SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

IDEOS 500 mg/400 IU, chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains 500 mg of calcium as 1250 mg calcium carbonate and 400 IU of cholecalciferol (vitamin D_3) as 4 mg cholecalciferol concentrate (in powder form).

Cholecalciferol concentrate in powder form contains among others alpha-tocopherol, hydrogenated soya bean oil, sucrose.

Excipients with known effect:
Each tablet contains 475.0 mg of sorbitol (E420), 1.52 mg of sucrose, and 0.3 mg of hydrogenated soybean oil.

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Chewable tablets
Square, white-grey tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

IDEOS is indicated only in adults for:
- The correction of vitamin D and calcium combined deficiency in elderly people.
- Vitamin D and calcium supplementation, as an adjunct to specific therapy for osteoporosis treatment in patients with established or at high risk of vitamin D and calcium combined deficiencies.

4.2 Posology and method of administration

Posology
Adults
One tablet twice a day.

Paediatric population
There is no relevant use of IDEOS in the paediatric population.

Method of administration
Oral use.
Chew or suck the tablets.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- This product contains hydrogenated soya bean oil. Patients should not take this medicinal product if they are allergic to peanut or soya.
- Hypercalcaemia, hypercalciuria, and diseases and/or conditions, which lead to hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases, primary hyperparathyroidism).
- Calcium lithiasis, nephrocalcinosis.
- Severe renal impairment (glomerular filtration rate < 30 ml/min). In patients with severe renal impairment, vitamin D3 in the form of cholecalciferol is not metabolised in the normal way and other forms of vitamin D3 must be used.
- Hypervitaminosis D.

4.4 Special warnings and special precautions of use

- The product should be prescribed with caution in patients with sarcoidosis because of possible increased of metabolism of vitamin D to its active form. These patients should be monitored for serum and urinary calcium.
- The product should be used with caution in renal impairment patients (glomerular filtration rate ≥ 30 ml/min) and with monitoring of calcium and phosphate homeostasis. The risk of soft tissue calcification must be taken into account.
- Calcium and alkali intake from other sources (foods, dietary supplements or other drugs) should be considered when prescribing IDEOS. If very high doses of calcium are taken in combination with absorbable alkaline agents (such as carbonates), there is a risk of Burnett syndrome (or milk-alkali syndrome) consisting of hypercalcemia, metabolic alkalosis, renal failure, and soft tissue calcification. In this case, frequent monitoring of serum calcium and calciuria may be necessary.
- In case of prolonged immobilisation in patients with hypercalciuria and/or hypercalcaemia, vitamin D and calcium treatment should only be resumed when the patient becomes mobile (see section 4.3).
- In case of longterm treatment, it is advisable to monitor serum and urinary calcium levels and kidney function (serum creatinine levels). It is advisable to reduce or interrupt treatment temporarily if urinary calcium exceeds 7.5 mmol/24 h,(300 mg/24h). This monitoring is particularly important in the elderly, in cases of combined treatment with cardiac glycosides or diuretics (see section 4.5) and in patients who are frequently subject to the formation of kidney stones. In the presence of hypercalcaemia or signs of problems with renal function, the dose must be reduced or treatment interrupted.
- Additional administration of vitamin D or calcium should be carried out under strict medical supervision. In such situation, weekly monitoring of serum and urinary calcium is absolutely necessary.

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Excipients :

- IDEOS contains sorbitol (E420). Patients with hereditary fructose intolerance (HFI) should not take this medicine.
- IDEOS contains sucrose (sucrose is present in small quantities in cholecalciferol concentrate). Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. The sucrose may be harmful to teeth if this product is taken chronically, e.g. for two weeks or more.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations requiring precautions for use:

Digoxin
Risk of serious dysrhythmia. Medical supervision and if necessary, monitoring electrocardiographic and calcaemia.

Bisphosphonates
Risk of decrease in the gastrointestinal absorption of bisphosphonates. It is advisable to take calcium salts apart from bisphosphonates (a minimum period of 30 minutes to more than 2 hours).

Strontium
Reduction in strontium gastrointestinal absorption on concomitant administration of calcium-containing products. It is advisable to take calcium more than two hours apart from strontium-containing medications.

