

**Summer Training at
Cadila Pharmaceuticals Limited,
Ahmedabad**

**To Assess the Calcium and Teriparatide Usage in Osteoporosis by
Orthopaedics in Hyderabad**

**By
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**Under the guidance of
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**MBA Pharmaceutical Management
2015-2017**



**The IIHMR University, Jaipur
2016**

CERTIFICATE

This is to certify that Mr. Hemanth koduri has undergone Summer Training in Cadila pharmaceutical limited, Ahmedabad from 1st April 2016 to 2nd June 2016.

The candidate himself completed the project assigned to him during Summer Training. His approach to the project was sincere and proactive. This summer training is partial fulfillment of the course requirement recommended for the award of MBA in Pharmaceutical Management.

I wish him success in all his future endeavors.



Dr. Seema mehta
Associate Professor

IIHMR, Jaipur



Col. (Dr.) Ashok Kaushik
Dean (Academic & Student Affair)

IIHMR, Jaipur

CPL/HR/Certificate/Internship-2016

02nd June, 2016**To Whom So Ever It May Concern**

This is to certify that **Mr. Hemanth Koduri** student of The IIHMR University, Jaipur successfully completed 8 weeks Summer Internship under the guidance of Mr. Kaushik Dasgupta.

During the period of training from **01st April 2016 to 02nd June 2016** **Hemanth Koduri**, was found to be sincere, dedicated and committed.

We wish his the very best in all his future endeavors.

For Cadila Pharmaceuticals Ltd


Johnson Mathew
GM/HR - Branded

Acknowledgment

“An endeavour over a period can be successful only with the advice and support of well-wishers. I take this opportunity to express my gratitude and appreciation to all those who encouraged me to complete this project.

First of all, I express my sage sense of gratitude and indebtedness to our Director, Dr.S.D.Gupta, IIHMR University, Jaipur.

I would like extend my sincere and heartfelt thanks to Mr. Kaushik dasgupta (General Manager-Marketing) Cadila Pharmaceuticals Ltd. For providing me an opportunity to learn and develop personally.

I would like to express my deep sense of gratitude for my faculty mentor Dr. Seema Mehta and Placement officer Dr. Sandeep Narula. I am greatly indebted to both of them for providing their valuable guidance at all stages of the study, their advice, constructive suggestions, positive and supportive attitude and continuous encouragement, without which it would not have been possible to complete this project.

To place on record, I owe a debt of gratitude to all my teachers for grooming me and my classmates for the inspiration needed to work with dedication and motivation throughout as an Intern at Cadila Pharmaceuticals Ltd.

I would like to present Sincere thanks to the respondents for sparing their valuable support and providing relevant information.

I hope that I can build upon the experience and knowledge that I have gained and make a valuable contribution towards the industry in coming future.

HEMANTH KODURI

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EXECUTIVE SUMMARY

The main of the project is to assess the calcium and teriparatide usage in osteoporosis by orthopaedic doctors

The project is conducted on two steps. One is face to face survey with the doctors and the second steps is the analysis

The main objectives the of the project is

- To assess the calcium and teriparatide usage in osteoporosis by orthopaedics.
- To assess the preference and criteria for prescribing the calcium and teriparatide.
- To assess the most preferred brand and molecule in treating the osteoporosis.

This project is cross sectional descriptive study and sampling method Non probability convenience Sampling

Main rationales of the study is the high incidence, long-term implications, high mortality, financial burden and dramatically decreased quality of life indicate the severity of osteoporosis in humans.

Sample population is orthopaedic doctors and questionnaire design was self and concentrated on usage, preferences, different criteria's, reasons for specific molecules and brands.

Limitation of the study is less time period and limited sample size.

The results shown that calcium and vitamin-D is mostly used as combinations and mostly used in cases of deficiencies, post menopausal women's, and high incidence in oldage people.

Teriparatide is mostly used for chronic cases of osteoporosis and prolonged fractures.

Bisphosphonates are cost effective and shown good improvement in patients.

INTRODUCTION

Osteoporosis is an important systemic disorder, affecting mainly women, with a diverse and multifactorial etiology. Osteoporosis is a multifactorial systemic skeletal disease characterized by a decrease in bone mass and micro architectural deterioration with enhanced bone fragility and results in the loss of mechanical strength and increased risk of fractures. The disorder can be localized or involve the entire skeleton. Traditionally, osteoporosis has been classified into primary and secondary osteoporosis.

- Primary osteoporosis is of two types; **Primary type 1** osteoporosis refers to decreased gonadal function such as decreased level of estrogen. It is post-menopausal osteoporosis, commonly seen in post-menopausal women.
- **Primary type 2** osteoporosis or senile osteoporosis is usually associated with aging and is seen in both females and males in the ratio of 2:1.
- Secondary osteoporosis may occur at any age and affects men and women equally. May be the consequence of endocrine and metabolism disorders (e.g., hypogonadism, hypercortisolism, hyperparathyroidism, anorexia), lymphoproliferative disorders, intestinal malabsorption conditions, rheumatoid arthritis, renal failure, collagenopathies, or certain drugs (e.g., corticosteroids, selective serotonin reuptake inhibitors (SSRI), anticoagulants and antidiabetic medications).

Osteoporotic fractures result in significant mortality and morbidity in all age groups and lead to considerable societal costs, including direct medical costs and indirect costs resulting from reduced quality of life, disability, and death.

- Mortality associated with osteoporotic fractures ranges from 15 to 30%, a rate similar to breast cancer and stroke.
- Furthermore, 50% of women with osteoporotic hip fractures develop disability, with significant impact on the capacity to live independently and, in most cases, institutionalization.
- Several risk factors have been identified for primary osteoporosis.

Risk factors for osteoporosis

Family history Parental history of hip fractures

Medical history Advanced age

Hyperthyroidism or hyperparathyroidism

Celiac and other malabsorption syndromes

Weight loss

Medical history particularly chronic glucocorticoid use and medications that decrease calcium and Vit D

Rheumatoid arthritis

Chronic liver disease

Low femoral neck BMD

Chronic obstructive pulmonary disease

Organ transplantation

Type 1 diabetic mellitus

For women Estrogen deficiency

Early menopause

Life style prolonged immobility and lack of weight-bearing exercise

Current smoking

Daily alcohol consumption

Inadequate calcium and vitamin D

Lack of sunlight exposure

Symptoms and Complication

Osteoporosis is an insidious disease. Some patients discover the disorder exists after sustaining a fracture. Vertebral fractures are painful and can take several months until pain subsides.

