Approved Professional Information for Medicines for Human Use: SOSKAIN

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

SOSKAIN 50 000 IU soft gelatin capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SOSKAIN 50 000 IU soft gelatin capsule

Each soft gelatin capsule contains 1,25 mg cholecalciferol (equivalent to 50 000 IU vitamin D_3)

Contains sugar: sorbitol 16,5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

SOSKAIN 50 000 IU soft gelatin capsules

Yellow coloured, clear transparent round shaped gelatin capsule with a clear, colourless liquid fill.

Capsule dimensions: approximate length is 7,36 mm and approximate width is 6,27 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of vitamin D deficiency (serum 25-hydroxycalciferol (25(OH)D) < 25 nmol/L).

4.2 Posology and method of administration

Posology

One SOSKAIN capsule contains 50 000 IU vitamin D_3.

Adults

- Treatment of vitamin D deficiency (< 25 nmol/L) 50 000 IU/week (1 capsule) for 6 – 8 weeks, followed by maintenance therapy (such as 1 capsule per month; follow up 25(OH)D measurements should be made upon completion of the treatment phase and approximately three to four months after initiating the maintenance therapy in order to confirm that blood levels have normalised or the set target level, within the normal range, has been achieved).

Higher doses may be required in certain situations, see below.

Certain populations are at high risk of vitamin D deficiency, and may require higher doses and monitoring of serum 25(OH)D:

- Institutionalised or hospitalised individuals
- Individuals with Fitzpatrick IV and upwards skin type
- Individuals with limited effective sun exposure due to protective clothing or consistent use of sunscreens
- Obese individuals
- Patients being evaluated for osteoporosis
- Use of certain concomitant medications (e.g. anticonvulsant medications, glucocorticoids)
- Patients with malabsorption, including inflammatory bowel disease and coeliac disease
- Those recently treated for vitamin D deficiency and requiring maintenance therapy.

Special populations

Renal impairment

SOSKAIN should not be used in combination with calcium in patients with severe renal impairment.

Hepatic impairment

No posology adjustment is required in patients with hepatic impairment.

Pregnancy and breastfeeding

Due to insufficient clinical data, SOSKAIN is not recommended (see section 4.3 and section 4.6).

Paediatric population

Due to insufficient clinical data, SOSKAIN should not be used in children under the age of 18 years (see section 4.3).

Method of administration

SOSKAIN is developed as per oral administration.

The capsules should be swallowed whole with water.

Patients should be advised to take SOSKAIN preferably with a meal (see section 5.2)

4.3 Contraindications

- Hypersensitivity to cholecalciferol or to any of the excipients listed in section 6.1
- Hypercalcaemia and/or hypercalciuria
- Nephrolithiasis and/or nephrocalcinosis
- Severe renal impairment
- Hypervitaminosis D

- Pseudohypoparathyroidism as the vitamin D requirement may be reduced due to phases of normal vitamin D sensitivity, involving the risk of prolonged overdose. Better-regulatable vitamin D derivatives are available for this.
- Pregnancy
- Children and adolescents (under 18 years of age)

4.4 Special warnings and precautions for use

Impaired renal function

Vitamin D should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account.

Cardiovascular disease

Caution is required in patients receiving treatment for cardiovascular disease (see section 4.5).

Sarcoidosis

SOSKAIN should be prescribed with caution in patients with sarcoidosis, due to a possible increase in the metabolism of vitamin D in its active form. In these patients the serum and urinary calcium levels should be monitored.

Vitamin D supplementation

Prescribers should take in account the dose of vitamin D by unit dose (50 000 IU) and any other prescription of vitamin D. Allowances should be made for the total dose of vitamin D in cases associated with treatments already containing vitamin D, foods enriched with vitamin D, cases using milk enriched with vitamin D, and the patient's

level of sun exposure. Additional administration of vitamin D should be carried out under strict medical supervision.

