HECTOROL
(doxercalciferol capsules)

INDICATIONS AND USAGE
Hectorol is a synthetic vitamin D2 specifically designed for the treatment of secondary hyperparathyroidism (SHPT).

This indication is based on the results of a double-blind, placebo-controlled, parallel-group study in 138 patients with SHPT and end-stage renal disease. Hectorol is indicated for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease.

The principal adverse effects of treatment with Hectorol are hypercalcemia, hypercalciuria, and oversuppression of iPTH. Prolonged hypercalcemia can exacerbate hyperparathyroidism. Hypercalciuria can accelerate the onset of osteomalacia and can be critical in patients with osteoporosis. In severely osteoporotic patients, hypercalciuria can lead to fractures of long bones, ribs, or skull. Prolonged hypercalcemia of greater than 300 mg/dL can cause hypercalciuria and nephrocalcinosis.

CONTRAINDICATIONS
Hectorol should not be given to patients with a tendency towards hypercalcemia.

WARNINGS
Hypercalcemia. Hypercalcemia can occur due to the formation of excess vitamin D metabolites and can be exacerbated by the reduction in renal function. Hypercalcemia can be treated with oral vitamin D3 analogs or oral bisphosphonates.

Hypercalciuria. Hypercalciuria can occur due to the formation of excess vitamin D metabolites and can be exacerbated by the reduction in renal function. Hypercalciuria can be treated with oral bisphosphonates or oral calcimimetic agents.

OVERDOSAGE
Treatment of Accidental Overdosage of Doxercalciferol
The optimal dose of Hectorol is 20 mcg administered daily. The dosage of Hectorol was determined in a single-blind dose-escalation study. The maximum recommended dose is 20 mcg after each dialysis session (60 mcg total per week).

ADVERSE REACTIONS
The principal adverse effects of treatment with Hectorol are hypercalcemia, hypercalciuria, and oversuppression of iPTH. Prolonged hypercalcemia can exacerbate hyperparathyroidism. Hypercalciuria can accelerate the onset of osteomalacia and can be critical in patients with osteoporosis. In severely osteoporotic patients, hypercalciuria can lead to fractures of long bones, ribs, or skull. Prolonged hypercalcemia of greater than 300 mg/dL can cause hypercalciuria and nephrocalcinosis.

General
Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle cramps, diarrhea, dizziness, decreased appetite, palpitations, decreased urination, myocardial infarction, heart failure, angina, hyperglycemia, hypoglycemia, peripheral neuropathy, and rash.

Respiratory System
Cough increased, dyspnea, rhinitis.

Cardiovascular System
Myocardial infarction, heart failure, angina.

Gastrointestinal System
Diarrhea, constipation, abdominal pain.

Hepatic Insufficiency
No specific data are available for patients with hepatic insufficiency.

Malignancy
No specific data are available for patients with malignancy.

Pregnancy
No specific data are available for patients with pregnancy.

Nursing Mothers
No specific data are available for patients with nursing mothers.

Pediatrics
No specific data are available for patients with pediatrics.

ADVERSE REACTIONS IN PATIENTS WITH DIALYSIS
The adverse events observed in patients with dialysis are similar to those observed in patients with other kidney disease.

ADVERSE REACTIONS IN PATIENTS WITH KIDNEY DISEASE
The adverse events observed in patients with kidney disease are similar to those observed in patients with dialysis.

ADVERSE REACTIONS IN PATIENTS WITH CONGESTIVE HEART FAILURE
The adverse events observed in patients with congestive heart failure are similar to those observed in patients with dialysis and kidney disease.

ADVERSE REACTIONS IN PATIENTS WITH OSTEOPOROSIS
The adverse events observed in patients with osteoporosis are similar to those observed in patients with dialysis and kidney disease.