In severe osteoporosis, vertebrae become so fragile they can collapse upon themselves without trauma. As vertebral bodies collapse the loss of vertebral height actually causes the patient to shrink.

Kyphosis (hump back)- physical deformity , this results from vertebral collapse in the thoracic spine. Kyphosis can cause severe pain, tingling, numbness, and weakness.



As the structural integrity of the vertebrae is compromised upper body height can be lost allowing the ribs to drop downward to the hips. This may compress the internal organs and causes the abdomen to protrude. Breathing can be impaired due to restricted lung expansion the symptoms of osteoporosis can devastate a patient's quality of life. Deformity often causes loss of self-esteem and may force the patient to give up activities that previously brought enjoyment. Even finding stylish clothing to fit properly can be difficult.

- Estrogen is important in maintaining bone density in women. When estrogen levels drop during menopause, loss of bone density accelerates.
- The accelerated bone loss starts the year before menopause and continues for another 3-4 years. Major cause of osteoporosis in women, referred to as **postmenopausal osteoporosis**
- The average decrease in BMD during the menopausal transition is about 10 percent so this means that half the women are losing even rapidly, perhaps as much as 10–20 percent in those 4-5 years around menopause.

- 25 percent of postmenopausal women can be classified as fast bone losers measured by rates bone loss and bone resorption markers.

Treatment

Bisphosphonates: - suppress bone turnover, prevent bone loss and preserve bone architecture by tightly adhering to bone surfaces and by inhibiting the enzyme farnesyl pyrophosphate synthase which is required for formation of the cytoskeleton in osteoclasts, thereby inhibiting bone resorption.

- Promotes apoptosis of osteoclast

Alendronate -first approved in 1995, daily

Risedronate- a third-generation bisphosphonate, weekly

Ibandronate- monthly

Zoledronic acidis - first and currently the only once-a-year commonly used along with calcium and vitamin D supplementation.

Limitations of bisphosphonates: Oral absorption is very low-less than 1 percent of the dose and must be taken on an empty stomach for maximal absorption, post-dose patients should sit upright.

- Gastrointestinal intolerability, ranging from mild acid reflux to serious esophageal ulcers.
Musculoskeletal pain

Denosumab:-

- Human monoclonal antibody that specifically reducing bone resorption and increasing bone density.
- Administered as a subcutaneous injection every 6 months.

Teriparatide: - (rDNA origin)

- Injection contains recombinant human parathyroid hormone PTH that has an identical sequence to the 34 N-terminal amino acids (the biologically active region) of the 84-amino acid human parathyroid hormone.
- Treatment with teriparatide is the only proven and approved method of increasing bone mass and improving bone architecture.

- Multiple cellular pathways in the osteoblast are activated by PTH.
- Activation of these pathways results in osteoblastic recruitment to the remodeling unit.
- Bone formation begins within the first month of treatment and peaks six to nine months .Bone resorption in patients on PTH begins at about six months and peaks after 12 months of treatment

Estrogen agonists-antagonists (SERMs)

- {Selective estrogen receptor modulators are competitive partial agonist} Compounds that act as estrogens on some tissues but anti-estrogens on others.
- The only approved second generation SERM for osteoporosis, raloxifene is an estrogen agonist at bone and liver maintains BMD and lowers LDL cholesterol concentrations.
- SERMs are an appropriate alternative for women who cannot take bisphosphonates due to side effects such as gastrointestinal intolerance, acid reflux and those who cannot adhere to the dosing requirements for bisphosphonates.

Lifestyle

- Exercise can be effective in preventing bone loss and improving balance, coordination and strength, thereby reducing risk of falls. Thirty minutes of weight-bearing exercise should be undertaken daily by patients who are able to tolerate it.
- Smoking cessation and minimizing alcohol consumption are also beneficial.
- Reducing medications and minimizing dosages, especially glucocorticoids, should be considered.

CALCIUM

Calcium is an essential nutrient that is involved in most metabolic processes and the phosphate salts of which provide mechanical rigidity to the bones and teeth, where 99% of the body's calcium resides. The calcium in the skeleton has the additional role of acting as a reserve supply of calcium to meet the body's metabolic needs in states of calcium deficiency. Calcium deficiency is easily induced because of the obligatory losses of calcium via the bowel, kidneys, and skin.

Loss of bone starts in women at the time of the menopause and in men at about age 55 and leads to an increase in fracture rates in both sexes. Individual fracture risk is inversely related to bone density, which in turn is determined by the density achieved at maturity (peak bone density) and the subsequent rate of bone

loss. At issue is whether either or both of these variables is related to calcium intake. The calcium requirement of adults may be defined as the mean calcium intake needed to preserve calcium balance, i.e., to meet the significant obligatory losses of calcium through the gastrointestinal tract, kidneys, and skin.

Calcium and vitamin D have long been recognized as important and required nutrients for bone health and maintenance. The continuation of calcium and vitamin D in a patient with bone loss is critical for optimal care. Unfortunately, 90% of women may not be getting enough calcium and over 50% of women treated for bone loss have inadequate vitamin D levels. Currently, there are a number of pharmacologic treatments for osteoporosis which provide improvements in bone mass and reduction in fracture risk. These treatments have been studied where adequate calcium and vitamin D supplementation had been achieved. Therefore, their use is predicated on proper calcium and vitamin D therapy. The goal of this manuscript is to review data related to calcium and vitamin D in the management of osteoporosis.

Vitamin D

Vitamin D is an important nutrient in the maintenance of bone health. The primary functions of vitamin D are the regulation of intestinal calcium absorption and the stimulation of bone resorption leading to the maintenance of serum calcium concentration. Sources of vitamin D include sunlight, diet, and supplements. The majority of Americans do not achieve adequate vitamin D levels. In fact, it is estimated that 90% of adults between 51 and 70 years of age do not get enough vitamin D from their diet.

RATIONALE

- The high incidence, long-term implications, high mortality, financial burden and dramatically decreased quality of life indicate the severity of osteoporosis in humans.
- Previous studies raised concerns that calcium supplements or high dietary calcium could increase death as a result of heart-related problems, such as heart attacks and sudden death; yet, calcium is a critical component in bone health, even in the elderly.
- Low intake of calcium in older men can significantly increase the risk of fractures, which can lead to a downward spiral in both physical and mental health, and even be fatal.
- These supplements are widely used by older women to maintain their bone health and prevent fractures.
- Due to its prevalence worldwide, osteoporosis is considered a serious public health concern. Currently it is estimated that over 200 million people worldwide suffer from this disease. Approximately 30% of all postmenopausal women have osteoporosis in the United States and in

Europe. At least 40% of these women and 15-30% of men will sustain one or more fragility fractures in their remaining lifetime.

