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R_x only

ANADROL®-50
 (oxymetholone)
50 mg Tablets



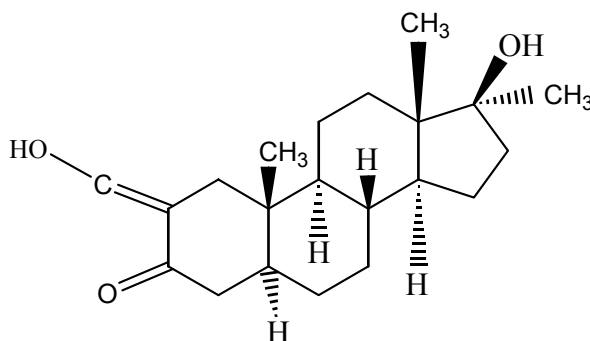
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4 **DESCRIPTION**

5 ANADROL® (oxymetholone) Tablets for oral administration each contain 50 mg of the
 6 steroid oxymetholone, a potent anabolic and androgenic drug.

7 The chemical name for oxymetholone is 17 β -hydroxy-2-(hydroxymethylene)-17-
 8 methyl-5 α -androstane-3-one. The structural formula is:

9



10

11 Inactive Ingredients: lactose
 12 magnesium stearate
 13 povidone
 14 starch

15

16 **CLINICAL PHARMACOLOGY**

17 Anabolic steroids are synthetic derivatives of testosterone. Nitrogen balance is improved
 18 with anabolic agents but only when there is sufficient intake of calories and protein.

19 Whether this positive nitrogen balance is of primary benefit in the utilization of protein-
 20 building dietary substances has not been established. Oxymetholone enhances the
 21 production and urinary excretion of erythropoietin in patients with anemias due to bone
 22 marrow failure and often stimulates erythropoiesis in anemias due to deficient red cell
 23 production.

24 Certain clinical effects and adverse reactions demonstrate the androgenic properties
 25 of this class of drugs. Complete dissociation of anabolic and androgenic effects has not
 26 been achieved. The actions of anabolic steroids are therefore similar to those of male sex
 27 hormones with the possibility of causing serious disturbances of growth and sexual
 28 development if given to young children. They suppress the gonadotropic functions of the
 29 pituitary and may exert a direct effect upon the testes.

30

31 **INDICATIONS AND USAGE**

32 ANADROL Tablets is indicated in the treatment of anemias caused by deficient red cell
 33 production. Acquired aplastic anemia, congenital aplastic anemia, myelofibrosis and the
 34 hypoplastic anemias due to the administration of myelotoxic drugs often respond.

35 ANADROL Tablets should not replace other supportive measures such as transfusion,
36 correction of iron, folic acid, vitamin B₁₂ or pyridoxine deficiency, antibacterial therapy
37 and the appropriate use of corticosteroids.

38

39 **CONTRAINDICATIONS**

- 40 1. Carcinoma of the prostate or breast in male patients.
- 41 2. Carcinoma of the breast in females with hypercalcemia; androgenic anabolic steroids
42 may stimulate osteolytic resorption of bones.
- 43 3. Oxymetholone can cause fetal harm when administered to pregnant women. It is
44 contraindicated in women who are or may become pregnant. If the patient becomes
45 pregnant while taking the drug, she should be apprised of the potential hazard to the
46 fetus.
- 47 4. Nephrosis or the nephrotic phase of nephritis.
- 48 5. Hypersensitivity to the drug.
- 49 6. Severe hepatic dysfunction.

50

51 **WARNINGS**

52 The following conditions have been reported in patients receiving androgenic anabolic
53 steroids as a general class of drugs:

54

Peliosis hepatis, a condition in which liver and sometimes splenic tissue is replaced with blood-filled cysts, has been reported in patients receiving androgenic anabolic steroid therapy. These cysts are sometimes present with minimal hepatic dysfunction, but at other times they have been associated with liver failure. They are often not recognized until life-threatening liver failure or intra-abdominal hemorrhage develops. Withdrawal of drug usually results in complete disappearance of lesions.

Liver cell tumors are also reported. Most often these tumors are benign and androgen-dependent, but fatal malignant tumors have been reported. Withdrawal of drug often results in regression or cessation of progression of the tumor. However, hepatic tumors associated with androgens or anabolic steroids are much more vascular than other hepatic tumors and may be silent until life-threatening intra-abdominal hemorrhage develops.