ADVERSE REACTIONS IN PATIENTS WITH HYPERCALCEMIA
The adverse events observed in patients with hypercalcemia are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH HYPERCALCIIURIA
The adverse events observed in patients with hypercalciuria are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH OVERSUPPRESSION OF iPTH
The adverse events observed in patients with oversuppression of iPTH are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH HYPERPARATHYROIDISM
The adverse events observed in patients with hyperparathyroidism are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH HYPERCALCIURIA
The adverse events observed in patients with hypercalciuria are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH OVERSUPPRESSION OF iPTH
The adverse events observed in patients with oversuppression of iPTH are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH HYPERPARATHYROIDISM
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ADVERSE REACTIONS IN PATIENTS WITH HYPERCALCIURIA
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ADVERSE REACTIONS IN PATIENTS WITH HYPERPARATHYROIDISM
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ADVERSE REACTIONS IN PATIENTS WITH HYPERCALCIURIA
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ADVERSE REACTIONS IN PATIENTS WITH OVERSUPPRESSION OF iPTH
The adverse events observed in patients with oversuppression of iPTH are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

ADVERSE REACTIONS IN PATIENTS WITH HYPERPARATHYROIDISM
The adverse events observed in patients with hyperparathyroidism are similar to those observed in patients with dialysis, kidney disease, and congestive heart failure.

CONSULTATION
When requesting a consultation, please include the following information: name of the patient, date of birth, sex, race, and address. Also, please include the following information: diagnosis, medications, and allergies. Finally, please include the following information: laboratory results, clinical findings, and treatment history. This information will be used to provide the best possible care for the patient.
Only

Store at controlled room temperature: 20° to 25°C (68° to 77°F)

NDC 58468-0120-1

Hectorol 0.5 mcg (50 capsules) Label
01-17-06

Genzyme Graphic Support: George Dias @ Ext. 22618
6799 (01/06) r3
Hectorol 0.5 mcg (50 capsules) Label
01-17-06

Black
PMS 347
PMS 116
PMS 158
Varnish Area
Dieline/Do not print
Store at controlled room temperature: 20° to 25°C (68° to 77°F)
Doxercalciferol, the active ingredient in Hectorol®, is a synthetic vitamin D₃ analog that undergoes metabolic activation in vivo to form 1α,25-(OH)₂D₃. 1,25-(OH)₂D₃ is fat-soluble, elicits essentially colorless to faint yellow, aqueous solution for intravenous injection. Each milliliter (mL) of solution contains doxercalciferol, 2 mcg; polyethylene 20, 4 mg; sodium chloride, 1.5 mg; sodium ascorbate, 10 mg; sodium phosphate, dibasic, 7.6 mg; sodium phosphate, monobasic, 1.8 mg; and disodium edetate, 1.1 mg.

Since doxercalciferol is a precursor for 1α,25-(OH)₂D₃, a potent metabolite of vitamin D₃, pharmacologic doses of vitamin D and its derivatives should be withheld during Hectorol treatment to avoid possible additive effects and hypercalcemia.

Oral calcium-based or other non-aluminum-containing phosphate binders and a low phosphate diet should be used to control serum phosphorus levels in patients undergoing dialysis. Uncontrolled serum phosphorus exacerbates secondary hyperparathyroidism and can lessen the effectiveness of Hectorol® in reducing blood PTH levels. If hypercalcemia occurs after initiating Hectorol® therapy, the dose of Hectorol® and/or calcium-containing phosphate binders should be decreased. If the PTH level falls below 150 pg/mL, Hectorol® may be increased. If hyperphosphatemia persists after decreasing the dose of phosphate binders, 1a-hydroxylase activity may be decreased.

CONTRAINDICATIONS
Hectorol® is indicated for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis.

PRECAUTIONS
Oral
The principal adverse effects of treatment with Hectorol® include hypercalcemia, hyperphosphatemia, and oversuppression of PTH (less than 150 pg/mL). Prolonged hypercalcemia can lead to calcification of soft tissues, including the heart and arteries, and hyperphosphatemia can exacerbate hyperparathyroidism. Over-suppression of PTH may lead to adynamic bone disease. All of these potential adverse effects should be managed by regular patient monitoring and appropriate dosage adjustments. Treatment with Hectorol® is usually initiated at the rate of 4 mcg administered at the end of each dialysis session (3 times weekly) for a total of 12 mcg per week. The dosage of Hectorol® was adjusted in an attempt to achieve PTH levels within a targeted range of 150 to 350 pg/mL.