- Ageing of populations worldwide (source: - <https://www.iofbonehealth.org/> international osteoporosis foundation) will be responsible for a major increase in the incidence of osteoporosis in postmenopausal women.

OBJECTIVES

- To assess the calcium and teriparatide usage in osteoporosis by orthopaedics.
- To assess the preference and criteria for prescribing the calcium and teriparatide.
- To assess the most preferred brand and molecule in treating the osteoporosis.

METHODOLOGY

Research design:

Cross sectional descriptive research design

Sample population: Doctors

Sampling unit: - Orthopaedic doctors

Sample area:

Hyderabad

Sampling method: -

Non probability purposive sampling

Sample size:

Total no of doctors: - 117

Response: - 107

Non Response: - 10

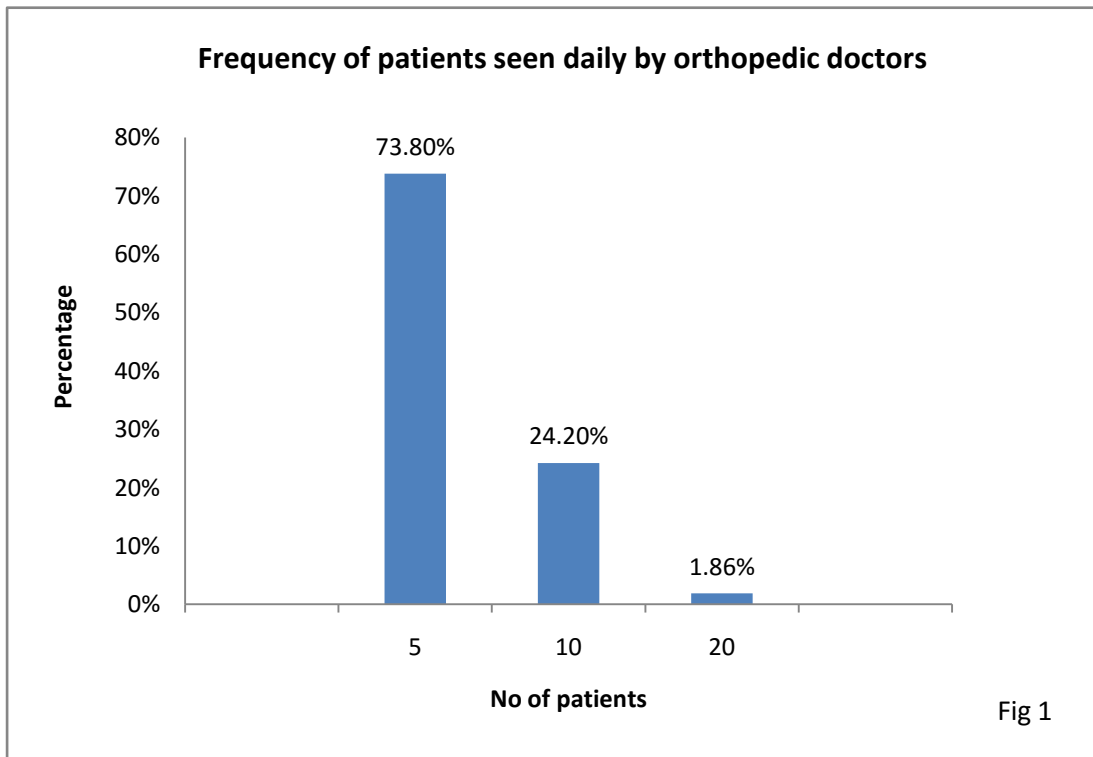
Questionnaire design: -

Questionnaire is mainly based on usage of calcium and teriparatide in osteoporosis.

- First two questions is about the no of patients and mostly whom suffering from osteoporosis.
- Third question is about symptoms regularly observed in patients.
- Fourth and fifth question is about first line treatment and duration of treatment.
- Sixth question is preferred brand, molecules and reasons for prescribing the molecules
- Seventh, eighth and ninth is about preference and criteria for prescribing the drugs.

ANALYSIS

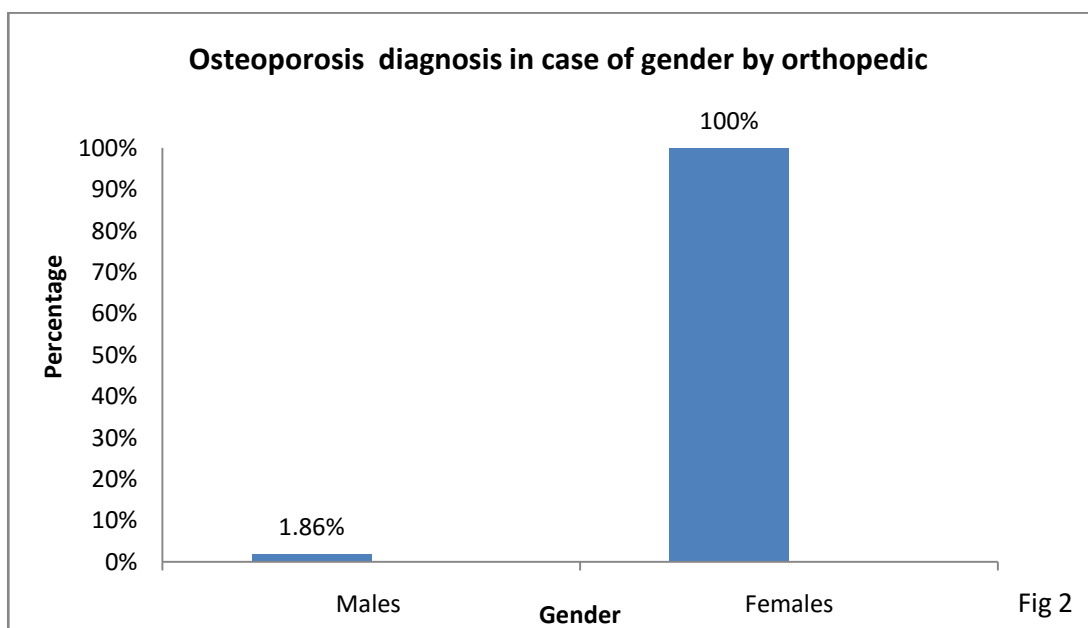
Q1 Frequency of patients seen for osteoporosis daily?



