Public Assessment Report

Calcitrol 0.25 microgram Capsules
Calcitrol 0.50 microgram Capsules

Calcitrol

PL 10622/0141
PL 10622/0142

Pliva Pharma Ltd

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Lay Summary

The MHRA has granted Pliva Pharma Ltd Marketing Authorisations (licences) for the medicinal products Calcitrol 0.25 microgram Capsules (PL 10622/0141) and Calcitrol 0.50 microgram Capsules (PL 10622/0142) on 27th November 2007. These are prescription only medicines and are used for the correction of abnormalities in calcium and phosphate metabolism in patients with renal osteodystrophy (defective bone formation) and in the treatment of those with established postmenopausal osteoporosis (reduction in bone mass causing weakening of the bones).

Calcitrol 0.25 microgram Capsules and Calcitrol 0.50 microgram Capsules were considered to be generic medical products of the reference products Rocaltrol 0.25 mcg and 0.5 mcg Capsules.
Scientific Discussion

INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted marketing authorisations for the medicinal products Calcitrol 0.25 microgram Capsules (PL 10622/0141) and Calcitrol 0.50 microgram Capsules (PL 10622/0142) on 27th November 2007.

The applications were standard abridged, according to Article 10.1 of Directive 2001/83/EC, claiming that the products were generic medical products to the UK products Rocaltrol 0.25 mcg and 0.5 mcg Capsules, respectively PLs 00031/0122 & 0123, granted 6 September 1979 to Roche Products Ltd.

Calcitrol, a vitamin D metabolite, is used for the correction of abnormalities in calcium and phosphate metabolism in patients with renal osteodystrophy and in the treatment of those with established postmenopausal osteoporosis. The proposed indications are consistent with those licensed for Rocaltrol 0.25 and 0.5 mcg Capsules.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Calcitrol

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Calcitrol is stored under argon in glass bottles with metal screw caps. It has been confirmed that the packaging materials afford protection from light.

Appropriate stability data have been generated supporting a retest period of 36 months, material to be stored at -18°C/Argon.
DRUG PRODUCT

Other Ingredients
The other ingredients of the products are listed below:

Capsule contents:
- Triglycerides, medium-chain
- Butyl hydroxyanisole
- Palmitoyl ascorbic acid

Capsule shell:
- Gelatin
- Glycerol (85 per cent)
- Sorbitol, liquid (non-crystallising)
- Titanium dioxide
- Sodium ethyl parahydroxybenzoate (E215)
- Sodium propyl parahydroxybenzoate (E217)
- Iron oxide red

All formulation excipients are tested for compliance with their respective Ph Eur monograph with the exception of red and yellow iron oxides that are tested to the USP monograph and sodium ethylparahydroxybenzoate that is tested for compliance with the monograph in the French Pharmacopoeia. The products contain gelatin and satisfactory evidence of compliance with current TSE requirements is addressed by the provision of Certificates of Suitability issued by EDQM.

Manufacture
A description and flow-chart of the manufacturing method has been provided. In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches of both strengths. The results are satisfactory.

Dissolution and impurity profiles
Dissolution tests were not performed and this is acceptable due to the nature of the product (oily formulation, insolubility in normal dissolution media and low dose active). Disintegration tests comparing the test products with the reference product found no differences between them. Impurity profiles for the drug products were found to be similar to those for the reference products.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used. Impurity profiles for both strengths of drug product were found to be similar to those for the reference products.

Container Closure System
The capsules are packaged in amber glass containers fitted with a polypropylene cover (note: the Expert states that this is a screw cap). Confirmation that all
immediate pack components comply with the relevant European regulations for packaging materials in contact with food is provided. Satisfactory details of the packaging materials are provided.

**Stability**
Satisfactory stability data was provided supporting a shelf-life of 2 years for product stored with the requirement not to store above 25°C and to store in the original package.

**ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY AND ADVICE**
A Marketing Authorisation was granted.
Pre-Clinical Assessment

No new preclinical data have been supplied with these applications and none are required for an application of this type.
MEDICAL ASSESSMENT

CLINICAL PHARMACOLOGY

Calcitriol has the greatest biological activity of the known vitamin D metabolites and is normally formed in the kidneys from its immediate precursor, 25-hydroxycholecalciferol. In physiological amounts it augments the intestinal absorption of calcium and phosphate and plays a significant part in the regulation of bone mineralisation. The defective production of calcitriol in chronic renal failure contributes to the abnormalities of mineral metabolism found in that disorder.

