SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
DESIFEROL PLUS 2000 IU+3333 IU+70 mg/ml oral drops, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml (30 drops) solution contains,

Active substance(s):

Vitamin A palmitate	2000 IU
Vitamin D_3 (obtained from sheep's wool)	3333 IU
Vitamin C	70 mg

Excipient(s):

PEG 40 hydrogenated castor oil	90 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Oral Drops
Yellowish, clear solution.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
DESIFEROL PLUS is indicated for use in patients with concomitant vitamin A, D and C deficiency.

4.2 Posology and method of administration
Posology/frequency of administration and duration of the treatment
1 ml of DESIFEROL PLUS solution is 30 drops.

Unless recommended otherwise by the physician, the daily dose is determined in accordance with the table below:

Age Group	**Number of drops per day**	**Vitamin D_3 (IU)**	**Vitamin A (microgram)**	**Vitamin C (mg)**
6 months – 1 year	20 drops	2222 IU	400 microgram	46 mg
1 – 3 years	30 drops	3333 IU	600 microgram	69 mg
4 – 12 years	45 drops	5000 IU	900 microgram	103 mg

1 drop of DESIFEROL PLUS contains 111.1 IU of Vitamin D3, 20 micrograms of Vitamin A, and 2.3 mg of Vitamin C.

Method of administration:
DESIFEROL PLUS is administered orally.
Oral route is preferred in infants or people who cannot be injected. It can be applied to infants by mixing with nutrients.

Additional information for special populations:
Renal/hepatic failure:
Since it contains vitamin D, it should not be used with calcium in patients with kidney failure.

Pediatric population:
It is applied as stated in Posology/frequency of administration and duration of the treatment.
It is not recommended for use in children under 6 months and over 12 years of age.

4.3. Contraindications
It is contraindicated in patients with hypersensitivity to any ingredient in its composition.

It is contraindicated in individuals with hypervitaminosis A and D, hypercalcemia, or those receiving retinoid therapy.

Vitamin C should not be used in cases of kidney stones with aciduria or normal urine pH and oxaluria.

It is contraindicated in cases of hypercalciuria and calcium hypersensitivity.

Long-term use is contraindicated in severe hypertension, advanced arteriosclerosis and active pulmonary tuberculosis.

4.4. Special warnings and precautions for use
A special warning should be made for patients with:
- restricted mobility
- treated with benzothiadiazine derivatives
- history of kidney stones
- sarcoidosis
- pseudohypoparathyroidism.

Ascorbic acid, at high doses, caused hemolysis in patients with G6PD (Glucose-6-phosphate dehydrogenase) deficiency.

If DESIFEROL PLUS is to be given together with other products containing vitamin D3, the total vitamin D dose should be considered carefully. Vitamin D is fat soluble and can accumulate in the body. This may cause toxic effects in overdose and in prolonged treatment with excessive doses.

Vitamins A and D cause hypervitaminosis if used in high doses for a long time.

High doses of ascorbic acid increase urinary oxalate levels and may cause the formation of calcium oxalate stones in the kidney. It should not be used in patients with impaired renal function or a history of kidney stones.

Since ascorbic acid increases iron absorption, high doses may be dangerous in patients with haemochromatosis, thalassaemia, polycythaemia, leukaemia or sideroblastic anaemia. In case of iron overload disease, ascorbic acid intake should be minimized.
High doses of ascorbic acid have been associated with sickle cell crises in patients with sickle cell anaemia.

Chronic use of high doses of ascorbic acid may lead to increased metabolism of the drug. Therefore, withdrawal symptoms may develop when the dosage is suddenly reduced. In such a case, high dosage should be resumed and the dosage should be reduced more slowly.

The diabetogenic effect of ascorbic acid is still controversial. However, blood glucose concentration should be monitored periodically in patients receiving long-term DESIFEROL PLUS treatment, especially in the initial period of treatment. The use of ascorbic acid in diabetic patients may cause false results to be obtained in urine glucose determination tests. Therefore, the use of ascorbic acid should be discontinued a few days before the performance of such tests.

Theoretically, high doses of ascorbic acid may cause gouty arthritis in susceptible patients due to its effect on uric acid excretion.

Ascorbic acid is thought to exacerbate rapidly proliferating and widely disseminated tumours. Therefore, caution should be exercised when prescribing ascorbic acid in advanced cancers.

