis A is characterized by cephalaeas, dizziness, hepatomegaly, vomiting, irritability and papilledema.

The symptoms of chronic toxicity include an increase in the intracranial tension, papilledema, polyuria, diplopia, cephalaeas, nausea, bone pains, hepatomegaly, hypercalcaemia, anaemia, anorexia, weight loss, fatigue, irritability, skin with yellowish pigmentation, sunlight sensitivity, alopecia and dizziness. In children, a premature closing of the epiphysis may take place.

The signs and symptoms of overdose are normally reversible when the administration of vitamin A is interrupted and, whenever necessary, by initiating a standardised

symptomatic treatment. In case of overdose in pregnant women, the risk of foetal toxicity must be assessed.

Hypervitaminosis B<sub>6</sub> (superior to 2g/day or a treatment for over two months) may cause reversible peripheral sensory neuropathy. Some of its characteristics are the development of a lack of orthostatic coordination and progressive sensory ataxia. After the interruption of the administration of vitamin B<sub>6</sub>, the neurological disorder will improve progressively.

Hypervitaminosis E (superior to 530 mg/day) may be characterized by diplopia, diarrhoea, dizziness, cephalaeas, nausea and fatigue. These effects disappear with the discontinuation of vitamin E.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 11.3.1.3 Vitamins association.

ATC code: A11BA

GERISO<sup>®</sup> is a vitaminic supplement which balances the increase in the need for vitamins that may occur in case of acute or chronic diseases or in case of an inappropriate diet, being useful in the prophylaxis of avitaminosis.

The pharmacologic reaction of GERISO<sup>®</sup> is due to its multivitaminic action.

Vitamins are crucial for keeping normal metabolic functions.

Vitamin A is essential for the functioning of the retina, bone growth, ovarian and testicular functions, embryonic growth and for the growth and differentiation of the epithelial tissues. Retinol and retinoic acid may act as a cofactor in biochemical reactions.

Vitamin B<sub>6</sub> is involved in the metabolism of the amino acids, carbohydrates and lipids. It is also necessary for the formation of haemoglobin.

Vitamin E is an antioxidant that prevents the oxidation of unsaturated fatty acid reacting with free radicals, which are responsible for the oxidative damages of the cellular membranes, and protects the erythrocytes from haemolyse.

Vitamin A acts as a cofactor of some enzymatic systems.

As far as lecithin is concerned, its favourable action in brain tissues is long and well known, increasing brain activity.

## 5.2 Pharmacokinetic properties

### Vitamin A

Vitamin A is a fat-soluble vitamin. Its absorption takes place in the small intestine and it depends on the amount of fat ingested in one's diet. In order to be absorbed, vitamin A is converted to retinol. After the absorption, retinol is esterified and is bound to chylomicrons reaching systemic circulation through the lymphatic way. Some retinol immediately reaches the circulation and is carried by means of a protein present in plasma.

The interval of normal plasmatic concentration for vitamin A is of 30 to 80 µg/dl.

Approximately 90% of vitamin A stored in the human body can be found in the liver.

It is metabolized in the liver and in the retina, originating the following active metabolites: 11-cis-retinal (retina); retinoic acid (other tissues); Retinaldehyde; tretinoin; isotretinoin (13-cis- retinoic acid); 4-oxo-tretinoin; 4-oxo-isotretinoin. Since it is a fat-soluble compound, it is likely to suffer accumulation in the organism, especially in fat-rich tissues.

There is no available data regarding the half-life of the elimination of vitamin A in the human being. It is only known that, in the mouse, the half-life of the elimination of vitamin A (under the form of retinol) is adjusted to a model of three compartments. It is also known that vitamin A is excreted in breast milk.