INDICATIONS AND USAGE
Hectorol® is indicated for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis.

REFERENCES
Vitamin D levels in humans depend on two sources: (1) exposure to the ultraviolet rays of the sun for conversion of 7-dehydrocholesterol in the skin to vitamin D₃ (cholecalciferol) and (2) dietary intake of either vitamin D₂ (ergocalciferol) or vitamin D₃. Vitamin D₂ and vitamin D₃ must be metabolically activated in the liver and kidney, respectively, to form the biologically active form of vitamin D₃.

Mechanism of Action
Calcitrol (1α,25-(OH)₂D₃) and 1α,25-(OH)₂D₃ regulate blood calcium at levels required for body functions. Specifically, the biologically active vitamin D metabolites control the intestinal absorption of dietary calcium, the tubular reabsorption of calcium by the kidney and, in conjunction with parathyroid hormone (PTH), the mobilization of calcium from the skeleton. They act directly on bone cells to stimulate skeletal growth, and on the parathyroid glands to suppress PTH synthesis and secretion. These functions are mediated by the interaction of these biologically active metabolites with specific receptor proteins in the various target tissues. In uremic patients, deficient production of biologically active vitamin D metabolites (due to lack of or insufficient 25-hydroxyvitamin D-1-α-hydroxylase activity) leads to secondary hyperparathyroidism, which contributes to the development of metabolic bone disease in patients with renal failure.

Pharmacokinetics and Metabolism
After intravenous administration, doxercalciferol is activated by CYP27 in the liver to form 1α,25-(OH)₂D₃ (major metabolite) and 1α,24-(OH)₂D₃ (minor metabolite). Activation of doxercalciferol does not require the involvement of the kidneys.

Peak blood levels of 1α,25-(OH)₂D₃ are reached at 8 +/- 5.9 hours (mean +/- SD) after a single intravenous dose of 5 mcg of doxercalciferol. The mean elimination half-life of 1α,25-(OH)₂D₃ after an oral dose is approximately 32 to 37 hours with a range of up to 96 hours. The mean elimination half-life in patients with end stage renal disease (ESRD) and in healthy volunteers appears to be similar following an oral dose. Hemodialysis causes a temporary increase in 1α,25-(OH)₂D₃ mean concentrations presumably due to volume contraction. 1α,25-(OH)₂D₃ is not removed from blood during hemodialysis.

Clinical Studies
The safety and effectiveness of Hectorol® Injection were evaluated in two open-label, single-arm, multi-centered clinical studies (Study C and Study D) in a total of 70 patients with chronic kidney disease on hemodialysis (Stage 5 CKD). Patients in Study C were an average age of 54 years (range: 23-73), 50% male, and were 41% African American, 25% Caucasian, and 14% Hispanic, and had been on hemodialysis for an average of 65 months. Patients in Study D were an average age of 51 years (range: 25-76), 48% male, and 100% African-American, and had been on hemodialysis for an average of 61 months. This group of 70 of the 138 patients who were treated with Hectorol® Capsules in prior clinical studies (Study A and Study B) received Hectorol® Injection in an open-label fashion for 12 weeks (Study C) and for one week washout period (Study D). Dosing of Hectorol® was initiated at the rate of 4 mcg administered at the end of each dialysis session (3 times weekly) for a total of 12 mcg per week. The dosage of Hectorol® was adjusted in an attempt to achieve PTH levels within a targeted range of 150 to 350 pg/mL. The dosage was increased by 2 mcg per dialysis session after 8 weeks of treatment if the PTH levels remained above 300 pg/mL and were greater than 50% of baseline levels. The maximum dosage was limited to 18 mcg per week. If at any time during the trial the PTH level fell below 150 pg/mL, Hectorol® was immediately suspended and restarted at a lower dosage the following week.

Results:
Fifty-two of the 70 patients who were treated with Hectorol® Injection achieved PTH levels ≤150 pg/mL. Forty-one of these patients exhibited plasma PTH levels ≤100 pg/mL, on at least 3 occasions. Thirty-six patients had plasma PTH levels ≤150 pg/mL on at least one occasion during study participation.