Calcitriol is a synthetic preparation of calcitriol. Oral administration of Calcitriol to patients with chronic renal failure compensates for impaired endogenous production of calcitriol which is decreased when the glomerular filtration rate falls below 30ml/min. Consequently, intestinal malabsorption of calcium and phosphate and the resulting hypocalcaemia are improved, thereby reversing the signs and symptoms of bone disease. In patients with established post-menopausal osteoporosis, Calcitriol increases calcium absorption, elevates circulating levels of calcitriol and reduces vertebral fracture frequency. The onset and reversal of the effects of Calcitriol are more rapid than those of other compounds with vitamin D activity and adjustment of the dose can be achieved sooner and more precisely. The effects of inadvertent overdosage can also be reversed more readily.

Calcitriol is efficiently absorbed following an oral dose, and peak serum levels are reached after 4 - 6 hours. Calcitriol concentrations return to the basal level with a half-life of 3 - 6 hours, although the duration of pharmacologic activity is approximately 3 - 5 days. Following oral administration of 1 microgram radiolabelled calcitriol to normal individuals, approximately 10% of the total radioactivity appears in the urine within 24 hours. Biliary excretion and enterohepatic recirculation also occur.

Bioequivalence Study

The study was a single dose, randomised, two-way cross over design in 24 healthy male volunteers who all completed the study. Following an overnight fast, volunteers ate a banana 30 minutes before drug administration (to induce bile production) before taking two capsules (2 x 0.50 mcg) of either Italian Rocaltrol or the test preparation on each study day. There was a washout period of 1 week. Blood samples were taken the night before, immediately before dosing and up to 24 hours after drug administration (16 test points). Urine samples were collected at pre-dose and post dose time intervals (0-6, 6-12, 12-24 hrs). Compliance with GCP Guidelines is claimed.

Blood serum levels of the parent drug were monitored and analysed using a radio immunoassay method. Various pharmacokinetic parameters were determined. The applicant has reported results for calcitriol levels, calcitriol levels after baseline correction and calcitriol levels after correcting for differences in assay values of
test/reference products (8.4% less for test). The latter correction is considered appropriate given the very low dose of drug substance in the formulation. The results for baseline and dose corrected pharmacokinetic parameters are summarised in Table 1 along with 90% confidence limits where appropriate. AUC\(_{0-\infty}\) and \(t_{1/2}\) cannot be determined due to the endogenous levels of calcitriol found in plasma (typically 20 to 40 pg/ml).

Table 1: Summary of blood serum calcitriol pharmacokinetic parameters (following baseline/dose correction) from biostudy no CRO-PK-99-24

<table>
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<th>Parameter</th>
<th>Geometric Mean</th>
<th>Frel</th>
<th>90% CI</th>
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<td></td>
<td>Test</td>
<td>Reference</td>
<td></td>
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<tr>
<td>C(\text{max} ) (pg/ml)</td>
<td>47.92 ± 28.395</td>
<td>49.448 ± 27.686</td>
<td>0.979</td>
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<tr>
<td>AUC(_{0-\infty}) (pg x h/ml)</td>
<td>428.971 ± 148.391</td>
<td>462.571 ± 144.732</td>
<td>-</td>
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<tr>
<td>Tmax (h)</td>
<td>4.8 ± 3.4</td>
<td>3.7 ± 2.4</td>
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The 90% confidence intervals for the ratios of AUC and \(C_{\text{max}}\) were within the accepted 0.8-1.25 range according to the CPMP Guidelines. These 0.50 mcg capsules tablets can be considered bioequivalent. The bioequivalence of the lower strength has been based on pharmaceutical extrapolations.

The results for urinary excretion of calcium show an increase in excretion rate after administration of both test and reference product. This increase was from 208±97 and 254±178 mmol/mol creatine to 659±466 and 630±234 mmol/mol creatine for the test and reference formulations, respectively. Statistical analyses showed no significant difference between treatment groups.

**Efficacy**

No formal efficacy data have been provided for this application and none are required.

**Safety**

The formulation of the products proposed for marketing is not expected to produce a different safety profile from the originator products. The adverse events that have been documented for the originator products are listed in the Summary of Product Characteristics.

**Clinical Expert Report**

There is a Clinical Expert Report from Professor D. Germano who is Professor of Occupational Medicine, University of Messina, Italy. Also a Preclinical Expert Report from Professor R. De Pasquale who is Professor of Toxicology at the same University.