Serum calcium levels may be monitored in patients with a history of kidney stones at high doses of vitamin D3 and close monitoring of these patients is recommended.

Vitamin D3 should be used with caution in patients with impaired renal function and its effect on calcium and phosphate levels should be monitored. Soft tissue calcification should be considered. In patients with severe renal impairment, vitamin D in the form of cholecalciferol is not metabolised normally and therefore a different form of vitamin D may be required.

In long-term treatment, serum and urine calcium levels, serum creatinine and renal function should be monitored every 3 to 6 months. These checks are particularly important in patients with a high propensity for kidney stone formation, in elderly patients and in concomitant treatment with cardiac glycosides or diuretics.

In case of symptoms of hypercalcaemia or decreased renal function, the dose should be reduced or treatment postponed.

If urinary calcium excretion exceeds 300 mg/24 h, the dose should be reduced or treatment temporarily discontinued.

The condition may be exacerbated in patients with impaired cardiac function due to the possibility of hypercalcaemia and elevated serum cholesterol concentration.

The active metabolite of vitamin D3 (125-dihydroxycholecalciferol) may affect phosphate balance.
Therefore, treatment with phosphate binders should be considered in case of increased phosphate levels.

Vitamin D3 should be given with caution in patients with sarcoidosis and other granulomatous disorders because of the risk of increased metabolism of vitamin D to its active form. These patients should be monitored for calcium content in serum and urine.
The therapeutic index of vitamin D is very low in infants and children. If hypercalcaemia lasts for a long time, it causes mental and physical developmental retardation in infants. There is a risk of hypercalcaemia in infants of nursing mothers who take more vitamin D than they need.

When it is considered to use vitamin A, the risk/benefit should be evaluated if the following medical problems are present:
-Cirrhosis
-Liver disease

-Viral hepatitis (use of vitamin A in these cases may exacerbate liver toxicity; however, this may not apply in cases of chronic cholestatic liver disease accompanied by vitamin A malabsorption)
-Chronic renal failure (serum vitamin A concentrations are increased)
-Sensitivity to vitamin A

High doses or prolonged use of vitamin A may cause bleeding gums, dry mouth or oral sensitivity, or dry, cracked or peeling lips.

Use should be carefully considered in hepatitis, active infectious conditions, inflammatory conditions of the intestinal tract such as enteritis, colitis, diverticulitis and ulcerative colitis, pancreatitis and peptic ulcer.

As it contains PEG 40 hydrogenated castor oil, it may cause nausea and diarrhoea.

4.5 4.5 Interactions with other medicinal products and other forms of interactions
Vitamin A
Calcium preparations (excessive intake of vitamin A [more than 25,000 IU per day] can stimulate bone loss and inactivate the calcium preparation and cause hypercalcaemia)

Cholestyramine, colestipol, mineral oil, oral neomycin (concomitant use may affect vitamin A absorption, recommended vitamin A intake may be increased)

Oral contraceptives (simultaneous use may increase vitamin A concentrations)

Etretinate, isotretinoin (concomitant use with vitamin A may result in additive toxic effects)

Tetracycline (concomitant use of 50,000 IU or more of vitamin A per day has been reported to cause benign intracranial hypertension)

Vitamin E (concomitant use of vitamin E may facilitate absorption, hepatic storage and utilisation of vitamin A and reduce toxicity; extremely high doses may deplete vitamin A stores)

Vitamin D_3
Aluminium-containing antacids (long-term use of aluminium-containing antacids as phosphate binders in vitamin D-related hyperphosphatemia has been found to increase blood levels of aluminium and may lead to bone aluminium toxicity, especially in patients with chronic renal failure)

Magnesium-containing antacids (concomitant use with vitamin D may result in hypermagnesaemia, especially in patients with chronic renal failure)

Vitamin D activity may decrease when used with anticonvulsants, hydantoin, rifampicin, barbiturates or pyrimidone which induce hepatic microsomal enzyme induction.
Mineral oils may reduce the absorption of vitamin D and reduce its effect.

Concomitant use with calcitonin, etidronate, gallium nitrate, pamidronate or pliamycin in the treatment of hypercalcaemia antagonises these drugs.

The risk of hypercalcaemia is increased when drugs containing high doses of calcium or diuretics and thiazide class diuretics are used concomitantly. However, this may be an advantage in the

elderly and in high-risk groups where vitamin D and calcium should be given together. Careful monitoring of serum calcium concentrations is necessary in such long-term treatment.