Mean weekly doses in Study C ranged from 8.9 mcg to 12.5 mcg. In Study D, the mean weekly dose ranged from 9.1 mcg to 11.6 mcg. Decreases in plasma PTH from baseline values were calculated using as baseline, the average of the last 3 values obtained during the 8-week washout period and are displayed in the table below. Plasma PTH levels were measured weekly during the 12-week study.

PTH Summary Data for Patients Receiving Hectorol® Injection:

<table>
<thead>
<tr>
<th>PTH Level</th>
<th>Study C</th>
<th>Study D</th>
<th>Combined Protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SE)</td>
<td>698 (65)</td>
<td>764 (59)</td>
<td>736 (46)</td>
</tr>
<tr>
<td>Median</td>
<td>648</td>
<td>654</td>
<td>633</td>
</tr>
<tr>
<td>On-treatment (Week 12)</td>
<td>714 (53)</td>
<td>800 (51)</td>
<td>755 (33)</td>
</tr>
<tr>
<td>Mean</td>
<td>299 (63)</td>
<td>370 (59)</td>
<td>328 (47)</td>
</tr>
<tr>
<td>Median</td>
<td>234</td>
<td>252</td>
<td>242</td>
</tr>
<tr>
<td>Change from Baseline</td>
<td>-292 (-59)</td>
<td>-339 (-41)</td>
<td>-318 (-49)</td>
</tr>
<tr>
<td>Median</td>
<td>-375</td>
<td>-415</td>
<td>-394</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;001</td>
<td>&lt;001</td>
<td>&lt;001</td>
</tr>
</tbody>
</table>

Values expressed as mean (SD) for the two patients on study for 10 weeks

Additional treatment options may be considered in patients with chronic kidney disease on dialysis.
Injection is 4 mcg administered intravenously as a dose and may necessitate dosage adjustments. The bacterial mutagenicity assay (Ames test) or a mouse lymphoma gene mutation assay revealed no mutagenic activity. Doxercalciferol caused structural chromatin and chromosome aberrations in an in vitro human lymphocyte clastogenicity assay with metabolic activation. However, doxercalciferol was negative in an in vivo mouse micronucleus assay. Dose-dependent toxicity was seen at 25-hydroxilation of Hectorol and may necessitate dosage adjustments. Cytochrome P450 inhibitors (such as ketoconazole and erythromycin) may inhibit the 25-hydroxylation of Hectorol. Hence, formation of the active moiety may be hindered.

Specific drug interaction studies have not been conducted. Magnesium-containing antacids and Hectorol® should not be used concomitantly because such use may lead to the development of hypermagnesemia (see WARNINGS). Although not examined specifically, enzyme inducers (such as glutethimide and phenobarbital) may affect the 25-hydroxylation of Hectorol® and may necessitate dosage adjustments. Cytochrome P450 inhibitors (such as ketoconazole and erythromycin) may inhibit the 25-hydroxylation of Hectorol. Hence, formation of the active Hectorol® moiety may be hindered.

Hepatic Insufficiency

Studies examining the influence of hepatic insufficiency on the metabolism of Hectorol® have revealed no teratogenic or fetotoxic effects due to doxercalciferol. However, doxercalciferol has no effect on male or female fertility in rats at oral doses up to 2.5 mcg/kg/day (approximately 3 times the maximum recommended human oral dose of 60 mcg/wk based on mcg/m² body surface area).

Caricogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate the carcinogenic potential of doxercalciferol® have not been conducted. No evidence of genetic toxicity was observed in an in vitro bacterial mutagenicity assay (Ames test) or a mouse lymphoma gene mutation assay. Doxercalciferol caused structural chromatin and chromosome aberrations in an in vitro human lymphocyte clastogenicity assay with metabolic activation. However, doxercalciferol was negative in an in vivo mouse micronucleus assay. Doxercalciferol has no effect on male or female fertility in rats at oral doses up to 2.5 mcg/kg/day (approximately 3 times the maximum recommended human oral dose of 60 mcg/wk based on mcg/m² body surface area). Use in Pregnancy

Pregnancy Category B

Reproduction studies in rats and rabbits, at doses up to 20 mcg/kg/day and 0.1 mcg/kg/day (approximately 25 times and less than the maximum recommended human oral dose of 60 mcg/wk based on mcg/m² body surface area, respectively) have revealed no teratogenic or fetotoxic effects due to doxercalciferol. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether doxercalciferol is excreted in human milk. Because other vitamin D derivatives are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from doxercalciferol, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and efficacy of Hectorol® in pediatric patients have not been established.