Usually most doctors analyse 5 patients daily suffering from osteoporosis

Q2. For whom you mostly treat?

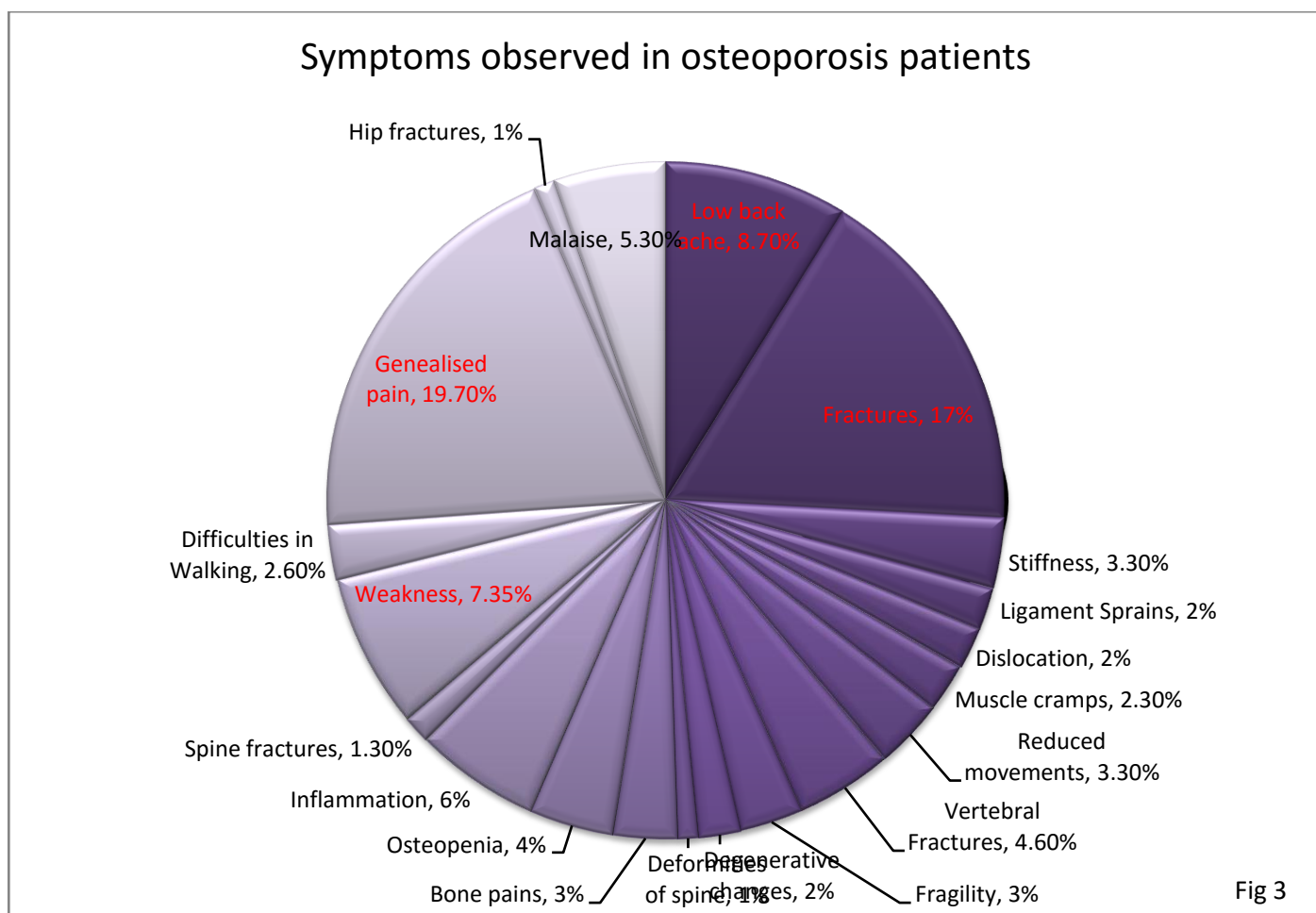
Among 107 form filled, all said that they treat mostly females. Only two doctors said they treat males along with the females.



Mainly females are most susceptible to osteoporosis

Oldage is affected more because osteoporosis is more prevails with age

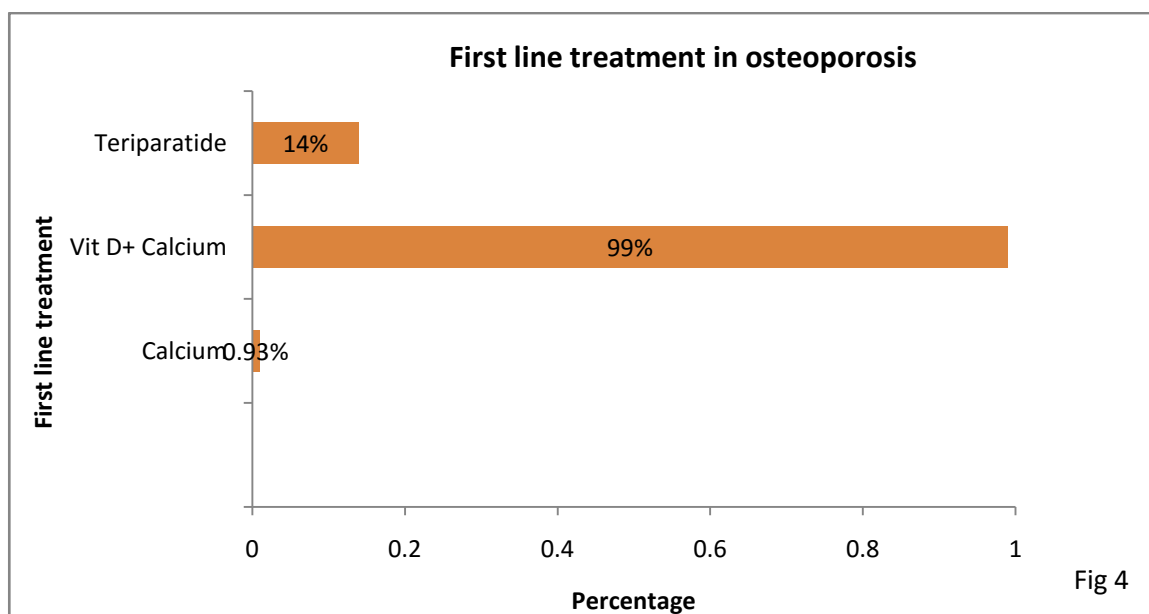
Q3. What are the symptoms you observe in patients?



