



DESCRIPTION:
Strontum ranelate is made up of 2 atoms of stable strontium and 1 molecule of ranelic acid, the organic part permitting the best compromise in terms of molecular weight, pharmacokinetics an acceptability of the medicinal product.

QUALITATIVE AND QUANTITITIVE COMPOSITION:

SIGTRO granular powder for oral suspensi SIGTRO Sachet 2g Each sachet contains Strontium Ranelate.....2g (Product Specs.: Sigma)

CLINICAL PHARMACOLOGY:

MECHANISM OF ACTION:

MELHANISM Or AL IDUS.
SIGTRO is an antiosteoporotic agent which both increases bone formation and reduces bone resorption, resulting in a rebalance of bone turnover in favor of bone formation by:

-Increases bone formation in bone tissue culture as well as osteoblast precursor replication and collagen synthesis in bone cell culture.

-Reduces bone resorption by decreasing osteoclast differentiation and resorbing activity.

PHARMACOKINETICS:

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Absorption:
Absorption:
Alter oral administration absolute bioavailability of strontium is about 25%. Maximum plasma Concentrations are reached 35 hours. Steady state is reached after 2 weeks of treatment. Intake of strontium ranelate with calcium or food reduces the bioavailability of strontium by approximat-4-6y 60-70%, compared with administration 3 hours after a meal. Due to the relatively slow absorption of strontium, food and calcium intake should be avoided both before and after administration of SIGTRO. Oral supplementation with vitamin D has no effect on strontium exposure.

Strontium has a volume of distribution of about 1L/kg. The binding of strontium to human plasma proteins is low (25%) and strontium has a high affinity for bone tissue.

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Metabolism:
As a divalent cation, strontium is not metabolized. Strontium ranelate does not inhibit cytochrome P450 enzymes.

Elimination:
Billiamiation:
Strontium is time and dose independent. The effective half-life of strontium is about 60 hours. Strontium excretion occurs via the kidneys and the gastrointestinal tract.
Special Populations:
Renal Impairment:
In patients with midt-to-moderate renal impairment (30-70 ml/min creatinine clearance), strontium clearance decreases and increases strontium plasma levels. No dosage adjustment is required in patients with mild-to-moderate renal impairment. There is no pharmacokinetic data in patients with severe renal impairment (creatinine clearance below 30 ml/min).

THERAPEUTIC INDICATIONS:
SIGTRO is indicated for the treatment of postmenopausal osteoporosis to reduce the risk of vertebral and hij fractures.

DOSAGE & ADMINISTRATION:

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The recommended dose is one 2 g sachet once daily by oral administration.
Method of Administration:
Food, milk and milk products reduce the absorption of strontium ranelate. It is recommended that you take SIGTRO only with water in-between meals, preferably at bedtime at least two hours after food, milk or milk products or calcium supplements.
Directions for Perparing Oral Suppension of Suppens

- Drink immediately, If for some reason, you do not drink the medicine immediately, make sure you stir it again before drinking. Use within 24 hours after preparation.
 Patients treated with strontium ranelae should receive vitamin D and calcium supplements if dietary intake is inadequate. Do not take calcium supplements at bedtime, at the same time as

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Special Populations:
Renal Impairment:
Strontium ranelate is not recommended for patients with severe renal impairment (creatinine clearance below 30 ml/min).
CONTRAINDICATIONS:
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Children and adolescents aged below 18 years. Renal Impairment:
Periodic assessment of renal function is recommended in patients with chronic renal impairment.
Continuation of treatment with SIGTRO in patients developing severe renal impairment should be considered on an individual basis.

Venous Thromboembolism:

Strontium ranelate should be used with caution in patients at increased risk of venous thromboembolic events (VTE), including patients with a past history of VTE.

Cardiac Ischaemic Events:

Patients with significant risk factors for cardiovascular events (e.g., hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with strontium ranelate after careful consideration and continue monitoring is recommended. Treatment should be stopped if the patient develops ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or if hypertension is uncontrolled. Skin Reactions:

Skin Reactions:

Cardiac disease or if hypertension is uncontrolled. Skin reactions cutaneous reactions (Stevens-Johnson syndrome, track epidermal necrolysis and drug rash with ensiphilia and systemic symptoms (DRESS)) have been reported with the use of strontium ranelate. Patients should be advised of the signs and symptoms of skin reactions and monitored closely for skin reactions. If signs and symptoms appear discontinued treatment with SIGTRO.

SIGTRO

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Interaction with Laboratory Test:
Strontium interferes with colorimetric methods for the determination of blood and urinary calcium concentrations. Alternate method used for testing.
SIGTRO contains aspartame, which may be harmful for people with phenylketonuria.

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Strontium ranelate is only intended for use in postmenopausal woman, no clinical data on exposed pregnancies are available for strontium ranelate if strontium ranelate is used Lactation:
SIGTRO should not be given to russing woman.
DRUG INTERACTIONES:
The administration of aluminum and magnesium hydroxides either two hours before or together with SIGTRO causes a slight decrease in the absorption of SIGTRO. It is together with SIGTRO causes a slight decrease in the absorption of SIGTRO. It is down the significant of the significant content of

Antibiotics:
Simultaneous administration of SIGTRO with oral tetracycline and quinolone is not recommended as these drugs may reduce absorption of SIGTRO. As a precautionary measure, SIGTRO treatment should be suspended during treatment with oral tetracycline control of SIGTRO.

or quinolone antibiotics.
ADVERSE REACTIONS:
Adverse events with SIGTRO are usually mild and transient. The most common adverse
events consisted of nausea and diarrhea, which are generally reported at the beginning of
treatment. Discontinuation of therapy is mainly due to nausea.

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Nervous System Disorders:
Common: headache.
Gastrointestiand Disorders:
Common: nausea, diarrhea, loose stools.
Skin and Subuctaneous Tissue Disorders:
Common: dermaitits, ezema.
OVERDOSAGE:
Administration of milk or antacids may be helpful to reduce the absorption of the active substance, in the event of substantial overdose, vomitting may be considered to remove unabsorbed active substance.

INSTRUCTIONS:

- Store below 30°C.
- Protect from light & moisture.
- Keep out of reach of children.
To be sold on prescription of a registered medical practitioner.

HOW SUPPLIED: SIGTRO 2g sachet is available in packs of 7's.

خداك: دُاكْرُى بدا - كه ملايق استعال كرير. وں نے وہ ہر کہا ہے۔ سے میں میں دی۔ ہا۔ وہ الوسالا کی اسٹی کی ہے کہ دید توارات رکھی۔ روشی اور کی سے کالی کی سے دور میں۔ صرف روز و اکثر کے تعمال آرو ' سریں۔

