DENSATE TABLETS
P1532291

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NOVAGEN
PHARMA

SKEDULERINGSTATUS

S3

EIENDOMSNAAM (en doseervorm)

DENSATE 70 mg (Tablet)

SAMESTELLING

DENSATE 70 mg:

Elke onbedekte tablet bevat natriumalendronaat gelykstaande aan 70 mg alendroniensuur.
Suikervry.

Die ander bestanddele is mikrokristallyne sellulose, magnesiumstearaat, mieliestysel, povidoon en natriumstyselglikolaat.

FARMAKOLOGIESE KLASSIFIKASIE

A.3.2. Bindweefselmiddels, Hormoonvry preparate.

FARMAKOLOGIESE WERKING

Bisfosfonate is sintetiese analoë van pirofosfaat wat bind aan die hidroksieapatiet wat in been voorkom. Natriumalendronaat is 'n aminobisfosfonaat watwerk as 'n spesifieke inhibeerdervan osteoklastbemiddelde beenresorpsie.

Alendronaat lokaliseer by voorkeur by areas van beenresorpsie, spesifiek onder osteoklaste, en inhibeer osteoklastiese beenresorpsie met geen regstreekse uitwerking op beenvorming nie. Gedurende blootstelling aan alendronaat, word normale been gevorm wat alendronaat by sy matriks inkorporeer, waar dit farmakologies onaktief is.

Farmakokinetika:

Absorpsie

Die gemiddelde biobeskikbaarheid van alendronaat in vroue is 0,57 % vir die 70 mg tablet, as dit na 'n oornagse vasting en twee ure voor 'n standaardontbyt toegedienword.

Biobeskikbaarheid na orale toediening in mans (0,6 %) is soortgelykas dié in vroue.

Biobeskikbaarheid neem met 40 % af indien alendronaat hetsy 30 minute of een uurvoor ontbyt toegedien word, in vergelyking met die tablette wat twee ure voordie inname van voedsel geneem word.

Biobeskikbaarheid is gering waar alendronaat tesame met of tot twee ure ná'n standaard ontbyt geneem word.

Waar alendronaat saam met koffie of sitrussap geneem word, verminderdie biobeskikbaarheid met 60 %.

Verspreiding

Alendronaat word tydelik na sagte weefsel versprei en dan vinnig herversprei na been of in die urien uitgeskei. Die volume van verspreiding is minstens 28 ℓ in mense.

Proteïenbinding

Ongeveer 78 % in menslike plasma.

Uitskeiding

Na 'n enkele intraveneuse dosis van 10 mg alendronaat, was die renale opruiming 71 ml per minuut. Binne 6 uur het die plasma-konsentrasie met meer as 95 % gedaal. Daar word beraam dat die terminale halfleeftyd in mense 10 jaar oorskry, wat vrystelling van alendronaat uit die skelet weerspieël.

Daar bestaan geen bewyse dat alendronaat in mense gemetaboliseer word nie.

INDIKASIES

DENSATE 70 mg is aangedui

- in vroue vir die behandeling van post-menopousale osteoporose om die risiko van frakture te verminder, insluitend heup- en ruggraatfrakture (vertebrale kompressiefrakture).
- vir die behandeling van primêre/idiopatiese osteoporose in mans en om die risiko van vertebrale frakture verwant aan primêre/idiopatiese osteoporose te verminder.

KONTRA-INDIKASIES

Hipersensitiwiteit vir alendronaat of enige ander komponente van die formule.

Erge belemmering van nierfunksie met kreatinien-opruiming van minder as 35 ml/minuut.

Abnormaliteite van die esofagus wat esofageale lediging vertraag, soos vernouing of achalasie.

Die onvermoë om vir 30 minute na inname van die medikasie regop te sit of te staan.

Pediatriese ouderdomsgroep: Veiligheid en doeltreffendheid is nie vasgestel nie.

Swangerskap en borsvoeding.

