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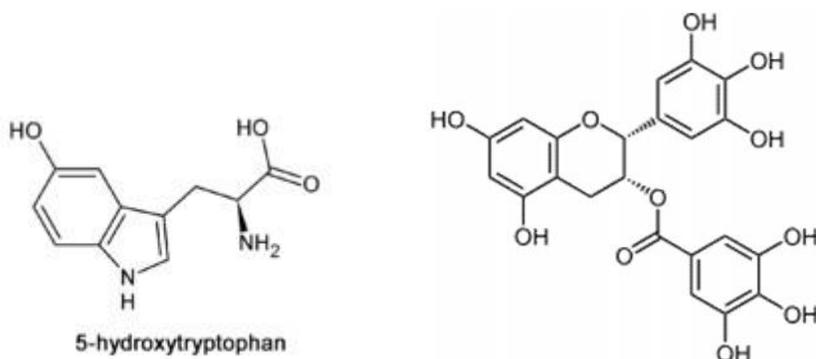
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CAPSULES

5 OTC – NATURAL SUPPLEMENT

6 DESCRIPTION

7 Bio-Slender is an orally administered agent for the treatment of obesity. Its composition is
8 formulated from natural products *Camellia sinensis*, *Taraxacum officinale*, *Garcinia cambogia*,
9 *Griffonia simplicifolia* Extract (20% 5-Hydroxytryptophan) , Guarana (*Paullinia cupana*).



10

11 Bio-Slender is beige to brownish powder (80 mesh) with a solubility of 2.5mg/ml in pH 5.2 water.
12 Each Bio-Slender capsule contains 420mg of the formulated natural components. Each capsule
13 shell contains gelatin, titanium dioxide and FD&C Blue No. 1.

14 CLINICAL PHARMACOLOGY

15 Mechanism of Action

16 Bio-Slender exerts its therapeutic effects on serotonin synthesis in central nervous system tissue.
17 It is believed that an artificially high supply of 5-HTP causes the brain's serotonin-producing
18 neurons to increase production. Increased serotonin production then leads to increased serotonin
19 release by acting as a precursor to serotonin. It provides the natural state for the brain to produce
20 more serotonin then inhibiting the reuptake such as SRI/MAOI products.

21 A principle constituent in Bio-slender is *Garcinia* which is hydroxycitric acid (HCA), or
22 hydroxycitrate. This important component makes up 10 - 30% of the dried fruit rind. *Garcinia* is
23 discussed essentially in terms of hydroxycitrate, with the majority of research focusing on this
24 chemical compound. *Garcinia* also contains a significant amount of beneficial flavonoids.

25 The exact mechanisms of action for hydroxycitrate's effect on physiologic and metabolic processes
26 are not fully known. Early studies showed that it inhibits the formation of fat in animals. HCA was
27 shown to be a potent inhibitor of ATP citrate lyase, an enzyme that catalyzes the
28 extramitochondrial cleavage of citrate to oxaloacetate and acetyl-CoA:

29 - citrate + ATP + CoA --> acetyl-CoA + ADP + P(i) + oxaloacetate -

30 The significance of this metabolic reaction is that inhibition limits the availability of acetyl-CoA
31 units required for fatty acid synthesis and lipogenesis; especially when a diet high in carbohydrates
32 is consumed. Furthermore, extensive animal studies indicated that (-)-HCA suppresses food intake
33 and induce weight loss.

34 Hydroxycitrate also appears to exert effects on processes other than fuel metabolism. One study
35 in rats showed that hydroxycitrate can inhibit [3H]-5-HT (hydroxy-tryptophan) uptake, while also
36 increasing 5-HT availability in isolated brain cortical slices; similar to the way SSRIs (selective
37 serotonin reuptake inhibitors) work. The authors conclude that these effects may be applicable in
38 controlling appetite, and other serotonin-deficient conditions

39

40 **Pharmacokinetics**

41 **Absorption**

42 Bio-Slender is rapidly absorbed from the GI tract (Tmax of 1.1 hours) following oral administration
43 and undergoes extensive first-pass metabolism in the liver. Following oral dosing with 300mg
44 Bio-slender plasma radioactivity peaked at approximately 3-4 hours; plasma concentrations of
45 intact Bio-Slender were near the limits of detection (<5ng/mL). On the basis of mass balance
46 studies, on average at least 74% of a single dose of Bio-Slender is absorbed. Bio-Slender well
47 absorbed from an oral dose, with about 70 percent ending up in the bloodstream. It easily crosses
48 the blood-brain barrier and effectively increases central nervous system synthesis of serotonin.