### Vitamin B<sub>6</sub>

Pyridoxine (Vitamin B<sub>6</sub>) is absorbed by the gastrointestinal tract (it is promptly absorbed in the jejunum, through passive diffusion). After being absorbed, pyridoxine in circulation is led to the liver by the hepatic portal vein where it will be metabolised, originating two active forms (pyridoxal phosphate, pyridoxamine phosphate) and an inactive form (4-pyridoxic acid) which is excreted in urine. Its main metabolite is pyridoxal phosphate because it is released in larger quantities in blood circulation (connected to serum albumine). This metabolite spreads across the liver and muscles, crosses the placenta and it is distributed in breast milk.

Pyridoxine is also metabolised in erythrocytes although in a lower quantity.

2% of pyridoxine (4-pyridoxic acid) is eliminated in bile and 35-63% is eliminated throughout the urinary tract (in urine). The primary inactive form of pyridoxine to be excreted in urine is 4-pyridoxic acid (water soluble metabolite). The half life time of elimination of vitamin B<sub>6</sub> in the human body is of 15 to 20 days.

### Vitamin E

Vitamin E is absorbed by the gastrointestinal tract with the help of bile.

Oral absorption varies because it depends on the amount of fat ingested in one's diet, on the hydrolysis rate of its salt (acetate) and on age. The therapeutic window of plasmatic concentrations for vitamin E, in a healthy adult, is of 0,5 a 2,5 mg/dl. Vitamin E is distributed through all body tissues (especially fat-rich ones as, for instance, adipose tissue) and it is mainly metabolised in liver (70%), being biotransformed in glucuronides of the tocopheronic acid. It presents a quite low renal elimination, since it is a fat soluble vitamin which is mainly excreted by the bile (70% to 80%).

### **Linoleic acid and Lecithin**

No elements regarding the Pharmacokinetic Properties of Linoleic Acid and Lecithin have been found.

## **5.3 Preclinical safety data**

### **Vitamin A**

Studies carried out in mice have demonstrated that the DL<sub>50</sub> of vitamin A palmitate, administrated orally, is of 4760 mg/kg, for the species studied. Teratogenic effects have also been observed in this species.

In the mutagenic tests carried out, no mutagenic effects have been observed.

### **Vitamin B<sub>6</sub>**

Studies carried out in mice have demonstrated that the DL<sub>50</sub> of pyridoxine hydrochloride, administered orally, is of 4000 mg/kg, for the studied species. There is no evidence regarding the possibility of teratogenic or embryotoxic effects.

### **Vitamin E**

No studies in animals regarding the acute or chronic toxicity of this substance have been found. However, it is known that the plasmatic concentration of vitamin E superior to 3,5mg/dl, may result in acute toxicity. It is also known that the plasmatic levels of prolonged 4,5mg/dl are associated with a raise in the occurrence of diseases such as bacterial sepsis and necrotizing enterocolitis.

### **Linoleic acid and Lecithin**

No studies in animals regarding the acute and chronic toxicity of these substances have been found. However, there are bibliographic references that declare that lecithin has not toxicity at all.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Butylated hydroxytoluene (E321), yellow wax, gelatine, glycerol, ethyl hydroxybenzoate (ethylparaben), propyl hydroxybenzoate (propylparaben) and Red Ponceau 4R (E124).

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

3 Years.

### **6.4 Special precautions for storage**

Store below 25°C.

### **6.5 Nature and contents of container**

PVC/PVDC/Aluminium blister.

Boxes containing 20 and 50 soft capsules.

### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

There are no particular precautions to be taken.

## 7. MARKETING AUTHORIZATION HOLDER

SIDEFARMA – Sociedade Industrial de Expansão Farmacêutica, S.A.  
Rua da Guiné, nº26  
2689-514 Prior Velho  
Portugal

## 8. MARKETING AUTHORIZATION NUMBER(S)

Register no. 9192013 - 20 Soft capsules, PVC/PVDC/Aluminium blister  
Register no. 9192005 - 50 Soft capsules, PVC/PVDC/Aluminium blister

## 9. DATE OF THE FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

3 May 1968

## 10. DATE OF REVISION OF THE TEXT