Blood lipid changes that are known to be associated with increased risk of atherosclerosis are seen in patients treated with androgens and anabolic steroids. These changes include decreased high density lipoprotein and sometimes increased low density lipoprotein. The changes may be very marked and could have a serious impact on the risk of atherosclerosis and coronary artery disease.

55

56 Cholestatic hepatitis and jaundice occur with 17-alpha-alkylated androgens at
57 relatively low doses. Clinical jaundice may be painless, with or without pruritus. It may
58 also be associated with acute hepatic enlargement and right upper-quadrant pain, which
59 has been mistaken for acute (surgical) obstruction of the bile duct. Drug-induced
60 jaundice is usually reversible when the medication is discontinued. Continued therapy

61 has been associated with hepatic coma and death. Because of the hepatotoxicity associated
62 with oxymetholone administration, periodic liver function tests are recommended.

63 In patients with breast cancer, anabolic steroid therapy may cause hypercalcemia by
64 stimulating osteolysis. In this case, the drug should be discontinued.

65 Edema with or without congestive heart failure may be a serious complication in
66 patients with pre-existing cardiac, renal or hepatic disease. Concomitant administration
67 with adrenal steroids or ACTH may add to the edema. This is generally controllable with
68 appropriate diuretic and/or digitalis therapy.

69 Geriatric male patients treated with androgenic anabolic steroids may be at an
70 increased risk for the development of prostate hypertrophy and prostatic carcinoma.

71 Anabolic steroids have not been shown to enhance athletic ability.

72

73 **PRECAUTIONS**

74 **General:**

75 Women should be observed for signs of virilization (deepening of the voice, hirsutism,
76 acne and clitoromegaly). To prevent irreversible change, drug therapy must be
77 discontinued when mild virilism is first detected. Such virilization is usual following
78 androgenic anabolic steroid use at high doses. Some virilizing changes in women are
79 irreversible even after prompt discontinuance of therapy and are not prevented by
80 concomitant use of estrogens. Menstrual irregularities, including amenorrhea, may also
81 occur.

82 The insulin or oral hypoglycemic dosage may need adjustment in diabetic patients
83 who receive anabolic steroids.

84 Anabolic steroids may cause suppression of clotting factors II, V, VII and X, and an
85 increase in prothrombin time.

86

87 **Information for the Patient:**

88 The health care provider should instruct patients to report immediately any use of
89 warfarin and any bleeding.

90 The health care provider should instruct patients to report any of the following side
91 effects of androgens.

92 **Adult or Adolescent Males:** Too frequent or persistent erections of the penis,
93 appearance or aggravation of acne.

94 **Women:** Hoarseness, acne, changes in menstrual periods or more hair on the face.

95 **All Patients:** Any nausea, vomiting, changes in skin color or ankle swelling.

96

97 **Laboratory Tests:**

98 Women with disseminated breast carcinoma should have frequent determination of urine
99 and serum calcium levels during the course of androgenic anabolic steroid therapy (see

100 **WARNINGS).**

101 Because of the hepatotoxicity associated with the use of 17-alpha-alkylated androgens,
102 liver function tests should be obtained periodically.

103 Periodic (every 6 months) x-ray examinations of bone age should be made during
104 treatment of prepubertal patients to determine the rate of bone maturation and the effects
105 of androgenic anabolic steroid therapy on the epiphyseal centers.

106 Anabolic steroids have been reported to lower the level of high-density lipoproteins
107 and raise the level of low-density lipoproteins. These changes usually revert to normal
108 on discontinuation of treatment. Increased low-density lipoproteins and decreased high-
109 density lipoproteins are considered cardiovascular risk factors. Serum lipids and high-
110 density lipoprotein cholesterol should be determined periodically.

111 Hemoglobin and hematocrit should be checked periodically for polycythemia in
112 patients who are receiving high doses of anabolics.

113 Because iron deficiency anemia has been observed in some patients treated with
114 oxymetholone, periodic determination of the serum iron and iron binding capacity is
115 recommended. If iron deficiency is detected, it should be appropriately treated with
116 supplementary iron.