49 The absolute bioavailability of Bio-Slender has not been determined.

50 **Distribution**

51 In vitro Bio-Slender was > 97% bound to human plasma proteins at plasma concentrations seen
52 following therapeutic doses.

53 **Metabolism**

54 Bio-Slender metabolism occurs both in nervous tissue and in the liver principally by the
55 cytochrome P450 (3A4) isoenzyme, to desmethyl metabolites, M₁ and M₂. These active
56 metabolites are further metabolized by hydroxylation and conjugation to pharmacologically
57 inactive metabolites M₅ and M₆. Following oral administration of radiolabeled Bio-Slender,
58 essentially of the peak radiolabeled material in plasma was accounted for by unchanged Bio-
59 Slender. (2.8%), M₁ (6%), M₂ (12.2) M₅ (54%) M₆ (25%).

60 The elimination half-live of Bio-Slender for a single dose of 300mg is 6-8 hours.

61

62 **Elimination**

63 Following a single dose of 300mg Bio-Slender in normal weight and obese subjects, fecal and urine
64 excretion of the unabsorbed product was found to be the major route of elimination.

65 Approximately 82% (range 68% - 95%) of the administered radiolabeled Bio-Slender was excreted
66 in urine and feces over a 12 day collection period with the majority of the dose (72% excreted in
67 the Urine. The primary route of excretion for M₁ and M₂ is hepatic metabolism and M₅ and M₆ is
68 renal excretion.

69 **Special Populations**

70 *Geriatrics:* Plasma concentrations of M₁ and M₂ were similar between elderly (ages 61 to 75yr) and
71 younger (ages 17-30) subjects following a single dose of 300mg oral Bio-Slender. Plasma
72 concentrations of inactive metabolites M₅ and M₆ were higher in elderly; these differences are
73 not likely to be of clinical significance. In general, dose selection for the elderly should be cautious,
74 reflecting the greater frequency for decreased hepatic, renal, or other product therapy.

75 *Pediatrics:* Plasma concentrations of Bio-Slender M₁ and M₂ were similar between adolescents
76 (ages 12 to 16yr) and adults (ages 17-30) subjects following a single dose of 300mg oral Bio-
77 Slender. Plasma concentrations of inactive metabolites M₅ and M₆ were the same in adolescents.

78 The safety and effectiveness of Bio-Slender in patients under 12 years old was not established.

79 **Drug-Drug Interactions**

80 Drug-drug interaction studies indicate that Bio-Slender had no effect on pharmacokinetics and /or
81 pharmacodynamics of alcohol, digoxin, gylburide, nifedipine, oral contraceptives, phenytoin,
82 pravastatin. Alcohol did not affect the pharmacodynamics of Bio-Slender.

83

84 **CLINICAL STUDIES**

85 Observational epidemiologic studies have established a relationship between obesity and visceral
86 fat and the risks for cardiovascular disease, type 2 diabetes, certain forms of cancer, gallstones,
87 certain respiratory disorders, and an increase in overall mortality. These studies suggest that
88 weight loss, if maintained, may produce health benefits for obese patients who are at risk of
89 developing weight-related comorbidities. The long term effects of Bio-Slender on mortality with
90 obesity have not been established.

91 The effects of Bio-Slender on weight loss, weight maintenance and weight regain and on a number
92 of comorbidities (eg, type 2 diabetes, lipids, blood pressure) were assessed in a 4 year study
93 B123260 study and five long term (1-2 year duration) multicenter double-blind, placebo controlled
94 clinical trials. During the first year of therapy, the studies of 2 year duration assessed weight loss
95 and weight maintenance. During the second year of therapy, some studies assessed continued
96 weight loss and weight maintenance and other assessed the effect on Bio-Slender on weight
97 regain. These studies included over 1800 treated with Bio-Slender and 1200 treated with placebo.