Concomitant use with other drugs containing vitamin D or its analogues is not recommended due to the increased likelihood of toxicity.

Isoniazid may reduce the effectiveness of vitamin D3 because it restricts the metabolic activation of vitamin D.

Patients treated with cardiac glycosides may be sensitive to high calcium levels and therefore ECG parameters and calcium levels of these patients should be monitored.

Drugs such as orlistat, colestipol and cholestramine, which may cause fat malabsorption, may reduce vitamin D absorption.

Corticosteroids (since corticosteroids may interfere with the activities of vitamin D, vitamin D preparations may be recommended by some physicians in long-term corticosteroid use)

Preparations containing high doses of phosphorus (since vitamin D increases phosphate absorption, concomitant use with vitamin D may increase the potential for hyperphosphataemia).

Vitamin C

Acetylsalicylic acid: With concomitant use, urinary excretion of ascorbic acid is increased and excretion of acetylsalicylic acid is decreased. Acetylsalicylic acid has been found to reduce ascorbic acid absorption by approximately 1/3.

Dicumarol: There is an exceptional case of shortening of prothrombin time after ascorbic acid ingestion.

Warfarin: Some cases have been reported in which ascorbic acid appeared to reduce the effects of warfarin.

Ethinylestradiol: Ascorbic acid at a dosage of 1 gram daily increases the bioavailability of ethinylestradiol from oral contraceptive preparations. Thus, low-dose contraceptives become similar in pharmaceutical and toxicological properties to higher-dose contraceptives. This effect is particularly important when ascorbic acid supplementation is discontinued, as the decrease in hormone absorption may lead to sudden bleeding and even impaired contraception.

Iron (oral): Ascorbic acid may increase iron absorption.

Desferrioxamine: Ascorbic acid may increase iron excretion when given concomitantly with desferrioxamine. However, cardiomyopathy and congestive heart failure have been observed in patients receiving concomitant treatment. This may be explained by increased iron accumulation in visceral organs as ascorbic acid mobilises iron from the spleen and other reticuloendothelial tissues.

Isoprenaline: The chronotropic effect of isoprenaline is reduced when given concomitantly with ascorbic acid.

Alcohol: Alcohol decreases blood levels of ascorbic acid.

Mexiletine: Renal excretion of mexiletine may be accelerated when high doses of ascorbic acid and mexiletine are administered simultaneously.

Barbiturates (Primidone): When given concomitantly with barbiturates (primidone), urinary excretion of ascorbic acid may increase.

Amphetamine and tricyclic antidepressants: Ascorbic acid decreased renal tubular reabsorption of amphetamines and tricyclic antidepressants.

Flufenazine and other phenothiazines: Ascorbic acid has been reported to reduce the therapeutic effect of phenothiazines. Flufenazine concentration may also be decreased.

Laboratory tests: Ascorbic acid interacts with laboratory tests involving oxidation and reduction reactions such as glucose oxidase test, copper sulphate test due to its reducing nature. Ascorbic acid interferes with the autoanalyser determination of serum transaminases and lactic dehydrogenase. It may also interfere with some tests for the determination of occult blood and serum theophylline levels.

Drugs that cause tissue desaturation of ascorbic acid include nicotine from smoking, some appetite suppressants, phenytoin, some anticonvulsant drugs and tetracyclines. High doses of ascorbic acid may lead to acidification of the urine, thus leading to unexpected renal tubular reabsorption of acidic drugs and an excessive response. On the other hand, basic drugs may show decreased reabsorption, resulting in a decrease in therapeutic effect.

Additional information for special populations:
There are no interaction studies.

Pediatric population:
There are no interaction studies**.**

4.6. Fertility, pregnancy and lactation
General advice:
Pregnancy category: C

In pregnancy, vitamin A, D and C intake in doses higher than the recommended daily dose should be avoided and should not be used without consulting a doctor.

Women of childbearing potential / Birth control (Contraception)
Data on women of childbearing potential and contraception are not available.

Pregnancy
Clinical information on the use of cholecalciferol in pregnancy is not available.

Ascorbic acid crosses the placenta. With the intake of high doses of ascorbic acid during pregnancy, the foetus may adapt to this and develop ascorbic acid deficiency in the form of postnatal withdrawal syndrome. Therefore, high doses of the drug (e.g. doses above 1 gram) should not be used in pregnant women or those likely to become pregnant unless the expected benefits outweigh the potential risk.