Hipokalsemie (sien **"WAARSKUWINGS"** en **"Spesiale Voorsorgmaatreëls"**)

WAARSKUWINGS

'n Tandheelkundige ondersoek met gepaste voorkomende tandheelkunde moet voor behandeling met bisfosfonate, insluitend **DENSATE 70 mg ,** oorweeg word in pasiënte met gepaardgaande risiko-faktore (bv. kanker, chemoterapie, kortikosteroïede, swak mondhigiëne).

Tydens die behandeling moet hierdie pasiënte indringende tandheelkundige prosedures vermy indien moontlik.

In pasiënte wat osteonekrose van die kakebeen ontwikkel terwyl hulle op terapie met **DENSATE 70 mg** is, kan tandheelkundige chirurgie die toestand vererger. In pasiënte wat tandheelkundige prosedures benodig, is daar geen data beskikbaar wat bevestig of staking van behandeling met **DENSATE 70 mg** die risiko van osteonekrose van die kakebeen verminder nie. Die kliniese oordeel van die dokter moet die bestuursplan van elke pasiënt rig, gebaseer op individuele voordeel/risiko-evaluering.

Die risiko-faktor moet oorweeg word waar gastroïntestinale probleme soos duodenitis, disfagie, gastritis, ulkusse of simptomatiese esofageale siektes aanwesig is.

Aangesien **DENSATE 70 mg** hipokalsemie en vitamien D-tekort kan vererger, moet hierdie toestande reggestel word voordat **DENSATE 70 mg** toegedien word.

Die risiko teenoor voordeel moet oorweeg word in pasiënte wat aan boonste gastroïntestinale siektes ly, soos disfagie, duodenitis, gastritis, ulkusse of simptomatiese esofageale toestande, weens die moontlik irriterende uitwerking van **DENSATE 70 mg** op die boonste gastroïntestinale mukosa en 'npotensiaal vir verergering van die onderliggende siekte.

Esofageale newe-effekte, soos esofagitis, esofageale ulkusse en esofageale erosies, in seldsame gevalle gevolg deur esofageale vernouing, is al aangemeld in pasiënte wat behandeling met **DENSATE 70 mg** ontvang. In party gevalle was hierdie toestande ernstig en het hospitalisasie vereis. Dokters moet dus bedag wees op enige tekens of simptome wat dalk op 'n moontlike esofageale reaksie kan dui, en pasiënte moet opdrag kry om **DENSATE 70 mg** te staak en mediese aandag te kry indien hul disfagie, odinofagie, retrosternale pyn of nuwe of verergerende sooibrand ontwikkel.

Die risiko van erge esofageale newe-effekte is klaarblyklik hoër in pasiënte wat gaan lê nadat hulle **DENSATE 70 mg** geneem het en/of wat versuim om dit met 'nvol glas waterte sluk, en/of wat voortgaan om **DENSATE 70 mg** te neem nadat hulle simptome ontwikkel hetwat op esofageale irritasie dui. Daarom is dit baie belangrik dat die volle doseringsinstruksies aan die pasiënt voorsien en deur die pasiënt verstaan word (sien "**DOSERING EN GEBRUIKSAANWYSINGS**").

INTERAKSIES

'n Toenemende voorkoms van boonste gastroïntestinale newe-effekte kan intree in pasiënte wat **DENSATE 70 mg** tesame met NSAIM's neem.

Bykomende hipokalsemiese effekte met aminoglikosiede kan voorkom.

Middels soos kalsiumaanvullings, osmotiese lakseermiddels, teensuurmiddels, voedsel en drinkgoed sal met die absorpsie van **DENSATE 70 mg** inmeng. Pasiënte word aangeraai om minstens 30 minute te wag nadat **DENSATE 70 mg** geneem is voordat enige ander medikasie of voedsel geneem word.

Geen newe-effekte te wyte aan die gelyktydige gebruik van alendronaat en estrogeen (intravaginaal, transdermaal of oraal) is in post-menopousale vroue geïdentifiseer nie.

SWANGERSKAP EN BORSVOEDING

Die veiligheid van **OENSATE 70 mg** tydens swangerskap of borsvoeding is nie bepaal nie.