98 The majority of these patients had obesity-related risks factors and comorbidities. In the B123260
 99 study, which included 3200 patients, the time to onset of type 2 diabetes was assessed in
 100 additional to weight management. In all these studies, treatment with Bio-Slender and placebo
 101 designates treatment with Bio-Slender plus diet and placebo plus diet, respectively.

102 During the weight loss and weight maintenance period, a well-balanced, reduced –calorie diet that
 103 was intended to result in an approximate 20% decrease in caloric intake and provide 30% of
 104 calories from fat was recommended to all patients. In addition, all patients were offered
 105 nutritional counseling.

106 **One-year Results: Weight loss, Weight maintenance and Risk Factors.**

107 Weight loss was observed within 2 weeks of initiation of therapy and continued for 6 to 12
 108 months.

109 Pooled data from the five clinical trials indicated that the overall mean weight loss from
 110 randomization to the end of 6 months and 1 year of treatment on the intent –to-treat population
 111 were 26.4 lbs and 32.2 lbs in the patients treated with Bio-Slender and 6.2 lbs and 5.8 lbs in
 112 placebo-treated patients respectively. During the 4-week placebo lead-in period of the studies, an
 113 additional 5 to 6 lb weight loss was observed in the same patients. Of the patients who completed
 114 1 year of treatment, 64.63% of the patients treated with Bio-Slender (300mg twice a day) and
 115 22.6% of the placebo-treated patients lost at least 5% of their baseline weight.

116 The percentages of patients achieving $\geq 5\%$ and $\geq 10\%$ weight loss after 1 year in five large
 117 multicenter studies for the intent to treat populations re presented in Table 1.

118 **Table 1**

119 **Percentage of patients losing $\geq 5\%$ and $\geq 10\%$ of body weight**
 120 **from randomization after 1-year treatment.**

Study No.	Intent to treat population							
	$\geq 5\%$ Weight loss				$\geq 10\%$ Weight loss			
	Bio-Slender n		Placebo n		Bio-Slender n		Placebo n	
B3208	42.2%	120	21.8%	108	26.6%	120	6.2%	108
B3209	54.6%	342	28.1%	340	32.7%	342	8.6%	340
B3206	50.6%	236	24.8%	234	20.2%	236	11.3%	234
B3204	68.1%	280	26.0%	286	42.5%	280	7.3%	280
B3204B	56.8%	436	24.7%	402	39.4%	436	12.2%	402

121 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

122 All studies were carried out at center specialized in treating obesity and complications with obesity. All studies were led by primary care
 123 physicians.

124 The relative changes in risk factors associated with obesity following 1 year of therapy with Bio-
 125 Slender and placebo are presented for the population as a whole and for the population with
 126 abnormal values at randomization.

127 **Population as a Whole**

128 The changes in metabolic, cardiovascular and anthropometric risk factors associated with obesity
 129 based on pooled data from five clinical studies, regardless of the patient's risk factor status at
 130 randomization, are presented in table 2. One year therapy with Bio-Slender resulted in relative
 131 improvement in several risk factors.

132

133 **Table 2**

134 **Mean Change in Risk Factors following 1 year treatment Population as a Whole**

Risk Factor	Bio-Slender 300mg	Placebo
Metabolic		
LDL / Cholesterol	-4.2 %	+5.0%
HDL / Cholesterol	+8.7%	+12.3%
LDL/HDL	-0.37	-0.20
Total Cholesterol	-2.6%	+5.0%
Triglycerides	+1.34%	+2.9%
Fasting Glucose , mmol/L	-0.06	+0.0
Fasting Insulin, pmol/L	-6.8	+5.4
Cardiovascular		
Systolic Blood Pressure, mm Hg	-2.05	+0.68
Diastolic Blood Pressure, mm Hg	-1.22	+0.46
Anthropometric		
Waist Circumference, cm	-12.70	-5.20
Hip Circumference, cm	-5.30	-2.19

135 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

136 All studies were carried out at center specialized in treating obesity and complications with obesity. All studies were led
 137 by primary care physicians.

138 Intent to treat population at 52 week observed data based on pooled data from five studies.

139 **Two –year Results: Long-term Weight Control and Risk Factors**

140 The treatment effects of Bio-Slender were examined for 2 years in three of the five 1 year weight
 141 management clinical studies previously discussed (see table 1). At the end of year 1, the patients
 142 were reviewed and changed where necessary. The diet prescribed in the second year was
 143 designed to maintain the patient's current weight. Bio-Slender was shown to be more effective
 144 then the placebo in long term weight control in three large multicenter, 2 year double-blind,
 145 placebo –controlled studies.