However, vitamin A may have a teratogenic effect when given to pregnant women above 5000 units per day.

There is insufficient data on the use of DESIFEROL PLUS in pregnant women.

Animal studies are insufficient for effects on pregnancy and/or embryonal/fetal development and/or natal and/or postnatal development (see section 5.3). The potential risk to humans is not known.

DESIFEROL PLUS should not be used during pregnancy unless necessary.

Breast-feeding
Only a small amount of vitamin D metabolites occur in human milk. Infants who are exclusively breastfed and have little contact with sunlight may require vitamin D supplementation.

The therapeutic index of vitamin D is very low in infants and children. If hypercalcaemia lasts for a long time, it causes mental and physical developmental retardation in infants as well as congenital heart and eye diseases. There is a risk of hypercalcaemia in infants of breastfeeding mothers who take more vitamin D than they need.

Ascorbic acid passes into breast milk. It is not known whether high doses have a harmful effect on the baby, but it is theoretically possible. It is therefore recommended that breastfeeding mothers should not exceed the maximum daily requirement unless the expected benefit outweighs the potential risk.

Reproduction ability/ Fertility
There are no known effects.

4.7 Effects on ability to drive and use of machines
There are no known effects.

4.8 Undesirable effects
Specified undesirable effects are classified as follows:
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); unknown (cannot be estimated based on the data available).

The incidence of undesirable effects is not known due to the lack of extensive clinical studies.

The possibility of side effects of DESIFEROL PLUS at normal doses and durations is low. The following undesirable effects may develop as a result of high doses of vitamin A, D3 and C and uncontrolled prolongation of the duration of treatment.

<u>Acute and chronic hypervitaminosis A</u>

Blood and lymphatic system disorders
Unknown: Nosebleeds, rarely hypoprothrombinemia

Psychiatric disorders
Unknown: Psychic disorders

Nervous system disorders
Unknown: Headache, dizziness, weakness, swelling of the fontanelles in infants (Maria-see syndrome), increased intracranial pressure in the form of benign intracranial hypertension called brain pseudotumour in adults, drowsiness, sleep disturbances, hyperirritability.

Eye disorders
Unknown: Papilla oedema, double vision

Gastrointestinal disorders
Unknown: Nausea, vomiting, loss of appetite

Hepato-biliary disorders
Unknown: Hepatomegaly and more rarely splenomegaly

Skin and subcutaneous tissue disorders
Unknown: Loss of epithelial tissues, itching, hair loss, dry skin, chapped lips

Musculoskeletal system, connective tissue and bone disorders
Unknown: Bone and joint pain, cortical hyperostosis in long bones, premature closure of epiphysis in children

Reproductive system and breast disorders
Very rare: Menstrual disorders

Vitamin D

Metabolism and nutritional disorders
Unknown: Hypercalciuria, hypercalcaemia and increased residual nitrogen in the blood.

Nervous system disorders
Unknown: Psychic symptoms, blurred consciousness

Cardiac disorders
Unknown: Arrhythmias

Gastrointestinal disorders
Unknown: Constipation, flatulence, nausea, abdominal pain, diarrhoea, anorexia, weight loss
Uncommon: Feeling of satiety

Skin and subcutaneous tissue disorders
Uncommon: Flushing
Very rare: Localised skin reactions
Rare: Hypersensitivity reactions such as itching, rash, urticaria

Kidney and urinary tract disorders
Unknown: Polyuria, polydipsia, anuria, kidney stone formation, nephrocalcinosis

General disorders and administration site conditions
Unknown: Fever

Vitamin C
Since excess vitamin C is excreted from the body, the potential for side effects is low. Undesirable effects due to Vitamin C observed during clinical trials are listed in order of frequency below.

Immune system disorders
Rare: Allergic reactions such as rash, itching, difficulty breathing, chest tightness, swelling of the mouth, face, lips and tongue

Nervous system disorders
Unknown: Headache, dizziness or drowsiness, fatigue, sleep disturbance

Gastrointestinal disorders
Unknown: Stomach cramps, diarrhoea, nausea or vomiting

Skin and subcutaneous tissue disorders
Unknown: Flushing or redness

Musculoskeletal system, connective tissue and bone disorders
Rare: Sensitivity, pain, fever or swelling in the extremities

Kidney and urinary tract disorders
Rare: Difficulty urinating
Unknown: Kidney stone formation, hyperoxaluria, diuresis

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 Turkish Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel.: 800 314 00 08; fax: 0 312 218 35 99).