DOSERING EN GEBRUIKSAANWYSINGS

Behandeling van post-menopousale osteoporose:

Die aanbevole dosis is een tablet van 70 mg een maal per week.

Behandeling van primêre/idiopatiese osteoporose in mans:

Die aanbevole dosering is een tablet van 70 mg een maal per week.

DENSATE 70 mg moet minstens 'n halfuur voor die eerste voedsel, drinkgoed of medikasie van die dag geneem word, en moet slegs met gewone water gesluk word. Ander drinkgoed (insluitend mineraalwater), voedsel en party medikasies sal waarskynlik die absorpsie van **DENSATE 70 mg** verminder (sien "**INTERAKSIES**").

Pasiënte behoort kalsium- en vitamien D-aanvullings te neem indien hulle dieetinname onvoldoende is (sien "**Spesiale Voorsorgmaatreëls**"). Dit moet minstens 30 minute ná die gebruikvan **DENSATE 70 mg** geneem word.

Pasiënte moet aangeraai word om vir 30 minute nadat **DENSATE 70 mg** tablette geneem is in 'nregop posisie te bly.

Om lewering aan die maag te vergemaklik en dus die potensiaal vir esofageale irritasie te verminder, moet **DENSATE 70 mg** slegs soggens na opstaantyd saam met 'n vol glas water afgesluk word en pasiënte moet vir minstens 30 minute daarna en tot na die eerste voedsel van die dag nie gaan lê nie. **DENSATE 70 mg** moet nie teen slaaptyd of soggens voor opstaantyd geneem word nie. Versuim om hierdie instruksies te volg, kan die risiko vir esofageale newe-effekte verhoog (sien "**Spesiale Voorsorgmaatreëls**").

Geen dosisaanpassing vir bejaardes of vir pasiënte met ligte tot matige renale ontoereikendheid is nodig nie (kreatinienopruiming 30 tot 80 ml/min) (sien "**KONTRA-INOIKASIES**").

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS

Newe-effekte:

Die volgende newe-effekte is met die gebruikvan **DENSATE 70 mg** aangemeld:

Hepatobiliêre versteurings

Minder dikwels: Verhoogte lewerensieme, hepatitis, hepatosellulêre skade.

Bloed- en limfstelselversteurings

Minder dikwels: Anemie, leukopenie, trombositopenie

Renale en urinêre versteurings

Minder dikwels: nierversaking

Kardiale versteurings

Minder dikwels: Artriale fibrillasie

Neoplasmas, goedaardig of kwaadaardig (insluitend siste en poliepe)

Minder dikwels: Esofageale kanker

Metabolisme- en voedingsversteurings:

Minder dikwels: Simptomatiese hipokalsemie, gewoonlik verbonde aan vooraf geneigde toestande (sien "**Spesiale Voorsorgmaatreëls**"), hipofosfatemie

Senuweestelselversteurings:

Dikwels: Hoofpyn

Oogversteurings:

Minder dikwels: Uveïtis, skleritis

Gastroïntestinale versteurings:

Dikwels: Abdominale pyn, dispepsie, esofageale ulkus, disfagie, opgeblase buik, esofagitis, esofageale erosies, naarheid, braking, hardlywigheid, diarree, winderigheid, suurregurgitasie en melena.

Minder dikwels: Esofageale vernouing, orofaringeale ulserasie, gastritis, gastriese en duodenale ulkusse, soms ernstig en gekompliseerd, esofageale perforasies.

(Sien "**Spesiale Voorsorgmaatreëls**" en "**DOSERING EN GEBRUIKSAANWYSINGS**").

Versteurings van die vel en subkutane weefsel:

Minder dikwels: Uitslag (by geleentheid met fotosensitiwiteit), eriteem en pruritus, erge velreaksies, insluitend Stevens-Johnson-sindroom en toksiese epidermale nekrolise

Muskuloskeletale, bindweefsel- en beenversteurings:

Dikwels: Muskuloskeletale (been-, spier- en gewrigs-) pyn, mialgie.