Tetracyclines per os
Possible reduction in the absorption of tetracycline. It is advisable to take calcium salts at least two hours apart from tetracyclines.

Rifampicin
Possible decrease in vitamin D concentrations. Vitamin D concentrations should be measured and supplementation provided if necessary.

Ciprofloxacin, norfloxacin
Risk of reduction in the intestinal absorption of these fluoroquinolones. It is advisable to take calcium more than two hours apart from ciprofloxacin or norfloxacin.

Dolutegravir
Risk of reduction in the intestinal absorption of dolutegravir. It is advisable to take calcium at least 2 hours after or 6 hours before dolutegravir intake.

Ferrous salt
Risk of reduced gastrointestinal absorption of ferrous salt. It is advisable to allow a period of more than two hours between calcium and ferrous salt.

Zinc

Risk of reduced gastrointestinal absorption of zinc. It is advisable to allow a period of more than two hours between calcium and zinc.

Estramustine
Risk of reduction in the gastrointestinal absorption of estramustine. It is advisable to allow a period of more than two hours between calcium and estramustine.

Thyroid hormones
Risk of reduction in the gastrointestinal absorption of thyroid hormones. It is advisable to allow a period of more than two hours between calcium and thyroid hormones.

Orlistat
Treatment with orlistat may potentially impair the absorption of vitamin D.

Thiazide diuretics
Risk of hypercalcemia due to a decrease in the urinary excretion of calcium.

Food
Possible interaction with food, e.g. foods containing oxalic acid (spinach, rhubarb, sorrel, cocoa, tea, etc.), phosphate (pork, ham, sausages, processed cheese, dessert cream, beverages containing cola, etc.) or phytic acid (wholemeal cereals, dry vegetables, oleaginous seeds, chocolate, etc.). It is therefore recommended that meals containing these foods be taken some time before or after ingestion of the product.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There are several case reports of administration of very high doses of vitamin D in hypoparathyroidism in the mother, where normal children were born.

In pregnancy, an overdose of cholecalciferol must be avoided:
- Overdoses of vitamin D during pregnancy have shown teratogenic effects in animals (see section 5.3).
- In pregnant woman: overdoses in vitamin D must be avoided as permanent hypercalcaemia can lead to physical and mental retardation, supravalvular aortic stenosis and retinopathy in the child.
Consequently, given the indication (see section 4.1), the use of IDEOS during pregnancy is not recommended.

Breast-feeding:
Vitamin D and its metabolites pass into the breast milk. Given the indication (see section 4.1) of IDEOS, the use during breastfeeding is not recommended

Fertility:
No data is available on the effects of IDEOS on fertility. However, normal endogenous calcium and vitamin D levels are not expected to have undesired effects on fertility.

4.7 Effects of ability to drive and use machine

IDEOS has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to < 1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Immune system disorders:
Not known: Hypersensitivity reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.
Not known: Milk-alkali syndrome (hypercalcaemia, alkalosis and renal impairment). Seen usually only in overdose (see sections 4.4 and 4.9).

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

Skin and subcutaneous tissue disorders
Rare: Pruritus, rash and urticaria.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Malta ADR Reporting Website: www.medicinesauthority.gov.mt/adrportal

4.9 Overdose

An overdose can lead to hypervitaminosis and hypercalcaemia.
Symptoms
The symptoms of hypercalcaemia can include: anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, hypertension, mental disturbances, polydipsia, polyuria, skeletal pain, renal calcinosis, kidney stones, and in severe cases, cardiac arrhythmia. Extreme hypercalcaemia may lead to coma and death. Continuous high calcium levels may lead to irreversible damage to the kidneys and soft tissue calcification.
The risk of overdose may be increased if other calcium containing products or alkaline agents are taken (Milk-alkali syndrome). See Section 4.4 and 4.8.