**Summary of Product Characteristics**

The Summary of Product Characteristics for the products was amended to reflect those of the reference products.
Patient Information Leaflet and Labelling
Satisfactory mock-ups of the PIL and labelling were provided.

Conclusion
The bioequivalence study supports the claim that the products are generic medical products of the reference products and there are no other clinical issues. Marketing authorisations were granted.
Overall Conclusion and Risk/Benefit Analysis

Quality
The important quality characteristics of Calcitrol 0.25 and 0.50 microgram Capsules are well defined and controlled. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

Pre-Clinical
No new preclinical data were submitted and none are required for applications of this type.

Clinical
Bioequivalence has been demonstrated between the applicant’s Calcitrol 0.25 and 0.50 microgram Capsules and the reference products Rocaltrol 0.25 mcg and 0.5 mcg Capsules.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Rocaltrol 0.25 mcg and 0.5 mcg Capsules.

Risk/Benefit Analysis
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s products and the innovator products are interchangeable. The risk benefit is, therefore, considered to be positive.
### Steps Taken During Assessment

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<td>1</td>
<td>The MHRA received the application on 10/07/2002.</td>
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<td>Following standard checks and communication with the applicant the MHRA considered the application valid on 13/09/2002.</td>
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<td>5</td>
<td>The application was determined on 27/11/2007.</td>
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Steps Taken after Assessment
None
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Calcitriol 0.25 microgram Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 0.25 mcg of calcitriol.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Capsule, soft.
Calcitriol 0.25 mcg are orange soft capsules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Calcitriol is indicated for the correction of the abnormalities of calcium and phosphate metabolism in patients with renal osteodystrophy. Calcitriol is also indicated for the treatment of established post-menopausal osteoporosis.

4.2 Posology and method of administration
The dose of Calcitriol should be carefully adjusted for each patient according to the biological response so as to avoid hypercalcaemia. The effectiveness of treatment depends in part on an adequate daily intake of calcium, which should be augmented by dietary changes or supplements if necessary. The capsules should be swallowed with a little water. Oral intermittent (pulse) therapy with Calcitriol two or three times weekly has been shown to be effective in patients with osteodystrophy refractory to continuous therapy.

Renal Osteodystrophy
Adults with renal osteodystrophy should take an initial daily dose of 0.25 mcg of Calcitriol. In patients with normal or only slightly reduced calcium levels, doses of 0.25 mcg every other day are sufficient. If no satisfactory response in the biochemical parameters and clinical manifestations of the disease is observed within 2 - 4 weeks, the dosage may be increased by 0.25 mcg daily at 2 - 4 week intervals. During this period, serum calcium levels should be determined at least twice weekly. As soon as the serum calcium levels rise to 1mg/100ml (250µmol/l) above normal (9 to 11mg/100ml, or 2250 - 2750µmol/l), or serum creatinine rises to > 120µmol/l, treatment with Calcitriol should be stopped immediately until normocalcemia ensues. Most patients respond to between 0.5 mcg and 1.0 mcg daily. Higher doses may be
necessary if barbiturates or anticonvulsant drugs are administered simultaneously.

Postmenopausal Osteoporosis
The recommended dose of Calcitriol for post-menopausal osteoporosis is 0.25 mcg twice daily. Serum calcium and creatinine levels should be determined at 4 weeks, 3 and 6 months and at 6 monthly intervals thereafter.

Use in the elderly
Clinical experience with Calcitriol in elderly patients indicates that the dosage recommended for use in younger adults may be given without apparent ill-consequence.

Use in Children
Dosage in children has not been established.
Calcitriol capsules are for oral administration only.

4.3 Contraindications
Calcitriol should not be given to patients with hypercalcaemia or evidence of metastatic calcification. The use of Calcitriol in patients with known hypersensitivity to calcitriol (or drugs of the same class) and any of the constituent excipients is contraindicated. Calcitriol is contraindicated if there is evidence of vitamin D toxicity.