Minder dikwels: Osteonekrose van die kakebeen (sien **"WAARSKUWINGS"**), sinovitis

Immuunstelselversteurings:

Minder dikwels: Hipersensitiwiteitsreaksies, insluitend urtikaria en angioedeem

Algemene versteurings en toestande by die plekvan toediening:

Minder dikwels: Ongesteldheid, koors

Spesiale Voorsorgmaatreëls:

Om distribusie na die maag te vergemaklik en dus die potensiaal vir esofageale irritasie te verminder, moet pasiënte aangeraai word om **DENSATE 70 mg** met 'n vol glas waterte sluken om vir minstens 30 minute daarna en tot na ontbyt nie te gaan lê nie.

Pasiënte moet nie die tablet kou of suig nie, weens die potensiaal vir orofaringeale ulserasie. Pasiënte moet aangeraai word om nie **DENSATE 70 mg** teen slapenstyd of voor opstaantyd te neem nie. Pasiënte moet ingelig word dat versuim om hierdie instruksies te volg hulle risiko vir die ontwikkeling van esofageale probleme kan verhoog. Pasiënte moet opdrag kry om **DENSATE 70 mg** te staak en hulle dokter te raadpleeg indien hulle simptome van esofageale siekte (soos pyn of moeilike sluk, retrosternale pyn, of die begin van of verergerende sooibrand) ontwikkel.

Oorsakevan osteoporose benewens estrogeengebrek, veroudering en gebruik van glukokortikoïede moet in ag geneem word.

Weens die positiewe uitwerking van **DENSATE 70 mg** op die toename in beenmineraal, kan klein asimptomatiese afnames in serumkalsium en -fosfaatvoorkom, veral in pasiënte wat glukokortikoïede ontvang, in wie die kalsiumabsorpsie kan afneem.

In pasiënte wat glukokortikoïede ontvang, is dit veral belangrik om te verseker dat genoegsame kalsium en vitamien D ingeneem word.

Gebruik in bejaardes:

Daar is geen ouderdomverwante verskille in die doeltreffendheid- of veiligheidsprofiele van **DENSATE 70 mg** nie.

Pasiënte moet aangeraai word dat as hulle 'n dosis van **DENSATE 70 mg** oorslaan, hulle een tablet moet neem in die oggend sodra hul onthou. Hulle moet nie twee tablette op dieselfde dag neem nie, maar moet terugkeer na die gebruik van een tablet een maal 'n week op hulle gekose dag, soos oorspronklikgeskeduleer.

Vermoë om te bestuur en met masjinerie te werk:

Daar is geen data wat daarop dui dat **DENSATE 70 mg** dievermoë om motorte bestuur of masjinerie te gebruik, aantas nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONOERHEDE VAN DIE BEHANDELING DAARVAN

Hipokalsemie, hipofosfatemie en boonste gastroïntestinale newe-effekte, soos omgekrapte maag, sooibrand, esofag tis gastritis of ulkus kan weens orale oordosering intree. Die toediening van melk of teensuurmiddels kan voordelig wees.

Weens die risiko van esofageale irritasie moet braking nie geïnduseerword nie. Hou die pasiënt in 'n regop posisie.

IDENTIFIKASIE

DENSATE 70 mg: Wit tot naaswit, ovaalvorminge, bikonvekse, onbedekte tablette, met 'F' aan die een kant en '21 aan d ander kant gebosseleer.

AANBIEDING

OENSATE 70 mg:

Tablette word verpak in gedrukte aluminiumfoelie met hitte-verseëlde lak en deursigtige PVC gelamineer met aklar of driedubbele gelamineerde aluminiumfoelie en PVC/PE/PVdC film strokie. Elke strokie bevat 4 tablette

Pakkiegrootte: 4's – Elke kartondosie bevat 1 strokie van 4 tablette.

BERGINGSINSTRUKSIES

Berg op 'n droë plek by of benede 25 °C. Moenie die strokies uit die kartondosie verwyder totdat dit vir gebruik vereis word nie. Hou oorspronklike houers dig toe.