Generalised pain and Fractures is the main symptoms that are frequently observed in patients

Followed by low back ache and malaise is observed in patients

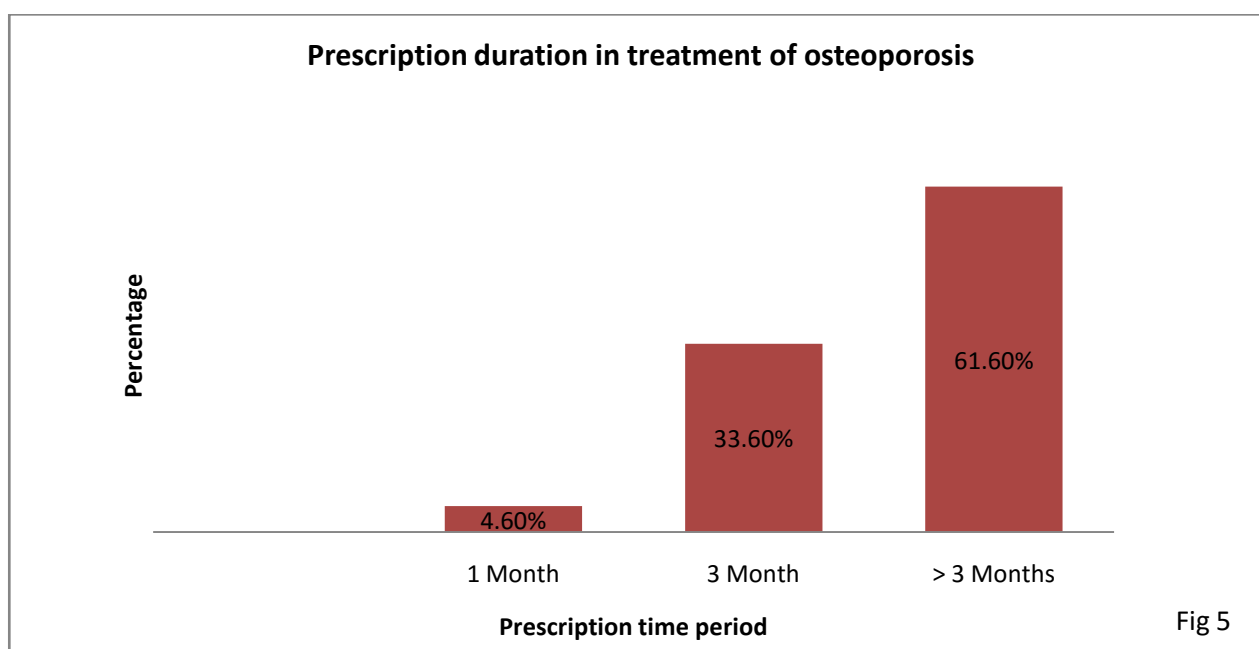
Q4. What is your first line treatment?



Most doctors prefer Vitamin D and calcium as their first line treatment because it is more effective

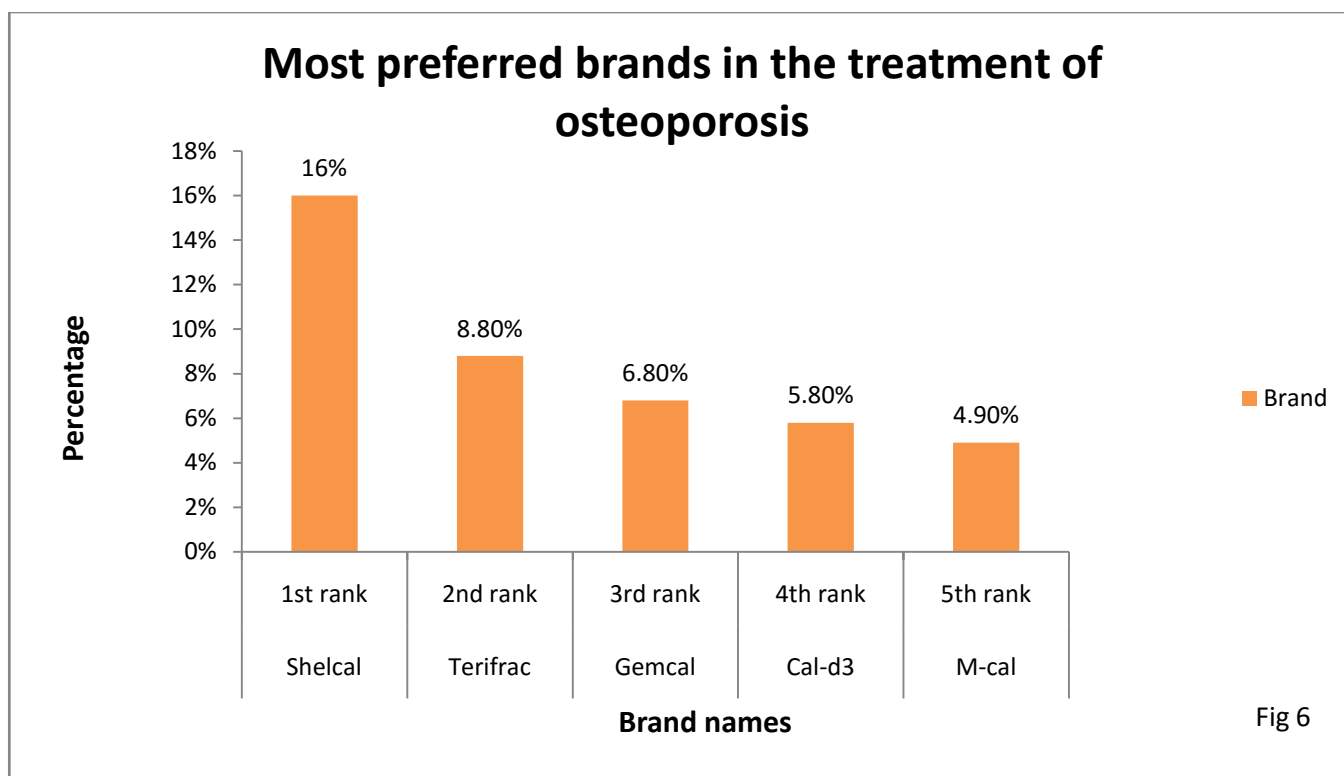
Teriparatide is used in severe cases of osteoporosis

Q5. For how much long duration you prescribe a drug for patient?