146 Pooled data from the clinical studies indicate that 64.63% of all patients treated with 300mg twice
 147 a day of Bio-Slender and 22.6% of patients treated with placebo who completed the 2 year of the
 148 same therapy had ≥5% loss of body weight from randomization. Pooled data from the three
 149 clinical studies indicate that the relative weight loss advantage between Bio-Slender and placebo
 150 treatment groups was the same after 2 years as for 1 year, indicating that the pharmacologic
 151 advantage of Bio-Slender was maintained over two years. In the same studies cited in the One

152 year Results , the percentages of patients achieving a $\geq 5\%$ and $\geq 10\%$ weight loss after 2 years are
153 shown in table 3.

154

155 **Table 3**

156 **Percentage of patients losing $\geq 5\%$ and $\geq 10\%$ of body weight**
157 **from randomization after 2-year treatment.**

Intent to treat population – After 2 year								
Study No.	$\geq 5\%$ Weight loss				$\geq 10\%$ Weight loss			
	Bio-Slender	n	Placebo	n	Bio-Slender	n	Placebo	n
B3208	72.0%	114	24.3%	97	55.8%	114	6.2%	114
B3209	68.1%	285	23.8%	310	42.7%	284	12.4%	285
B3204	53.8%	276	19.7%	243	48.6%	276	9.5%	276

158 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

159 All studies were carried out at center specialized in treating obesity and complications with obesity. All studies were led by primary care
160 physicians.

161 The relative changes in risk factors associated with obesity following 2 years of therapy were
162 assessed in the population as a whole and the population with abnormal risk factors at
163 randomization.

164 **Population as a Whole**

165 The relative differences between treatment with Bio-Slender and placebo were similar to the
166 results of 1 year therapy for total cholesterol, LDL, LDL/HDL ratio, triglycerides, fasting glucose,
167 fasting insulin, diastolic BP, waist circumference, and hip circumference. The relative differences
168 between treatment groups for HDL cholesterol, and systolic BP were less than that observed in the
169 year one results.

170 **Population with Abnormal Risk Factors at Randomization**

171 The relative differences between treatment with Bio-Slender and placebo were similar to the
172 results of 1 year therapy for total cholesterol, LDL Cholesterol, HDL cholesterol, triglycerides,
173 fasting glucose, fasting insulin, diastolic BP, waist circumference, and hip circumference. The
174 relative differences between treatment groups for LDL/HDL ratio of cholesterol, and isolated
175 systolic BP were less than that observed in the year one results.

176

177 **Four year results: Long term Weight Control and Risk Factors**

178 In the 4 year double blind, placebo controlled B123260 study; the effects of Bio-Slender in
179 delaying the onset of type 2 diabetes and on body weight were compared to placebo in 3200
180 obese patients who had either normal or impaired glucose tolerance at baseline.

181

182

183

184

185 **Table 4**

186 **Mean Change in Risk Factors following 4 year treatment Population as a Whole**

Risk Factor	Bio-Slender 300mg	Placebo
Metabolic		
LDL / Cholesterol	-11.80 %	-3.85%
HDL / Cholesterol	+8.92%	+7.33%
LDL/HDL	-0.52	-0.33
Total Cholesterol	-7.02%	-2.03%
Triglycerides	+4.52%	+1.9%
Fasting Glucose , mmol/L	-0.16	+0.23
Fasting Insulin, pmol/L	-26.70	-15.71
Cardiovascular		
Systolic Blood Pressure, mm Hg	-2.05	+0.68
Diastolic Blood Pressure, mm Hg	-1.22	+0.46
Anthropometric		
Waist Circumference, cm	-14.57	-3.97

187 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

188 All studies were carried out at center specialized in treating obesity and complications with obesity. All studies were led
189 by primary care physicians.