4.4 Special warnings and precautions for use
All other vitamin D compounds and their derivatives, including proprietary compounds or foodstuffs which maybe 'fortified' with vitamin D, should be withheld during treatment with Calcitriol.
Treatment does not obviate the need to control plasma phosphate with phosphate-binding agents. Since calcitriol affects phosphate transport in the gut and bone, the dose of phosphate-binding agents may need to be modified. Patients with tertiary hyperparathyroidism, renal failure, or on regular haemodialysis are particularly prone to develop hypercalcaemia from using this product.
Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Calcitriol must be used with caution in patients receiving medications known to increase the serum calcium level, such as thiazide diuretics. Caution must also be exercised in patients receiving calcium supplements or high doses of vitamin D.
Other vitamin D compounds and their derivatives, including proprietary compounds or foodstuffs which maybe 'fortified' with vitamin D, should be withheld during treatment with Calcitriol.

4.6 Pregnancy and lactation
The safety of Calcitriol during pregnancy has not been established. Studies of reproductive toxicology in animals have not yielded unequivocal findings, and no controlled studies on the effect of exogenous calcitriol on pregnancy and foetal development have been performed in human subjects. Consequently,
Calcitriol should be given only when the potential benefit has been weighed against the possible hazard to the foetus. The usual caution in prescribing any drug for women of childbearing age should be observed. It should be assumed that exogenous calcitriol passes into breast milk. Mothers may breastfeed while taking Calcitriol, provided that the serum calcium levels of the mother and infant are monitored.

4.7 Effects on ability to drive and use machines
Patients who suffer from hypercalcaemia may suffer from headache, apathy and somnolence, and therefore should not drive or operate machinery.

4.8 Undesirable effects
The number of adverse effects reported from clinical use of Calcitriol over a period of 15 years in all indications is very low with each individual effect, including hypercalcaemia, occurring rarely. Hypercalcaemia and hypercalciuria are the major side-effects of Calcitriol and indicate excessive dosage. The clinical features of hypercalcaemia include anorexia, nausea, vomiting, headache, weakness, apathy and somnolence. More severe manifestations may include thirst, dehydration, polyuria, nocturia, abdominal pain, paralytic ileus and cardiac arrhythmias. Rarely, overt psychosis and metastatic calcification may occur. In patients with normal renal function, chronic hypercalcemia may be associated with an increase in serum creatinine. Mild, non-progressive and reversible elevations in levels of liver enzymes (SGOT, SGPT) have been noted in a few patients treated with Calcitriol, but no pathological changes in the liver have been reported. Hypersensitivity reactions may occur in susceptible individuals.

4.9 Overdose
In acute overdosage gastric lavage should be considered as soon after ingestion as possible provided that the drug was taken within the previous 6 - 8 hours. Should hypercalcaemia occur, Calcitriol should be discontinued until plasma calcium levels have returned to normal. A low-calcium diet will speed this reversal. Calcitriol can then be restarted at a lower dose or given in the same dose but at less frequent intervals than previously. Severe hypercalcaemia may be treated by ensuring adequate hydration, inducing a diuresis where practicable and by general supportive measures. Calcitonin may increase the rate of fall of serum calcium when bone resorption is increased. In patients treated by intermittent haemodialysis, a low concentration of calcium in the dialysate may also be used. The relatively short biological half-life of Calcitriol permits rapid elimination of the compound when treatment is stopped and hypercalcaemia will recede within 2 - 7 days. This rate of reversal of biological effects is more rapid than when other vitamin D derivatives are used.
5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Calcitriol has the greatest biological activity of the known vitamin D metabolites and is normally formed in the kidneys from its immediate precursor, 25-hydroxycholecalciferol. In physiological amounts it augments the intestinal absorption of calcium and phosphate and plays a significant part in the regulation of bone mineralisation. The defective production of calcitriol in chronic renal failure contributes to the abnormalities of mineral metabolism found in that disorder.
Calcitriol is a synthetic preparation of calcitriol. Oral administration of Calcitriol to patients with chronic renal failure compensates for impaired endogenous production of calcitriol which is decreased when the glomerular filtration rate falls below 30ml/min. Consequently, intestinal malabsorption of calcium and phosphate and the resulting hypocalcaemia are improved, thereby reversing the signs and symptoms of bone disease. In patients with established post-menopausal osteoporosis, Calcitriol increases calcium absorption, elevates circulating levels of calcitriol and reduces vertebral fracture frequency. The onset and reversal of the effects of Calcitriol are more rapid than those of other compounds with vitamin D activity and adjustment of the dose can be achieved sooner and more precisely. The effects of inadvertent overdosage can also be reversed more readily.