Most doctors prescribe drugs for more than 3 months

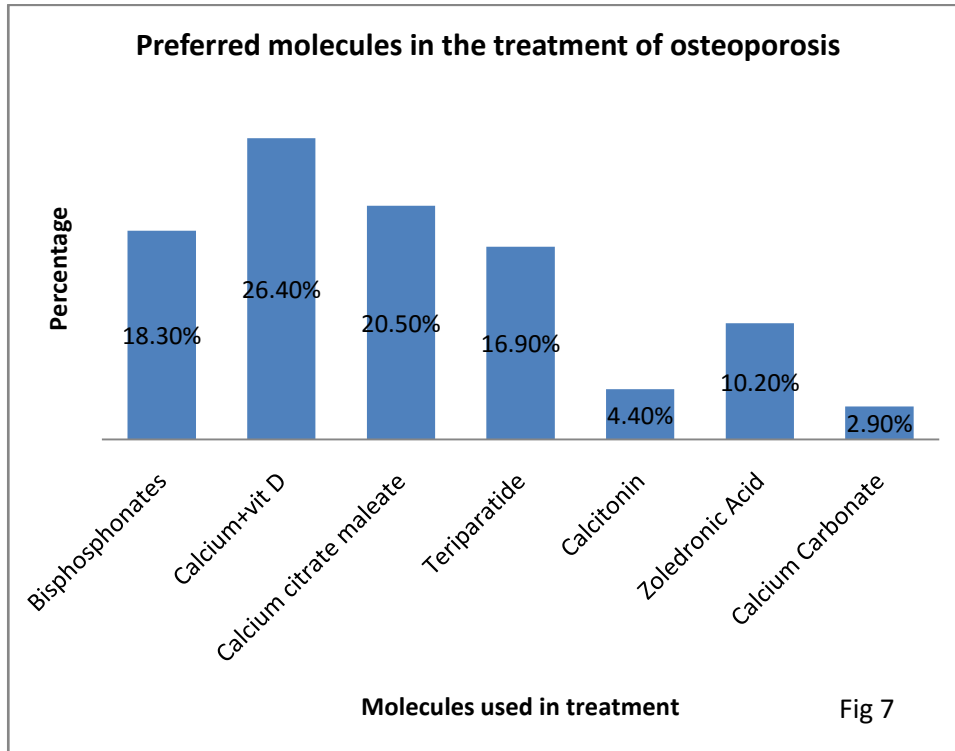
Q6. What is your preferred brand and molecule treatment of osteoporosis?



Most preferred in calcium and vitamin D is Shelcal

Followed by Gemcal, Cal D3, M-Cal, Cipcal

Terifrac (teriparatide) is more commonly used brand



Calcium and vitamin-D and calcium citrate maleate is most preferred molecules

Bisphosphonates and teriparatide is almost equally used in treatment.

Among bisphosphonates, Zoledronic acid is most commonly used.

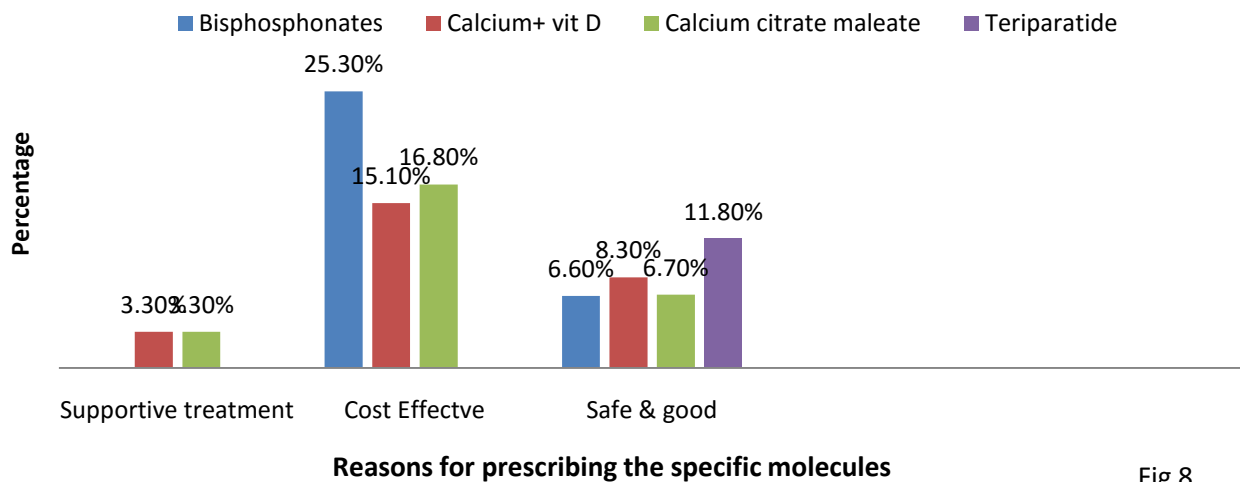
Mostly Calcium is used for supportive treatment.

Bisphosphonates is more economic than teriparatide and more effective too because of fewer side effects when compared to the teriparatide.

Calcium + vitamin-D is having a good results on prolonged treatment.

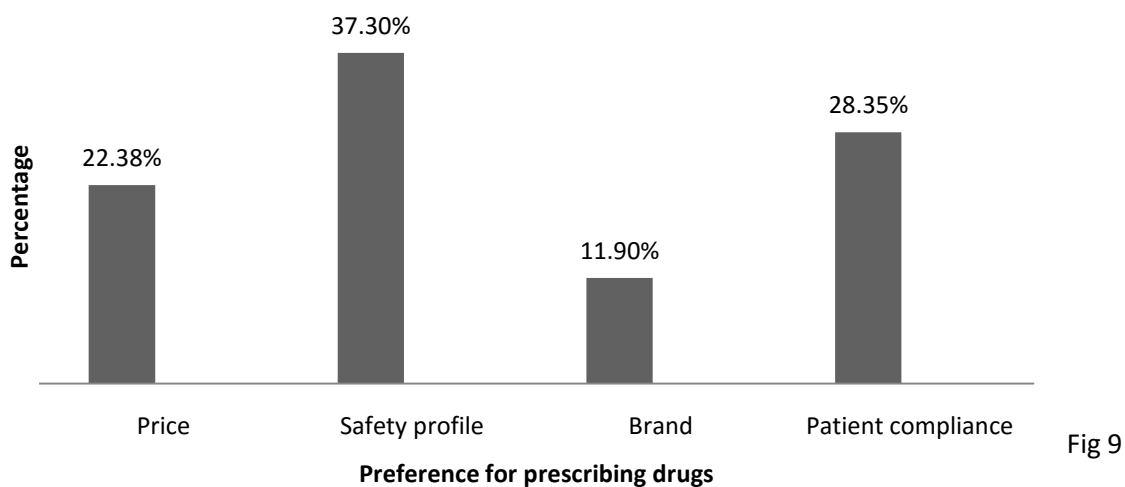
Calcium citrate maleate is having fewer side effects.