117 Oxymetholone has been shown to decrease 17-ketosteroid excretion.

118

119 **Drug Interactions:**

120 **Warfarin:** Clinically significant pharmacokinetic and pharmacodynamic interactions
121 between anabolic steroids and warfarin have been reported in healthy volunteers. When
122 anabolic steroid therapy is initiated in a patient already receiving treatment with warfarin,
123 the INR (international normalized ratio) or prothrombin time (PT) should be monitored
124 closely and the dose of warfarin adjusted as necessary until a stable target INR or PT has
125 been achieved. Furthermore, in patients receiving both ANADROL Tablets and warfarin,
126 careful monitoring of the INR or PT and adjustment of the warfarin dosage, if indicated,
127 are recommended when the ANADROL dose is changed or discontinued. Patients
128 should be closely monitored for signs and symptoms of occult bleeding.

129

130 **Anticoagulants:** Anabolic steroids may increase sensitivity to oral anticoagulants.
131 Dosage of the anticoagulant may have to be decreased in order to maintain the desired
132 prothrombin time. Patients receiving oral anticoagulant therapy require close monitoring,
133 especially when anabolic steroids are started or stopped.

134

135 **Drug/Laboratory Test Interferences:**

136 Therapy with androgenic anabolic steroids may decrease levels of thyroxine-binding
137 globulin resulting in decreased total T₄ serum levels and increased resin uptake of T₃ and
138 T₄. Free thyroid hormone levels remain unchanged and there is no clinical evidence of
139 thyroid dysfunction. Altered tests usually persist for 2 to 3 weeks after stopping anabolic
140 therapy.

141 Anabolic steroids may cause an increase in prothrombin time.

142 Anabolic steroids have been shown to alter fasting blood sugar and glucose tolerance
143 tests.

144

145 **Carcinogenesis, Mutagenesis, Impairment of Fertility:**

146 A two-year carcinogenicity study in rats given oxymetholone orally was conducted under
147 the auspices of the US National Toxicology Program (NTP). A wide spectrum of
148 neoplastic and non-neoplastic effects was observed. In male rats, no effects were
149 classified as neoplastic in response to doses up to 150 mg/kg/day (5 times therapeutic
150 exposures with 5 mg/kg based on body surface area). Female rats given 30 mg/kg/day (1
151 fold the maximum recommended clinical dose of 5 mg/kg/day based on the body surface

152 area) had increased incidences of lung alveolar/bronchiolar adenoma and adenoma or
153 carcinoma combined. At 100 mg/kg/day (about 3 fold the maximum recommended
154 clinical dose of 5 mg/kg/day based on BSA), female rats had increased incidences of
155 hepatocellular adenoma and adenoma or carcinoma combined; the combined incidence of
156 squamous cell carcinoma and carcinoma of the sweat glands also was increased.

157
158 Human data: There are rare reports of hepatocellular carcinoma in patients receiving
159 long-term therapy with androgens in high doses. Withdrawal of the drugs did not lead to
160 regression of the tumors in all cases.

161 Geriatric patients treated with androgens may be at an increased risk of developing
162 prostatic hypertrophy and prostatic carcinoma although conclusive evidence to support
163 this concept is lacking.

164 In studies conducted under the auspices of the US National Toxicology Program, no
165 evidence of genotoxicity was found using standard assays for mutagenicity, chromosomal
166 aberrations, or induction of micronuclei in erythrocytes.

167 Impairment of fertility was not tested directly in animal species. However, as noted
168 below under **ADVERSE REACTIONS**, oligospermia in males and amenorrhea in
169 females are potential adverse effects of treatment with ANADROL Tablets. Therefore,
170 impairment of fertility is a possible outcome of treatment with ANADROL Tablets.

171

172 **Pregnancy:**

173 Pregnancy category X (see **CONTRAINDICATIONS**).

174

175 **Nursing Mothers:**

176 It is not known whether anabolics are excreted in human milk. Because of the potential
177 for serious adverse reactions in nursed infants from anabolics, women who take
178 oxymetholone should not nurse.

179

180 **Pediatric Use:**

181 Anabolic/androgenic steroids should be used very cautiously in children and only by
182 specialists who are aware of their effects on bone maturation.

183 Anabolic agents may accelerate epiphyseal maturation more rapidly than linear
184 growth in children, and the effect may continue for 6 months after the drug has been
185 stopped. Therefore, therapy should be monitored by x-ray studies at 6-month intervals in
186 order to avoid the risk of compromising the adult height.