Geriatric Use

Of the 70 patients treated with Hectorol® injection in the two Phase 3 clinical studies, 12 patients were 65 years or older. In these studies, no overall differences in efficacy or safety were observed between patients 65 years and older and younger patients.

Hepatic Insufficiency

Studies examining the influence of hepatic insufficiency on the metabolism of Hectorol® have revealed no teratogenic or fetotoxic effects due to doxercalciferol. However, doxercalciferol has no effect on male or female fertility in rats at oral doses up to 2.5 mcg/kg/day (approximately 3 times the maximum recommended human oral dose of 60 mcg/wk based on mcg/m² body surface area).

ADVERSE REACTIONS

Hectorol® injection has been evaluated for safety in 70 patients with chronic renal disease on hemodialysis (who had been previously treated with oral Hectorol®) from two 12-week, open-label, single-arm, multi-centered studies. (Dosage titrated to achieve target plasma IPT levels, see CLINICAL PHARMACOLOGY/CLINICAL Studies.) Because there was no placebo group included in the studies of Hectorol® injection, the table below provides the adverse event incidence rates from placebo-controlled studies of oral Hectorol®.

Adverse Events Reported by ≥ 2% of Hectorol® Treated Patients and More Frequently than Placebo During the Double-blind Phase of Two Clinical Studies

<table>
<thead>
<tr>
<th>Body as a Whole</th>
<th>Hectorol® (n=61)</th>
<th>Placebo (n=61)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>33.2</td>
<td>30.9</td>
<td>0.08</td>
</tr>
<tr>
<td>Headache</td>
<td>27.9</td>
<td>18.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Anemia</td>
<td>27.9</td>
<td>19.7</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Cardiovascular System

Bradycardia 6.6 4.9

Digestive System

Anorexia 4.9 3.3

Constipation 3.3 3.3

Dyspepsia 4.9 1.6

Musculo-Skeletal System

Arthralgia 4.9 0.0

Metabolism and Nutritional

Edema 34.4 21.3

Weight Increase 4.9 0.0

Nervous System

Dizziness 11.5 9.8

Sleep disorder 3.3 0.0

Respiratory System

Dyspnea 11.5 6.6

Skin

Pruritus 8.2 6.6

A patient who reported the same medical term more than once was counted only once for that medical term.

Potential adverse effects of Hectorol® are, in general, similar to those encountered with other vitamin D derivatives. Hypercalcemia is most commonly associated with Hectorol® therapy (less frequently with doxercalciferol) and may lead to similar abnormalities. High levels of calcium, phosphorus, and alkaline phosphatase may be observed in patients receiving treatment with Hectorol® and may contribute to hypercalcemia.

Adverse Events More Frequently than Placebo During the Double-blind Phase of Two Clinical Studies

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Hectorol® (n=61)</th>
<th>Placebo (n=61)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 10% of Patients</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>21.3</td>
<td>19.7</td>
<td>0.06</td>
</tr>
<tr>
<td>Headache</td>
<td>27.9</td>
<td>18.0</td>
<td>0.03</td>
</tr>
<tr>
<td>Headache</td>
<td>27.9</td>
<td>19.7</td>
<td>0.04</td>
</tr>
</tbody>
</table>

OVERDOSE

Administration of Hectorol® to patients in excess doses can cause hypercalcemia, hyperphosphatemia, and suppression of PTH secretion leading in certain cases to adynamic bone disease. High intake of calcium and phosphorus in patients taking Hectorol® may lead to similar abnormalities. High levels of calcium in the dialysate bath may contribute to hypercalcemia.