HOU BUITE DIE BEREIKVAN KINDERS.

REGISTRASIENOMMER

45/3.2/0581

NAAM EN BESIGHEIDSAORES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

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DATUM VAN PUBLIKASIE VAN DIE PAKKIEVOUBILJET

01 Maart 2013

NOVAGEN
PHARMA

SCHEDULING STATUS

S3

PROPRIETARY NAME (and dosage form)

DENSATE 70 mg (Tablet)

COMPOSITION

DENSATE 70 mg:

Each uncoated tablet contains sodium alendronate equivalent to alendronic acid 70 mg.

Sugar free.

The other ingredients are cellulose microcrystalline, magnesium stearate, maize starch, povidone and sodium starch glycolate.

PHARMACOLOGICAL CLASSIFICATION

A.3.2. Connective tissue medicines, non-hormonal preparations.

PHARMACOLOGICAL ACTION

Bisphosphonates are synthetic analogues of pyrophosphate that bind to the hydroxyapatite found in bone. Alendronate sodium is an aminobisphosphonate that acts as a specific inhibitor of osteoclast–mediated bone resorption.

Alendronate localises preferentially at sites of bone resorption, specifically under osteoclasts, and inhibits osteoclastic bone resorption with no direct effect on bone formation. During exposure to alendronate, normal bone is formed that incorporates alendronate into its matrix where it is pharmacologically inactive.

Pharmacokinetics:

Absorption

The mean oral bioavailability of alendronate in women is 0,57 % for the 70 mg tablet when administered after an overnight fast and two hours before a standardised breakfast.

Bioavailability after oral administration in men (0,6 %) is very similar to that in women.

Bioavailability is decreased by 40 % when alendronate is given either 30 minutes or one hour before breakfast, when compared to taking the tablets two hours before eating.

Bioavailability is negligible whether alendronate is administered with or up to two hours after a standardised breakfast.
When alendronate is taken with coffee or citrus juice, bioavailability is reduced by 60 %.

Distribution

Alendronate is transiently distributed to soft tissue and then rapidly redistributed to bone or excreted in the urine. The volume of distribution is at least 28 ℓ in humans.

Protein binding

Approximately 78 % in human plasma.

Elimination

Following a single intravenous dose of 10 mg alendronate, the renal clearance was 71 ml per minute. Within 6 hours the plasma concentrations fell by more than 95 %. The terminal half-life in humans is estimated to exceed 10 years, reflecting release of alendronate from the skeleton.
There is no evidence that alendronate is metabolised in humans.

INDICATIONS

DENSATE 70 mg is indicated

- in women for the treatment of postmenopausal osteoporosis to reduce the risk of fractures, including those of the hip and spine (vertebral compression fractures).
- for the treatment of primary/idiopathic osteoporosis in men and to reduce the risk of vertebral fractures associated with primary/idiopathic osteoporosis.

CONTRA-INDICATIONS

Hypersensitivity to alendronate or any other components of the formulation.

Severe renal function impairment when creatinine clearance is less than 35 ml/minute.

Abnormalities of the oesophagus which delay oesophageal emptying such as stricture or achalasia.

The inability to stand or sit upright for 30 minutes after taking the medicine.

Paediatric age group: Safety and efficacy have not been established.

Pregnancy and lactation.

Hypocalcaemia (see **"WARNINGS"** and **"Special Precautions"**)

WARNINGS

A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates, including **DENSATE 70 mg**, in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene).

While on treatment, these patients should avoid invasive dental procedures if possible.

For patients who develop osteonecrosis of the jaw while on **DENSATE 70 mg** therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of **DENSATE 70 mg** treatment reduces the risk of osteonecrosis of the jaw. Clinical judgement of the treating doctor should guide the management plan of each patient based on individual benefit/risk assessment.

The risk factor should be considered when gastrointestinal problems such as duodenitis, dysphagia, gastritis, ulcers or symptomatic oesophageal diseases are present.