4.9 Overdose and treatment
Symptoms
Dosage adjustment should be made in individuals receiving treatment with vitamins A and D, overdoses of which may cause hypervitaminosis.

Chronic toxicity with vitamin A may occur with intake of 1 million units of vitamin A for 3 days, 500,000 units daily for 2 months, 50,000 units daily for more than 18 months.

High doses of Vitamin C may cause gastrointestinal disorders, including diarrhoea. High doses may also cause hyperoxaluria and kidney stone formation if the urine is acidic. Daily doses of 600 mg or more have a diuretic effect. In case of overdose, treatment should be stopped and symptomatic treatment should be performed.
Acute and chronic overdose of vitamin D causes hypercalcaemia. Symptoms of hypercalcaemia include fatigue, psychiatric symptoms (euphoria, drowsiness, confusion), nausea, vomiting, loss of appetite, weight loss, thirst, early diarrhoea and later constipation, abdominal pain, headache,

muscle and joint pain, muscle weakness, polyuria, kidney stone formation, nephrocalcinosis, bone calcification and renal failure, soft tissue calcification, ECG changes, arrhythmia and pancreatitis.

Overdose in pregnancy
Vitamin D:
Massive doses during pregnancy have been related to the occurrence of aortic stenosis syndrome and idiopathic hypercalcaemia in newborns. Facial anomalies, physical and mental retardation, strabismus, enamel defects, craniosynostosis, super valvular aortic stenosis, pulmonary stenosis, inguinal hernia, cryptorchidism in boys and early development of secondary sex characteristics in girls have also been reported.

However, several cases of normal newborns born to mothers with hypoparathyroidism using high doses of vitamin D have been reported.

Vitamin A may have teratogenic effects when given to pregnant women at doses above 5000 units per day.

If high doses of ascorbic acid are ingested during pregnancy, the foetus may adapt and develop ascorbic acid deficiency in the form of postnatal withdrawal syndrome.

Treatment
There is no specific information on the treatment of vitamin A and C overdose.

In case of vitamin A and C overdose, treatment should be stopped and symptomatic and supportive treatment should be performed.

In case of intoxication caused by vitamin D analogues, vitamin D and calcium support is discontinued, low calcium diet is applied and i.v. fluid administration is performed.

Serum calcium concentrations are reduced by using calcuric diuretics (such as furosemide and ethacrynic acid) when necessary. Haemodialysis or peritoneal dialysis may also be used against calcium-free dialysate. If vitamin D has just been ingested, gastric lavage or vomiting may be used to prevent further absorption. Hypercalcaemia caused by chronic high doses of cholecalciferol may resolve in 2 months or more.
If massive doses have been taken, ventricular emptying with carbon administration should be considered. Sunlight and continued vitamin D administration should be avoided.
Rehydration and treatment with diuretics such as furosemide should be used to ensure adequate diuresis. In case of hypercalcaemia, bisphosphonates or calcitonin and corticosteroids may be given. Treatment is symptomatic.

5. PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin Combinations
ATC Code: A11JA

Cholecalciferol (Vitamin D3) increases serum phosphate and calcium concentrations, mainly through increasing their absorption. It allows calcium formation in bones. It increases reabsorption of calcium and phosphate through tubular cells, thus reduces the elimination of calcium and phosphate. Cholecalciferol ensures normalized calcium and phosphate levels along with parathyroid hormone.

Cholecalciferol also stimulates bone resorption and is essential for normal mineralisation of bone. In physiological doses, cholecalciferol also increases renal reabsorption of calcium. It inhibits parathyroid hormone (PTH) secretion indirectly through increased intestinal absorption of calcium. The normal daily requirement of the body is 400-800 IU.
These vitamins, which are also found together in nature, complement each other in terms of their functions on the metabolism of cells, especially the cells of the nervous system. It stabilises the development of rickets in children and osteomalacia in adults.

Vitamin A is responsible for growth and development of epithelial tissue. It regulates the immune system and plays a role in protecting the body from infections. It is important for the protection of mucous membranes against keratinisation, the growth and development of long bones and the function of the gonads.

Vitamin D3 has the strongest therapeutic effect in the prophylaxis and treatment of rickets. By participating in calcium and phosphorus metabolism, it ensures the storage of calcium in the bones and prevents decalcification.