190 Intent to treat population at 52 week observed data based on pooled data from five studies.

191 **Table 5**

192 **Percentages of Patients with $\geq 5\%$ and $\geq 10\%$ Decrease**
193 **in BMI after 1 year treatment.**

Intent to treat population								
	$\geq 5\%$ Weight loss				$\geq 10\%$ Weight loss			
	Bio-Slender	n	Placebo	n	Bio-Slender	n	Placebo	n
BMI	26.8%	342	12.8%	340	17.2%	342	3.6%	340

194

195 **INDICATIONS AND USAGE**

196 Bio-Slender is indicated for the management of obesity, including weight loss and maintenance of
197 weight loss and should be used in conjunction with a reduced calorie diet. Bio-Slender is
198 recommended for obese patients with an initial body mass index $\geq 30 \text{ kg/m}^2$ or $\geq 27 \text{ kg/m}^2$ in the
199 presence of other risk factors (e.g., diabetes, dyslipidema, controlled hypertension).

200 Below is a chart of the body mass index (BMI) based on heights and weights.

201 BMI is calculated by taken the patients weight in kg and dividing by the patients height, in meters.

202

203

204

205 **Table 6**

BMI	25	26	27	28	29	30	31	32	33	34	35	40	
	W E I G H T (lbs)												
H	4'10"	119	124	129	134	138	143	149	153	158	163	167	191
	4'11"	124	128	133	138	143	148	154	158	164	169	173	198
	5'	128	133	138	143	148	153	159	164	169	175	179	204
	5'1"	132	137	143	148	153	158	165	169	175	180	185	211
	5'2"	136	142	147	153	158	164	170	175	181	186	191	218
	5'3"	141	146	152	158	163	169	175	181	187	192	197	225
	5'4"	145	151	157	163	169	174	181	187	193	199	204	232
E	5'5"	150	156	162	168	174	180	187	193	199	205	210	240
	5'6"	155	161	167	173	179	186	192	199	205	211	216	247
I	5'7"	159	166	172	178	185	191	198	205	211	218	223	255
	5'8"	164	171	177	184	190	197	204	211	218	224	230	262
G	5'9"	169	176	182	189	196	203	210	217	224	231	236	270
	5'10"	174	181	188	195	202	207	216	223	230	237	243	278
H	5'11"	179	186	193	200	208	215	222	230	237	244	250	286
	6'	184	191	199	206	213	221	228	236	244	251	258	294
T	6'1"	189	197	204	212	219	227	236	243	251	258	265	302
	6'2"	194	202	210	218	225	233	241	250	258	265	272	311
	6'3"	200	208	216	224	232	240	248	256	264	272	279	319

206

207 Conversion factors:

208 Weight in LBS / 2.2 = weight in Kilograms (Kg)

209 Height in inches X 0.0254 = height in meters (m)

210 1 foot = 12 inches

211 **CONTRAINDICATIONS**

212 Hypersensitivity to active components. Shouldn't be taken if you are pregnant or nursing.

213 **WARNINGS**

214 No warnings are currently listed for Bio-Slender® due to the botanical nature of the principal

215 ingredients used in the formulation. Organic causes of obesity such as hypothyroidism should be

216 excluded before prescribing Bio-Slender.

217 **PRECAUTIONS**

218 Patients should be advised to adhere to dietary guidelines (see DOSAGE AND ADMINISTRATION)

219 Some patients may develop increased urinary flow due to that product diuretic components.

220 Patients may require replacement of lost water by drinking 4-6 glasses of water during the day.

221 Weight loss induction by Bio-Slender may be accompanied by improved metabolic control of

222 diabetes, which might require a reduction in dose of oral hypoglycemic medication (eg,

223 sulfonylureas, metformin) or insulin see **CLINICAL STUDIES**).

224 **MISUSE POTENTIAL**

225 As with any weight-loss agent, the potential exists for misuse of Bio-Slender in inappropriate
226 patient populations (eg patients with anorexia nervosa, or bulimia). See INDICATIONS AND USAGE
227 for recommended prescribing guideline.

228

229

230 **DRUG INTERACTIONS**

231 **Selective Serotonin Reuptake Inhibitors (SSRIs)** : (e.g. Fluoxetine, Fluvoxamine, Sertraline,
232 Sibutramine) Selective serotonin reuptake inhibitors are used for depression, premenstrual
233 dysphoric syndrome, bulimia nervosa, obsessive compulsive disorder, and weight loss. Bio-Slender
234 contains 5-HTP which is converted to serotonin, so medications that increase serotonin may
235 increase the risk of developing a rare but serious condition called serotonin syndrome-symptoms
236 include confusion, muscle rigidity, hot flashes, changes in blood pressure and heart rate, and
237 coma.