Calcium supplements

There is no clear evidence for causation between vitamin D supplementation and renal stones, but the risk is plausible, especially in the context of concomitant calcium supplementation. The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.

Fractures

Oral administration of high-dose vitamin D (500 000 IU by single annual bolus) was reported to result in an increased risk of fractures in elderly subjects, with the greatest increase occurring during the first 3 months after dosing.

4.5 Interaction with other medicines and other forms of interaction

Anticonvulsants: i.e. phenytoin and barbiturates

Concomitant use of anticonvulsants (such as phenytoin) or barbiturates (and possibly other medicines that induce hepatic enzymes) may reduce the effect of vitamin D by metabolic inactivation.

Thiazide diuretics

In cases of treatment with thiazide diuretics, which decrease urinary elimination of calcium, monitoring of serum calcium concentration is recommended.

Glucocorticoids

Concomitant use of glucocorticoids can decrease the effect of vitamin D.

Cardiac glycosides

In cases of treatment with medicines containing digitalis and other cardiac glycosides, the administration of vitamin D may increase the risk of digitalis toxicity (dysrhythmia).

Serum calcium concentrations

Strict medical supervision is needed, together with serum calcium concentration and electrocardiographic monitoring if necessary.

Reduced bioavailability

Simultaneous treatment with ion exchange resin such as cholestyramine, colestipol hydrochloride, orlistat or laxative such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

Actinomycin and imidazole antifungal medicines

The cytotoxic medicine actinomycin and imidazole antifungal medicines interfere with vitamin D activity by inhibiting the conversion of the cholecalciferol metabolite, calcifediol (25-OHD_3), to the primary active metabolite calicitriol (1α,25-$(OH)_2D_3$) by the kidney enzyme, 25-OH-D_3-1-hydroxylase. See section 5.2.

4.6 Fertility, pregnancy and lactation

Pregnancy

SOSKAIN should not be used in pregnancy. See section 4.3.

Breastfeeding

SOSKAIN should not be taken by mothers who are breastfeeding.

Fertility

There is no data regarding treatment with vitamin D_3 and its effects on fertility.

4.7 Effects on ability to drive and use machines

There are no data on the effects of SOSKAIN on the ability to drive. However, an effect on this ability is unlikely.

4.8 Undesirable effects

The table below shows all Adverse Drug Reactions (ADRs) observed as per reported clinical trials and post-market spontaneous reports with cholecalciferol.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Metabolism and nutrition disorders		Hypercalcaemia and hypercalciuria	
Skin and subcutaneous tissue disorders		Pruritus, rash, and urticaria.	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms

Ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) have a relatively low therapeutic index. The threshold for vitamin D intoxication is between 40 000 and 100 000 IU daily for 1 to 2 months in adults with normal parathyroid function. Infants and small children may react sensitively to far lower concentrations. Therefore, it is warned against intake of SOSKAIN without medical supervision.

Overdose leads to increased serum and urinary phosphorus levels, as well as hypercalcaemic syndrome and consequently calcium deposits in the tissues and above all in the kidneys (nephrolithiasis, nephrocalcinosis) and the vessels.

Discontinue SOSKAIN when calcaemia exceeds 10,6 mg/dL (2,65 mmol/L) or if the calciuria exceeds 300 mg/24 hours in adults or 4 – 6 mg/kg/day in children.

Chronic overdosage may lead to vascular and organ calcification, as a result of hypercalcaemia.

The symptoms of intoxication are characteristic and manifest as nausea, vomiting, initially also diarrhoea, later constipation, loss of appetite, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, ataxia, confusion, uraemia, polydipsia and polyuria and, in the final stage, dehydration. Typical biochemical findings include hypercalcaemia, hypercalciuria, as well as increased serum 25 hydroxy cholecalciferol concentrations.

Treatment

Symptoms of chronic SOSKAIN overdosage may require forced diuresis as well as administration of glucocorticoids or calcitonin.