Ascorbic acid, a water-soluble vitamin, is essential for the formation of collagen and intercellular material. It is therefore essential for the development of cartilage, bone, teeth and wound healing. It is also involved in the conversion of folic acid to folinic acid and facilitates the absorption of iron from the gastrointestinal tract. It is effective in haemoglobin formation and maturation of erythrocytes.

5.2 Pharmacokinetic properties
General characteristics
Absorption:
Cholecalciferol is well absorbed in gastrointestinal tract.
Vitamin A is absorbed from the gastrointestinal tract, especially from the duodenum and jejunum, in the presence of bile salts and pancreatic lipase, proteins and fats.
Ascorbic acid is absorbed predominantly in the upper part of the small intestine via a sodium-dependent active transport mechanism. When ascorbic acid is present in high concentrations, absorption is by passive diffusion.

Distribution:
Vitamin D and its metabolites in blood bind to a specific a-globulin. Vitamin D is stored in adipose tissues and muscles for a long time and slowly released from these storage sites. Cholecalciferol has a long-term activity despite a slow start. Half-life is 19 to 25 hours.
The binding rate of ascorbic acid to plasma proteins is approximately 24%. Serum concentrations are normally 10 mg/L (60 μmol/L). Concentrations below 6 mg/L (35 μmol/L) indicate that vitamin C intake is not always adequate. Concentrations below 4 mg/L (20 μmol/L) indicate inadequate vitamin C intake. In clinical ascorbic acid deficiency, serum concentrations are below 2 mg/L (10 μmol/L).

Biotransformation:
Vitamin A is metabolised in the liver and vitamin D in the kidney and liver.
In the liver, cholecalciferol is converted to its 25-hydroxy derivative by the enzyme 25-hydroxylase in the mitochondria. This metabolite is hydroxylated once more in the kidneys by vitamin D 1-a hydroxylase enzyme and becomes active. When the concentration of 1-25 hydroxylated metabolite reaches a sufficient level, it is converted to 24, 25 hydroxylated metabolite with minimal biological activity in the kidneys.

Ascorbic acid is partly metabolised to oxalic acid via dehydroascorbic acid. However, in excessive amounts, ascorbic acid is excreted largely unchanged in urine and faeces. Ascorbic-acid-2-sulphate is also found in the urine as a metabolite.

Elimination:
Vitamin D compounds and metabolites are excreted mainly in bile and faeces. Small amounts are excreted in the urine. The main metabolite excreted in urine is calcitroic acid.
Vitamin A is excreted in faeces and urine.
Excretion of ascorbic acid is related to its half-life, route of administration, amount administered and absorption rate.

Linearity/Non-linearity:
Pharmacokinetics are linear. Plasma levels increase depending on the doses given.

5.3. Preclinical safety data
Vitamin D3 overdose during pregnancy causes malformations in mice, rats and rabbits (skeletal disorders, microcephaly, cardiac malformations).

Animal studies are inadequate with regard to effects on pregnancy /and/or/ embryonal/fetal development /and/or/ perinatal /and/or/ postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Potassium sorbate
PEG 40 hydrogenated castor oil
Glycerin
Sucralose
Povidone K90
Sodium bicarbonate
Sodium chloride
Disodium EDTA
Orange flavour
Purified water

6.2. Incompatibilities
Not available.

6.3. Shelf life
24 months

6.4 Special precautions for storage
Store at room temperature below 25°C, tightly closed, and away from light.

6.5 Nature and contents of container
DESIFEROL is marketed in amber colored glass bottles (Type III) closed with pilfer-proof HDPE closure and LDPE dropper seal in a cardboard box..

DESIFEROL PLUS is available in bottles containing 20 ml, 30 ml and 45 ml solution.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with “Directive on Control of Medical Waste” and “Directive on the Control of Packaging and Packaging Waste”.

7. MARKETING AUTHORIZATION HOLDER

Berko İlaç ve Kimya Sanayi A.Ş.
Yenişehir Mah. Özgür Sok. No: 16-18 Ataşehir/İstanbul
0 216 456 65 70 (Pbx)
0 216 456 65 79 (Fax)
info@berko.com.tr

8. MARKETING AUTHORIZATION NUMBER(S)

2019/72

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION

Date of the first authorization: 08.02.2019
Date of the renewal of the authorization: -

10. DATE OF REVISION OF THE TEXT

02.06.2021