5.2 Pharmacokinetic properties
Calcitriol is efficiently absorbed following an oral dose, and peak serum levels are reached after 4 - 6 hours. Calcitriol concentrations return to the basal level with a half-life of 3 - 6 hours, although the duration of pharmacologic activity is approximately 3 - 5 days. Following oral administration of 1 microgram radiolabelled calcitriol to normal individuals, approximately 10% of the total radioactivity appears in the urine within 24 hours. Biliary excretion and enterohepatic recirculation also occur.

5.3 Preclinical safety data
No relevant information additional to that described elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Capsule contents:
- Triglycerides, medium-chain
- Butyl hydroxyanisole
- Palmitoyl ascorbic acid
Capsule shell:
- Gelatin
- Glycerol (85 per cent)
Sorbitol, liquid (non-crystallising)
Titanium dioxide
Sodium ethyl parahydroxybenzoate (E215)
Sodium propyl parahydroxybenzoate (E217)
Iron oxide red

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container
Type III amber glass bottle and polypropylene/ polyethylene cap with PVC seal, containing 30 or 100 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
PLIVA Pharma Ltd.
Vision House
Bedford Road
Petersfield
Hampshire
GU32 3QB
UK.

8 MARKETING AUTHORISATION NUMBER(S)
PL 10622/0141

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
27/11/2007

10 DATE OF REVISION OF THE TEXT
27/11/2007
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Calcitriol 0.50 microgram Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 0.50 mcg of calcitriol.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Capsule, soft
Calcitriol 0.50 mcg are red-orange soft capsules

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Calcitriol is indicated for the correction of the abnormalities of calcium and phosphate metabolism in patients with renal osteodystrophy. Calcitriol is also indicated for the treatment of established post-menopausal osteoporosis.

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Renal Osteodystrophy
Adults with renal osteodystrophy should take an initial daily dose of 0.25 mcg of Calcitriol. In patients with normal or only slightly reduced calcium levels, doses of 0.25 mcg every other day are sufficient. If no satisfactory response in the biochemical parameters and clinical manifestations of the disease is observed within 2 - 4 weeks, the dosage may be increased by 0.25 mcg daily at 2 - 4 week intervals. During this period, serum calcium levels should be determined at least twice weekly. As soon as the serum calcium levels rise to 1mg/100ml (250µmol/l) above normal (9 to 11mg/100ml,or 2250 - 2750µmol/l), or serum creatinine rises to > 120µmol/l, treatment with Calcitriol should be stopped immediately until normocalcemia ensues. Most patients respond to between 0.5 mcg and 1.0 mcg daily. Higher doses may be
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Clinical experience with Calcitriol in elderly patients indicates that the dosage recommended for use in younger adults may be given without apparent ill-consequence.

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Dosage in children has not been established.
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5 PHARMACOLOGICAL PROPERTIES

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Calcitriol is a synthetic preparation of calcitriol. Oral administration of Calcitriol to patients with chronic renal failure compensates for impaired endogenous production of calcitriol which is decreased when the glomerular filtration rate falls below 30ml/min. Consequently, intestinal malabsorption of calcium and phosphate and the resulting hypocalcaemia are improved, thereby reversing the signs and symptoms of bone disease. In patients with established post-menopausal osteoporosis, Calcitriol increases calcium absorption, elevates circulating levels of calcitriol and reduces vertebral fracture frequency. The onset and reversal of the effects of Calcitriol are more rapid than those of other compounds with vitamin D activity and adjustment of the dose can be achieved sooner and more precisely. The effects of inadvertent overdosage can also be reversed more readily.

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5.3 Preclinical safety data
No relevant information additional to that described elsewhere in the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Capsule contents:
Triglycerides
Butyl hydroxyanisole
Palmitoyl ascorbic acid
Capsule shell:
Gelatin
Glycerol (85 per cent)
Sorbitol, liquid (non-crystallising)
Titanium dioxide
Sodium ethyl parahydroxybenzoate (E215)
Sodium propyl parahydroxybenzoate (E217)
Iron oxide red
Iron oxide yellow.

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container
Type III amber glass bottle and polypropylene/ polyethylene cap with PVC seal, containing 30 or 100 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
None.

7 MARKETING AUTHORISATION HOLDER
PLIVA Pharma Ltd.
Vision House
Bedford Road
Petersfield
Hampshire
GU32 3QB
UK.

8 MARKETING AUTHORISATION NUMBER(S)
PL 10622/0142

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
27/11/2007

10 DATE OF REVISION OF THE TEXT
27/11/2007
Labels and Leaflet

INTENT INFORMATION LEAFLET

Calcitrol 0.25 and 0.5 microgram Capsules

Calcitrol Capsules

Please read this leaflet carefully before you start to use your capsules.