As **DENSATE 70 mg** may exacerbate hypocalcaemia or vitamin D deficiency, these conditions should be corrected before **DENSATE 70** mg is administered.

The risk benefit should be considered in patients suffering from upper gastrointestinal diseases, such as dysphagia, duodenitis, gastritis, ulcers or symptomatic oesophageal conditions, because of possible irritant effects of **DENSATE 70 mg** on the upper gastrointestinal mucosa and a potential for worsening of the underlying disease.

Oesophageal adverse experiences, such as oesophagitis, oesophageal ulcers and oesophageal erosions, infrequently followed by oesophageal stricture, have been reported in patients receiving treatment with **DENSATE 70 mg**. In some cases these have been severe and required hospitalisation. Doctors should therefore be alert to any signs or symptoms signaling a possible oesophageal reaction and patients should be instructed to discontinue **DENSATE 70 mg** and seek medical attention if they develop dysphagia, odynophagia, retrosternal pain or new or worsening heartburn.

The risk of severe oesophageal adverse experiences appears to be greater in patients who lie down after taking **DENSATE 70 mg** and/or who fail to swallow it with a full glass of water, and/or who continue to take **DENSATE 70 mg** after developing symptoms suggestive of oesophageal irritation. Therefore, it is very important that the full dosing instructions are provided to, and understood by the patient (see "**DOSAGE AND DIRECTIONS FOR USE**").

INTERACTIONS

An increased incidence of upper gastrointestinal adverse events may occur in patients taking **DENSATE 70 mg** concomitantly with NSAIDs.

There may be additive hypocalcaemic effects with aminoglycosides.

Substances such as calcium supplements, osmotic laxatives, antacids, food and beverages will interfere with the absorption of **DENSATE 70 mg**. Patients are advised to wait at least 30 minutes after taking **DENSATE 70 mg** before taking any other medication, or food.

No adverse experiences attributable to the concomitant use of alendronate and oestrogen (intravaginal, transdermal, or oral) in postmenopausal women have been identified.

PREGNANCY AND LACTATION

The safety of **DENSATE 70 mg** has not been established in pregnancy or lactation.

DOSAGE AND DIRECTIONS FOR USE

Treatment of postmenopausal osteoporosis:
The recommended dosage is one 70 mg tablet once weekly.

Treatment of primary/idiopathic osteoporosis in men:
The recommended dosage is one 70 mg tablet once weekly.

DENSATE 70 mg must be taken at least half an hour before the first food, beverage, or medication of the day with plain water only. Other beverages (including mineral water), food, and some medications are likely to reduce the absorption of **DENSATE 70 mg** (see "**INTERACTIONS**").

Patients should take calcium and vitamin D supplements if their dietary intake is inadequate (see "**Special Precautions**"). These should be taken at least 30 minutes after taking **DENSATE 70 mg**.

Patients should be advised to remain in an upright position for 30 minutes after taking **DENSATE 70 mg** tablets.

To facilitate delivery to the stomach and thus reduce the potential for oesophageal irritation, **DENSATE 70 mg** should only be swallowed upon arising for the day with a full glass of water and patients should not lie down for at least 30 minutes and until after their first food of the day. **DENSATE 70 mg** should not be taken at bedtime or before arising for the day. Failure to follow these instructions may increase the risk of oesophageal adverse experiences (see "**Special Precautions**").

No dosage adjustment is necessary for the elderly or for patients with mild-to-moderate renal insufficiency (creatinine clearance 30 to 80 ml/min) (see "**CONTRA-INDICATIONS**").

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Side-effects:

The following side-effects have been reported with **DENSATE 70 mg**:

Hepato-biliary disorders

Less frequent: Raised liver enzymes, hepatitis, hepatocellular damage.

Blood and lymphatic system disorders

Less frequent: Anaemia, leucopenia, thrombocytopenia

Renal and urinary disorders

Less frequent: Renal failure

Cardiac disorders

Less frequent: Artrial fibrillation

Neoplasms benign/ malignant (including cysts and polyps)

Less frequent: Oesophageal cancer

Metabolism and nutrition disorders:

Less frequent: Symptomatic hypocalcaemia, generally in association with predisposing conditions (see "**Special Precautions**") hypophosphataemia.