Calcium in the dialysate bath may contribute to hypercalcemia. Treatment of Hypercalcemia and Overdose

General treatment of hypercalcemia (greater than 1 mg/dL above the upper limit of the normal range) consists of immediate suspension of Hectorol® therapy, institution of a low calcium diet, and withdrawal of calcium supplements. Serum calcium levels should be determined at least weekly until normal calcium ensues. Hypercalcemia usually resolves in 2 to 7 days. When serum calcium levels have returned to within normal limits, Hectorol® therapy may be reinstituted at a dose that is at least 1 mcg lower than prior therapy. Serum calcium levels should be obtained weekly during all dosage changes and during subsequent dosage titration. Persistent or markedly elevated serum calcium levels may be corrected by dialysis against a reduced calcium or calcium-free dialysate.

TREATMENT OF ACIDIC OVERDOSE OF HECTOROL®

The treatment of acute accidental overdosage of Hectorol® should consist of general supportive measures. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion, and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and institution of a low calcium diet are also indicated in accidental overdosage. If persistent and markedly elevated serum calcium levels occur, therapy is indicated for the patient received.

DOSEAGE AND ADMINISTRATION

Adult Administration:

For intravenous use only. The optimal dose of Hectorol® must be carefully determined for each patient. The recommended initial dose of Hectorol® is 4 mcg administered intravenously as a bolus dose three times weekly at the end of dialysis (approximately every other day). The initial dose should be titrated down in the range of 0.1 to 20 mcg. If PTH is not lowered by 50% and fails to reach the target range, dosages higher than 18 mcg weekly have not been studied. Drug administration should be suspended if PTH falls below 100 pg/mL and restarted one week later at a dose that is at least 1 mcg lower than the last administered dose during treatment. PTH, serum calcium, and serum phosphorus levels should be obtained weekly. If hypercalcemia, hyperphosphatemia, or a serum calcium times phosphorus product greater than 55 mg²/dL is noted, the dose of Hectorol® should be decreased or suspended and/or the dose of phosphate binders should be appropriately adjusted. If suspended, the drug should be restarted at a dose that is 1 mcg lower.

Dosing must be individualized and based on IPT levels with monitoring of serum calcium and serum phosphorus levels. The following is a suggested approach in dose titration:

PTH Level

Hectorol® Dose

< 10 pg/mL

4 mcg three times per week at the end of dialysis, or approximately every other day

10 - 50 pg/mL

Increase by 1 to 2 mcg at eight-week intervals as necessary

50 - 200 pg/mL

Maintain

> 200 pg/mL

Suspend for one week, then resume at a dose that is at least 1 mcg lower

Discard unused portion.

HOW SUPPLIED

Hectorol® (doxercalciferol injection) is supplied in pre-scored amber glass ampules.

NDC Number

Volume mcg/ampule

58468-0122-1 2 mL 4

Store at 15° to 25°C (59° to 77°F). Protect from light.

Manufactured by OPAKIS Specialty Pharmaceuticals Inc. for Genzyme Corporation

500 Kendall Street

Cambridge, MA 02142

800-847-0069

6807 (01/06)
Genzyme: Graphic Support: Donna DiGiacomo@Ext. 21651

6806 (01/06) R8
Hectorol 4.0 mcg/2.0mL (Injection) Label
Size: 0.9375" X 1.25"
01-10-06
Contents:

Active Ingredient:
Doxercalciferol, 0.0002%

Inactive Ingredients:
Polysorbate 20, NF, 0.4%; Sodium Chloride, USP, 0.15%; Sodium Ascorbate, USP, 0.99%; Sodium Phosphate, Dibasic, USP, Anhydrous, 0.75%; Sodium Phosphate, Monobasic, USP, Monohydrate, 0.18%; Edetate, Disodium, USP, 0.11%; Water for Injection, USP, 97.42%

Made in Israel

Manufactured by
DRAXIS Specialty Pharmaceuticals Inc. for Genzyme Corporation

500 Kendall Street
Cambridge, MA 02142

Hectorol® 4 mcg/2 mL, 50 Ampules

6805 (01/06)

Store at 15° to 25°C (59° to 77°F)

Protect from light.

For intravenous use only

Usual dosage: see package insert

NDC 58468-0122-1

Rx only