Reasons for prescribing specific molecules in the treatment of osteoporosis



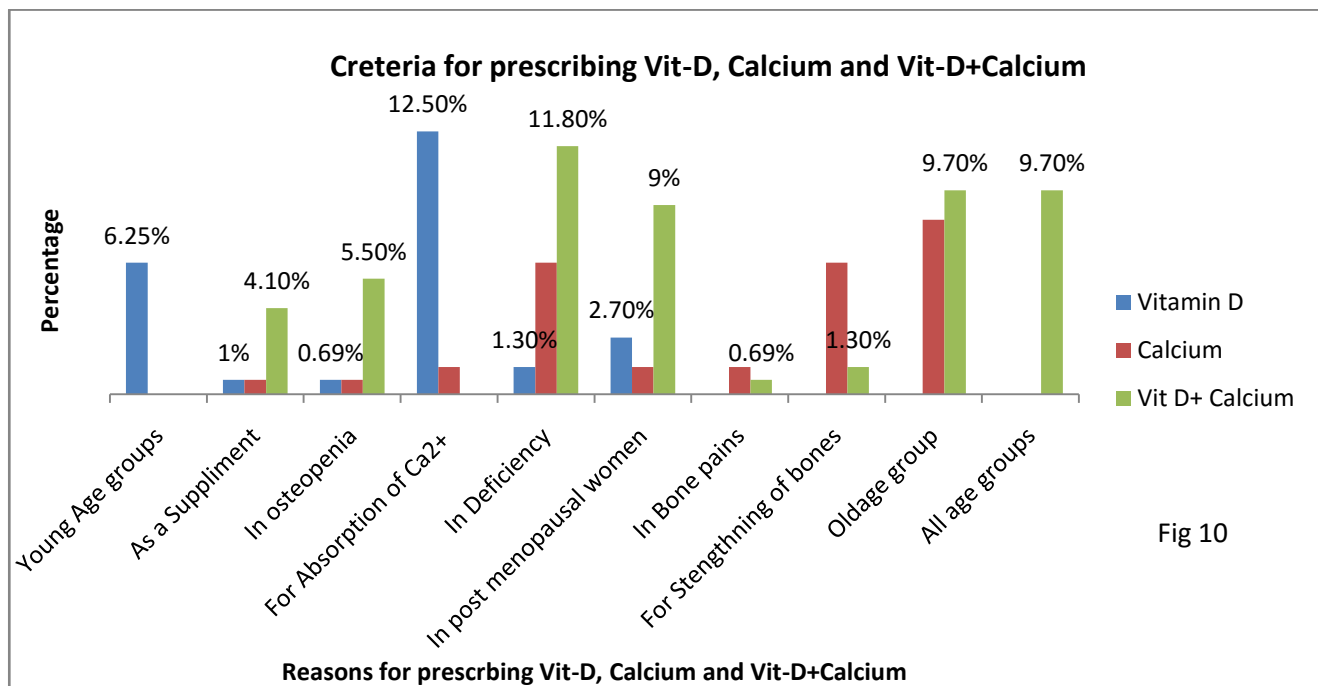
Q7. What are your preference criteria for osteoporosis drug?

Preference for prescribing specific molecules



Safety profile is main criteria for prescribing the drugs followed by patient compliance, price and brand.

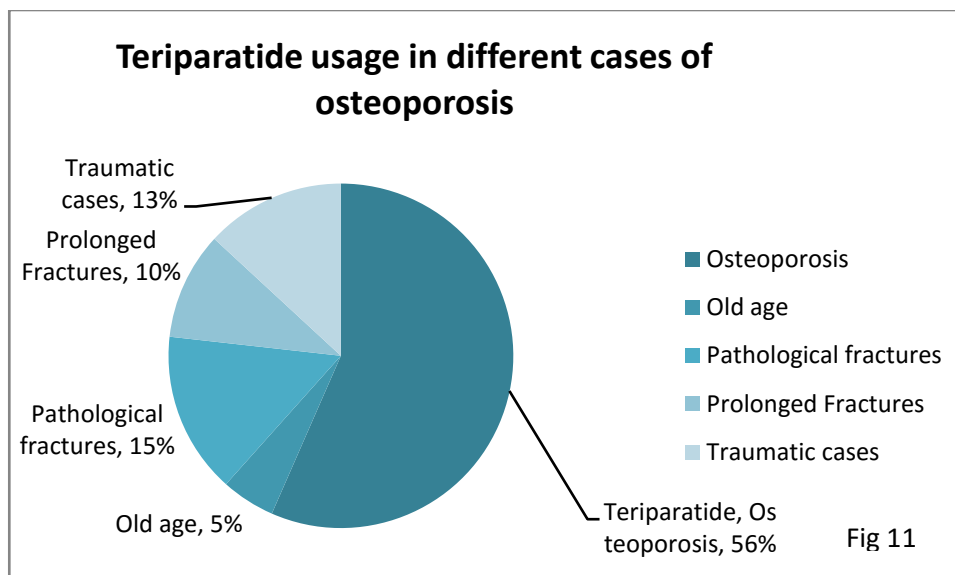
Q8. What are the criteria for prescribing these following molecules/products?



Vitamin D is mainly used in young ages and mostly used for absorption of calcium.