Management
Treatment of hypercalcaemia: all calcium and vitamin D_3 treatments must be stopped. The need to continue all other concomitant medicines should be reconsidered by the physician. Gastric lavage should be performed on patients with problems affecting consciousness. Rehydrate and, depending on severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Peritoneal dialysis should be considered in patients with renal failure or in patients refractory to other therapies.
Serum electrolytes, kidney function and diuresis must be monitored. In severe cases, ECG and calcaemia should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: CALCIUM, COMBINATIONS WITH VITAMIN DAND/OR OTHER DRUGS, ATC code: A12AX.

Vitamin D corrects an insufficient intake of vitamin D.
It increases intestinal absorption of calcium and its fixation on osteoid tissue.

Calcium intake corrects a lack of calcium in the diet.
The commonly accepted requirement of calcium in the elderly is 1500 mg/day.
The optimal amount of vitamin D in the elderly is 500 to 1000 IU/day.
Vitamin D and calcium correct secondary senile hyperparathyroidism.

5.2 Pharmacokinetic properties

Calcium carbonate
In the stomach, calcium carbonate releases calcium ion as a function of pH.
Calcium is essentially absorbed in the proximal part of the small intestine.
The rate of absorption of calcium in the gastrointestinal tract is of the order of 30 % of the dose ingested.
Calcium is eliminated in sweat and gastrointestinal secretions.
The urinary calcium excretion depends on the glomerular filtration and rate of tubular reabsorption of calcium.

Vitamin D3
Vitamin D_3 is absorbed from the intestine and transported by protein binding in the blood to the liver (first hydroxylation) and to the kidney (2^{nd} hydroxylation).
Non hydroxylated vitamin D_3 is stored in reserve compartments such as muscle and adipose tissues.
Its plasma half-life is of the order of several days; it is eliminated in faeces and urine.

5.3 Preclinical safety data

In acute toxicity studies, calcium was very low toxic by oral route in the mouse and in the rat (LD50 = 6450 mg/kg bw).

For calcium carbonate, no genotoxic properties are observed in several *in vitro* tests, neither carcinogenic nor reprotoxic potential are described in the dedicated studies.

Acute toxicity studies with vitamin D3 showed essentially that vitamin D3 in doses far higher than the human therapeutic dose (in the range of 10 mg/kg bw) in the dog and the rabbit by the oral route, has toxic effects (multifunctional defect), as cardiac effects in the rat.

Toxicologically significant effects in repeat-dose toxicity studies with vitamin D3 were observed only at doses or exposures that were sufficiently in excess of the maximum human dose or exposure, indicating that these effects were limited or of no relevance to clinical use. These included: the possible induction of focal adrenal medullary proliferative lesions observed in rats fed up to 6 months by vitamin D3.

In carcinogenicity studies, vitamin D induced biphasic growth response: induction of proliferation in malignant cell lines at low doses and inhibition at higher dose (reduction of cancer’s growth).

At very high doses, vitamin D3 has been found to be teratogenic in rabbits (at doses 4 to 15 times the recommended human dose), and to induce change in sexual behavior in juvenile rats treated neonatally.

These data show that the non-clinical data with calcium and/or vitamin D reveal no specific risk for human.

6. PHARMACEUTICAL PARTICULARS

6.1 List of the excipients

Xylitol, sorbitol (E420), povidone, lemon flavouring *, magnesium stearate.

**composition of lemon flavouring: flavouring preparations, natural flavouring substances, maltodextrin, acacia, sodium citrate, citric acid, butylated hydroxyanisole.*

Excipients of cholecalciferol concentrate in powder form: alpha-tocopherol, hydrogenated soya bean oil, gelatin, sucrose, corn starch.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special conditions of storage

Do not store above 25°C

6.5 Nature and contents of container:

Polypropylene tube and polyethylene stopper with silica gel desiccant containing 10 or 15 tablets.

Packs of 2, 5 or 10 tubes of 10 tablets.
Packs of 2, 4, 6 or12 tubes of 15 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratoire Innotech International

22, avenue Aristide Briand
94110 ARCUEIL
FRANCE

8. MARKETING AUTHORISATION NUMBER

MA093/00201

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11th August 2006

10. DATE OF REVISION OF THE TEXT

11th January 2022

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

Detailed information on this medicinal product is available on the website of Malta
http://www.medicinesauthority.gov.mt