This leaflet contains important information about your treatment. If you have any doubts or questions, or are not sure about anything, ask your doctor or pharmacist.

Keep your leaflet. You may need to read it again or as your treatment continues. It may help others who are taking the same treatment.

This leaflet contains the following information:
1. What are Calcitrol capsules and what are they used for?
2. Information to read BEFORE taking Calcitrol Capsules.
3. How to take your medicine.
4. Can you use this medicine more than once?
5. Storing your medicine.

The name of your medicine is Calcitrol Capsules.

Calcitrol 0.25 microgram capsules are orange soft gel capsules.
Calcitrol 0.5 microgram capsules are orange soft gel capsules.

The active substance in your capsules is calcitrol.

Other ingredients are medium chain triglycerides, hypromellose and

Calcitrol is a vitamin product. The capsule can only be taken with food, drinks and all other vitamins and medicines the label tells you to take. Do not take calcitrol capsules in place of any other medicines the label tells you to take.

Calcitrol is a vitamin product. Take your capsules as you are told on the label. The capsules contain a vitamin product with food, drinks and all other medicines you are taking the treatment continues. Do not take calcitrol capsules in place of any other medicines the label tells you to take.

Calcitrol has been prescribed for you. Do not take calcitrol capsules in place of any other medicines the label tells you to take.

Calcitrol contains a vitamin product. Take your capsules as you are told on the label. The capsules contain a vitamin product with food, drinks and all other medicines you are taking the treatment continues. Do not take calcitrol capsules in place of any other medicines the label tells you to take.

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Calcitriol 0.25 microgram Capsules

30 capsules
Each capsule contains 0.25 micrograms of calcitriol.
Also contains: sorbitol and parahydroxybenzoates.
For oral use as directed by the physician.
To be swallowed whole with a little water.
Please read the enclosed leaflet.
Do not store above 25°C. Store in the original package.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

MA Holder: PLIVA Pharma Ltd.
Vision House, Bedford Road, Petersfield,
Hampshire GU32 3QB, United Kingdom.

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Calcitriol 0.25 microgram Capsules

100 capsules
Each capsule contains 0.25 micrograms of calcitriol.
Also contains: sorbitol and parahydroxybenzoates.
For oral use as directed by the physician.
To be swallowed whole with a little water.
Please read the enclosed leaflet.
Do not store above 25°C. Store in the original package.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

MA Holder: PLIVA Pharma Ltd.
Vision House, Bedford Road, Petersfield,
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POM
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UKPAR Pliva Pharma Ltd, Calcitrol 0.25 and 0.50 microgram Capsules
Calcitriol 0.25 microgram Capsules
100 capsules
Each capsule contains 0.25 micrograms of calcitriol.

Calcitriol 0.25 microgram Capsules
100 capsules
Each capsule contains 0.25 micrograms of calcitriol.

Calcitriol 0.25 microgram Capsules
100 capsules
Each capsule contains 0.25 micrograms of calcitriol.
Calcitriol 0.5 microgram Capsules
100 capsules
Each capsule contains 0.5 micrograms of calcitriol.
Also contains: sorbitol and parahydroxybenzoates.
For oral use as directed by the physician.
To be swallowed whole with a little water.
Please read the enclosed leaflet.
Do not store above 25°C. Store in the original package.
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[PL 10620/0142]

Calcitriol 0.5 microgram Capsules
30 capsules
Each capsule contains 0.5 micrograms of calcitriol.
Also contains: sorbitol and parahydroxybenzoates.
For oral use as directed by the physician.
To be swallowed whole with a little water.
Please read the enclosed leaflet.
Do not store above 25°C. Store in the original package.
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[PL 10620/0142]
Also contains cortisol and parathyroid hormone.
See leaflet enclosed for further information.
For oral use as directed by the physician.
To be swallowed whole with a little water.
Please read the enclosed leaflet.
Do not store above 25°C.
Store in the original package.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN.

Calcitriol
0.5 microgram
Capsules
30 capsules
Each capsule contains
6.5 micrograms of calcitriol

Calcitriol
0.5 microgram
Capsules
30 capsules
Each capsule contains
3.5 micrograms of calcitriol