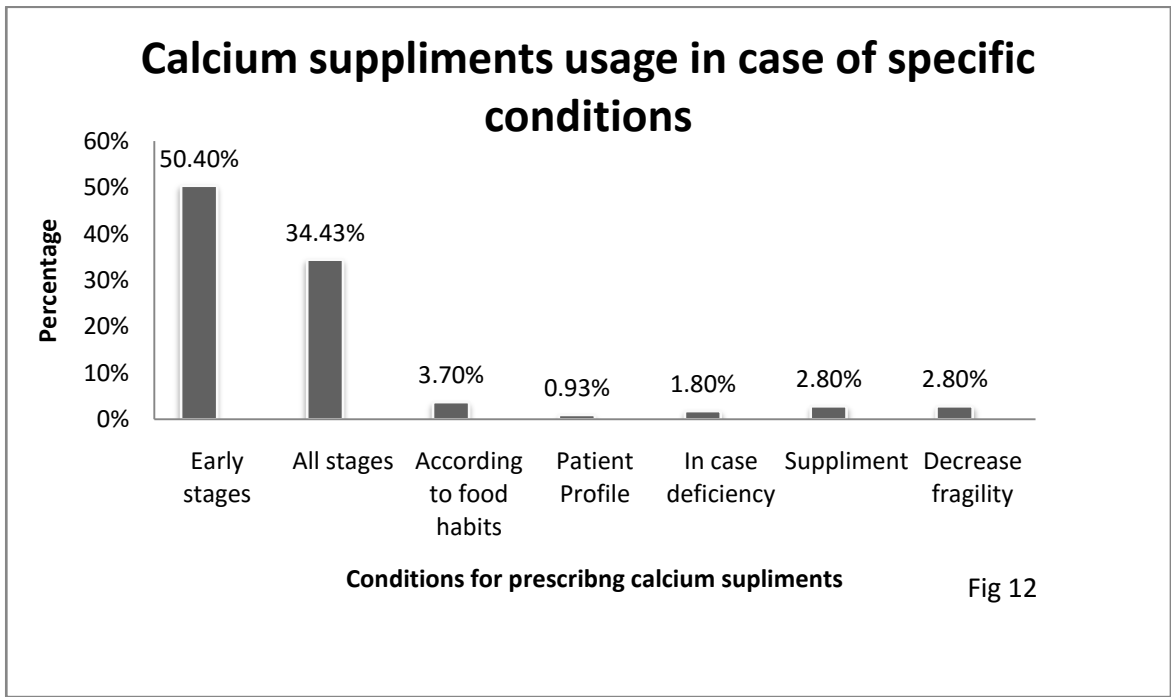
Calcium is mostly used in old ages, deficiency and strengthening of bones

Vitamin D and calcium is used in combination in many cases like every age group people, post menopausal women's, deficiency, osteopenia and for supplementation.



Mostly teriparatide is used in osteoporosis and followed by pathological fractures, prolonged fractures, and traumatic cases.

Q9. What is the preference for prescribing calcium supplements in treating osteoporosis?



Calcium is mainly preferred in initial stages of osteoporosis and also used along the treatment.

LIMITATIONS

- Sample size is small.
- Time period for study is limited.
- Less time of interaction with doctors.

CONCLUSION

Mostly calcium is used as a supplement for the management of osteoporosis and also used in the case of deficiency.

Vitamin D is used for absorption of calcium and now-a-day's young ages given vitamin D because of reduced sunlight exposure.

Teriparatide is costly but more effective in cases of severe osteoporoses. Some doctors said that it shows better results.

Bisphosphonates is economic and mostly used because of its fewer side effects when compared to the teriparatide. Zoledronic acid is most commonly used among the bisphosphonates.

Mostly calcium and vitamin D is combinely used for postmenopausal women's because they are more susceptible for osteoporosis and also deficiency cases.

Among the calcium salts calcium citrate maleate is more used and then calcium carbonate.

Osteoporosis is young ages (juvenile osteoporosis) is rarely seen by doctors.

SUGGESTIONS

Mostly females are affected with osteoporosis, so early diagnosis (frequent checking of bone density) and proper maintenance of diet is better than long term treatments with potent drugs.

Proper care should be taken in post menopausal women's and old people, as themselves are most susceptible to osteoporosis.

Shelcal is the leading brand (Region: - Hyderabad) so company should focus on best promotional activities to acquire the good market share.

Calcium and vitamin D is mostly used in combinations. So instead of releasing single molecules, afford should be made on combinations along with good promotional strategies.

Teriparatide is used for effective treatment in the late phases of osteoporosis. Rather than the high cost, low cost of teriparatide will acquire a good market share.

Calcium is used for long term treatment, so give more preference to safety profile and should be cost effective.

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- j. <http://www.iofbonehealth.org/>
- k. <http://www.asbmr.org/About/PressReleases/Detail.aspx?cid=285ee54c-d6c1-4940-930a-4f9e87176a7c>

ANNEXURE

QUESTIONNAIRE

A. Personal Details:

Name: _____

Experience/ Practice: _____

Place: _____

B. Questions:

Q1. How often you see patient suffering from osteoporosis daily?

5	☐	10	☐
20	☐	30	☐

Q2. To whom you mostly analyze?

Gender:

Male	☐	Female	☐
------	--------------------------	--------	--------------------------

Age Group:

Child	☐	Young	☐
Old	☐		

Q3. What are the symptoms you observe in patients?

1. _____

2. _____

3. _____

Q4. What is your first line treatment?

Vitamin D	☐	Calcium Supplement	☐
Vit D + Calcium supplements	☐	Teriparatide	☐

Q5. For how much long duration you prescribe a drug for patient?

1) 15 days	2) 1 month
3) 3 months	4) More than 3 months

Q6. What is your preferred brand and molecule treatment of osteoporosis?

Brand Name	Molecule/Combination	Reason

Q7. What are your preference criteria for osteoporosis drug?

Price Safety Profile
Brand Patient Compliance

Q8. What are the criteria for prescribing these following molecules/products?

1. Vitamin D: _____
2. Calcium: _____
3. Teriparatide: _____

Q9. What is the preference for prescribing calcium supplements in treating osteoporosis?

Inform Consent Form:

Informed Consent Form



The following is a consent form for a capstone research project. It is a project on “**Market Research of Osteoporosis drug Teriparatide in hyderabad**”, carried out by the student investigator of this project from the IIHMR University, Jaipur.

I, the undersigned, confirm that:

- I have read and understood the information about the project, as provided in the Information Sheet dated.
- I have been given the opportunity to ask questions about the project and my participation.
- I voluntarily agree to participate in the project.
- I understand I can withdraw at any time without giving reasons and that I will not be penalised for withdrawing nor will I be questioned on why I have withdrawn.
- The procedures regarding confidentiality have been clearly explained (e.g. use of names, pseudonyms, anonymisation of data, etc.) to me.
- If applicable, separate terms of consent for interviews, audio, video or other forms of data collection have been explained and provided to me.
- The use of the data in research, publications, sharing and archiving has been explained to me.
- I understand that other researchers will have access to this data only if they agree to preserve the confidentiality of the data and if they agree to the terms I have specified in this form.
- I, along with the Researcher, agree to sign and date this informed consent form.

Participant:

Name of Participant

Signature

Researcher:

Name of Researcher

Signature