Nervous system disorders:

Frequent: Headache

Eye disorders:

Less frequent: Uveitis, scleritis

Gastrointestinal disorders:

Frequent: Abdominal pain, dyspepsia, oesophageal ulcer, dysphagia, abdominal distention, oesophagitis, oesophageal erosions, nausea, vomiting, constipation, diarrhoea, flatulence, acid regurgitation and melaena.

Less frequent: Oesophageal stricture, oropharyngeal ulceration, gastritis, gastric and duodenal ulcers, some severe and with complications, oesophageal perforations.

(See "**Special Precautions**" and "**DOSAGE AND DIRECTIONS FOR USE**").

Skin and subcutaneous tissue disorders:

Less frequent: Rash (occasionally with photosensitivity), erythema and pruritus, severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis.

Musculoskeletal, connective tissue and bone disorders:

Frequent: Musculoskeletal (bone, muscle or joint) pain, myalgia.

Less frequent: Osteonecrosis of the jaw (see "**WARNINGS**"), synovitis.

Immune system disorders:

Less frequent: Hypersensitivity reactions, including urticaria and angioedema

General disorders and administrative site conditions:

Less frequent: Malaise, fever

Special Precautions:

To facilitate delivery to the stomach and therefore reduce the potential for oesophageal irritation, patients should be instructed to swallow **DENSATE 70 mg** with a full glass of water and not to lie down for at least 30 minutes and until after their first food of the day.

Patients should not chew or suck the tablet because of a potential for oropharyngeal ulceration. Patients should be specifically instructed not to take **DENSATE 70 mg** at bedtime or before arising for the day. Patients should be informed that failure to follow these instructions may increase their risk of oesophageal problems. Patients should be instructed that if they develop symptoms of oesophageal disease (such as difficulty or pain upon swallowing, retrosternal pain or new or worsening heartburn) they should stop taking **DENSATE 70 mg** and consult their doctor.

Causes of osteoporosis other than oestrogen deficiency, aging and glucocorticoid use should be considered.

Due to the positive effects of **DENSATE 70 mg** to increase bone mineral, small, asymptomatic decreases in serum calcium and phosphate may occur, especially in patients receiving glucocorticoids, in whom calcium absorption may be decreased.

Ensuring adequate calcium and vitamin D intake is especially important in patients receiving glucocorticoids.

Use in the Elderly:

There is no age-related difference in the efficacy or safety profiles of **DENSATE 70 mg**.

Patients should be instructed that if they miss a dose of **DENSATE 70 mg**, they should take one tablet on the morning after they remember. They should not take two tablets on the same day but should return to taking one tablet once a week on their chosen day, as originally scheduled.

Effects on ability to drive and use machines:

There are no data to suggest that **DENSATE 70 mg** affects the ability to drive or use machines.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Hypocalcaemia, hypophosphataemia and upper gastrointestinal adverse events, such as upset stomach, heartburn, oesophagitis, gastritis, or ulcer, may result from oral overdosage. The administration of milk or antacids may be of benefit.

Because of the risk of oesophageal irritation, vomiting should not be induced. Keep the patient in an upright position.

IDENTIFICATION

DENSATE 70 mg: White to off-white, oval shaped, biconvex, uncoated tablets, debossed with 'F' on one side and '21' on the other side.

PRESENTATION

DENSATE 70 mg:

Tablets are packed in printed aluminium foil with heat seal lacquer and clear PVC laminated with aclar or triple laminated aluminium foil and PVC/PE/PVdC film blisters. Each blister contains 4 tablets.
Pack size: 4's –Each carton contains 1 blister of 4 tablets each.

STORAGE INSTRUCTIONS

Store in a dry place at or below 25 °C. Do not remove blisters from carton until required for use. Keep original containers well closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

45/3.2/0581

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Novagen Pharma (Pty) Ltd.
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DATE OF PUBLICATION OF THE PACKAGE INSERT

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