187

188 **Geriatric Use:**

189 Clinical studies of ANADROL Tablets did not include sufficient numbers of subjects
190 aged 65 and over to determine whether they respond differently from younger subjects.
191 Other reported clinical experience has not identified differences in responses between the
192 elderly and younger patients. In general, dose selection for an elderly patient should be
193 cautious, usually starting at the low end of the dosing range, reflecting the greater
194 frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or
195 other drug therapy.

196

197 **ADVERSE REACTIONS**

198 **Hepatic:** Cholestatic jaundice with, rarely, hepatic necrosis and death. Hepatocellular
199 neoplasms and peliosis hepatis have been reported in association with long-term
200 androgenic anabolic steroid therapy (see **WARNINGS**).

201

202 **Genitourinary System:**

203

In Men:

204

Prepubertal: Phallic enlargement and increased frequency of erections.

205

Postpubertal: Inhibition of testicular function, testicular atrophy and oligospermia,
206 impotence, chronic priapism, epididymitis, bladder irritability and decrease in
207 seminal volume.

208

In Women:

209

Clitoral enlargement, menstrual irregularities.

210

In Both Sexes:

211

Increased or decreased libido.

212

213 **CNS:** Excitation, insomnia.

214

215 **Gastrointestinal:** Nausea, vomiting, diarrhea.

216

217 **Hematologic:** Bleeding in patients on concomitant anticoagulant therapy, iron-
218 deficiency anemia.

219

Leukemia has been observed in patients with aplastic anemia treated with
220 oxymetholone. The role, if any, of oxymetholone is unclear because malignant
221 transformation has been seen in patients with blood dyscrasias and leukemia has been
222 reported in patients with aplastic anemia who have not been treated with oxymetholone.

223

224 **Breast:** Gynecomastia.

225

226 **Larynx:** Deepening of the voice in women.

227

228 **Hair:** Hirsutism and male-pattern baldness in women, male-pattern of hair loss in
229 postpubertal males.

230

231 **Skin:** Acne (especially in women and prepubertal boys).

232

233 **Skeletal:** Premature closure of epiphyses in children (see **PRECAUTIONS, Pediatric**
234 **Use**), muscle cramps.

235

236 **Body as a Whole:** Chills.

237

238 **Fluid and Electrolytes:** Edema, retention of serum electrolytes (sodium, chloride,
239 potassium, phosphate, calcium).

240

241 **Metabolic/Endocrine:** Decreased glucose tolerance (see **PRECAUTIONS**), increased
242 serum levels of low-density lipoproteins and decreased levels of high-density lipoproteins
243 (see **PRECAUTIONS, Laboratory Tests**), increased creatine and creatinine excretion,

244 increased serum levels of creatinine phosphokinase (CPK). Reversible changes in liver
245 function tests also occur, including increased Bromsulphalein (BSP) retention and
246 increases in serum bilirubin, glutamic-oxaloacetic transaminase (SGOT), and alkaline
247 phosphatase.

248

249 **DRUG ABUSE AND DEPENDENCE**

250 ***Controlled Substance:***

251 ANADROL Tablets is considered to be a controlled substance and is listed in Schedule
252 III.

253

254 **OVERDOSAGE**

255 There have been no reports of acute overdosage with anabolics.

256

257 **DOSAGE AND ADMINISTRATION**

258 The recommended daily dose in children and adults is 1-5 mg/kg body weight per day.
259 The usual effective dose is 1-2 mg/kg/day but higher doses may be required, and the dose
260 should be individualized. Response is not often immediate, and a minimum trial of three
261 to six months should be given. Following remission, some patients may be maintained
262 without the drug; others may be maintained on an established lower daily dosage. A
263 continued maintenance dose is usually necessary in patients with congenital aplastic
264 anemia.

265

266 **HOW SUPPLIED**

267 ANADROL (oxymetholone) Tablets is supplied in bottles of 100 white scored tablets
268 imprinted with 8633 and UNIMED (NDC 0051-8633-33).

269

270 Store at controlled room temperature 20° to 25°C (68° to 77°F); excursions permitted to
271 15° to 30°C (59° to 86°F) [See USP].

272

273 *Manufactured for*

274 *Unimed Pharmaceuticals, Inc.*

275 *by Solvay Pharmaceuticals, Inc*

276 *Marietta, GA 30062*

277

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