Overdosage requires measures for treating the often persisting and under certain circumstances life-threatening hypercalcaemia.

The first measure is to discontinue taking SOSKAIN, it takes several weeks to normalise hypercalcaemia caused by vitamin D intoxication.

Depending on the degree of hypercalcaemia, measures include a diet that is low in calcium or free of calcium, abundant liquid intake, increase of urinary excretion by means of the medicine furosemide, as well as the administration of glucocorticoids and calcitonin.

If kidney function is adequate, calcium levels can be reliably lowered by infusions of isotonic sodium chloride solution (3 - 6 litres in 24 hours) with addition of furosemide and, in some circumstances, also 15 mg/kg body weight/hour sodium edetate accompanied by continuous calcium and ECG monitoring. In oligoanuria, in contrast, haemodialysis (calcium-free dialysate) is necessary.

No special antidote exists.

It is recommended to point out the symptoms of potential overdose to patients under chronic therapy with higher doses of vitamin D (nausea, vomiting, initially also diarrhoea, later constipation, anorexia, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, azotaemia, polydipsia and polyuria).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 22.2 Vitamins – Others

Pharmacotherapeutic group: Vitamin D and analogues, cholecalciferol

ATC Code: A11CC05

In its biologically active form vitamin D_3 stimulates intestinal calcium absorption, incorporation of calcium into the osteoid, and release of calcium from bone tissue. In the small intestine it promotes rapid and delayed calcium uptake. The passive and active transport of phosphate is also stimulated. In the kidney, it inhibits the excretion of calcium and phosphate by promoting tubular resorption. The production of parathyroid hormone (PTH) in the parathyroids is inhibited directly by the biologically active form of vitamin D_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D_3.

5.2 Pharmacokinetic properties

The pharmacokinetics of vitamin D_3 is well known.

Absorption

Vitamin D_3 is well absorbed from the gastro-intestinal tract in the presence of bile, so the administration with the major meal of the day might therefore facilitate the absorption of vitamin D_3.

Distribution and biotransformation

Cholecaliciferol is hydroxylated in the liver by vitamin D 25-hydroxylase to form 25-hydroxy-cholecalciferol (calcifediol). Calcifediol undergoes further hydroxylation in the kidney by vitamin D 1-hydroxylase to form the active metabolite 1,25-dihydroxy-cholecalciferol (calcitriol). Additional further hydroxylation occurs prior to elimination.

Vitamin D_3 and metabolites circulate in the blood bound to a specific α – globin. Vitamin D_3 can be stored- and subsequently be released from adipose and muscle tissue.

Elimination

Vitamin D_3 and its metabolites are excreted mainly in the bile and faeces, with small amounts excreted in the urine.

Characteristics in specific groups of subjects or patients

Hepatic or biliary dysfunction may impair vitamin D absorption. Patients who have had intestinal bypass surgery or otherwise have severe shortening or inflammation of the small intestine may fail to absorb vitamin D sufficiently to maintain normal levels.
A reduced metabolic clearance rate is reported in subjects with renal impairment as compared with that of healthy volunteers.
Decreased absorption and increased elimination of vitamin D occurs in subjects with malabsorption.
Obese subjects are less able to maintain vitamin D levels with sun exposure and are likely to require larger oral doses of vitamin D to replace deficits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Vitamin E acetate (α-tocopheryl acetate)

Medium chain triglycerides (MCT)

Capsule shell

Gelatin (E441)

Glycerol (E422)

Sorbitol liquid, partially dehydrated

Quinoline yellow (E104)

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 30 °C.

Store in the original packaging until required for use.

6.5 Nature and contents of container

White PVC / PVDC aluminium blister strip packages of 10,12, 50 or 100 tablets packed in an outer carton (10 or 12 capsules per blister strip).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBER

To be allocated by the Authority upon registration.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated by the Authority upon authorisation.

10. DATE OF REVISION OF THE TEXT

To be allocated by the Authority