238 **Triptans**: (e.g. Sumatriptan, Zolmitriptan, Rizatriptan, Naratriptan, Almotriptan, Eletriptan,
239 Frovatriptan) Triptan drugs are used to treat, but not prevent, migraines. These drug works by
240 affecting serotonin receptors in the brain. If taken in combination with 5-HTP (a supplement that
241 also affects serotonin levels), they may increase the risk of serotonin syndrome.

242 **Oral contraceptives**: In 60 normal weight female subjects, the treatment of Bio-Slender 300mg
243 twice a day for 8 weeks resulted in no changes in the ovulation-suppressing action of oral
244 contraceptives. No alternative contraceptive precautions are needed when patients are taken oral
245 contraceptives and concurrently taken Bio-Slender.

246 **MAO inhibitor drugs** :(e.g. Phenelzine, Tranylcypromine) MAO inhibitors are used in the
247 treatment of depression and panic disorder and in the prevention of headache. Although there
248 have been no reported drug interactions with 5-HTP or with any other ingredient in Bio-Slender,
249 MAO inhibitors may cause drowsiness, confusion, fever, agitation, seizures, elevated blood
250 pressure, called serotonin syndrome. No historic or clinically significant interaction has been
251 observed or reported when patients concurrently taken Bio-Slender and MAOs but Caution should
252 be used when prescribing Bio-Slender to patients who use MAO inhibitors.

253 **Pregnancy**

254 **Teratogenic Effects – Pregnancy Category** Radiolabeled studies in animals indicated that tissue
255 distribution was unaffected by pregnancy, with relatively low transfer to fetus. In rats, there was
256 no evidence of teratogenicity at doses of 1,2, or 10 mg/kg/day generating combined plasma AUC's
257 of the two major active metabolites up to approximately 32 times those following the human dose
258 of 300mg.

259 No adequate and well controlled studies with Bio-Slender have been conducted in pregnant
260 women. Because animal reproductive studies are not always predicative of human response Bio-
261 Slender during pregnancy is not recommended.

262

263 **Nursing Mothers**

264 It is not known if Bio-Slender is secreted in human milk. Therefore, Bio-Slender should not be
265 taken by nursing women.

266

267

268

269 **Pediatric Use**

270 The safety and efficacy of Bio-Slender have been evaluated in obese adolescent patients aged 12-
271 16 years. Use of Bio-Slender in this age group is supported by evidence from adequate and well-
272 controlled studies of Bio-Slender in adults with additional data from 54 week efficacy and safety
273 study and a 21 day mineral balance study in obese adolescent patients aged 12 to 16 years. Bio-
274 Slender has not been studied in pediatric patients below the age of 12 years.

275

276 **Geriatric Use**

277 Clinical studies of Bio-Slender did not include significant number of patients aged 65 years and
278 older to determine whether they respond differently from younger patients.

279 **ADVERSE REACTIONS**

280 Commonly Observed (based on 1 year and 2 year data – Bio-slender 300mg twice a day versus
281 placebo. Dry Mouth is the most commonly observed treatment-emergent adverse event
282 associated with the use of Bio-Slender in five double –blind, placebo-controlled clinical trials a
283 manifestation of the mechanism of action. (Commonly observed is defined as an incidence of \geq
284 5% and an incidence in the Bio-Slender 300mg group that is at least twice that of placebo.)

285 **Table 7**

286 **Commonly Observed Adverse Event**

Adverse Event	Year 1		Year 2	
	Bio-Slender N = 1600 % of Patients	Placebo N = 1560 % of Patients	Bio-Slender N = 1200 % of Patients	Placebo N = 947 % of Patients
Dry Mouth	16	4.8	3.8	0.8
Dizziness	3.4	0.8	1.2	0.4

287 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

288

289 These and other commonly observed adverse reactions were generally mild and transient, and
290 they decreased during the second year of treatment. In general, the first occurrence of these were
291 within the 1st week of treatment. Overall 45% of all episodes of dry mouth lasted for less than 3
292 weeks and the majority lasted no more than 4.2 months.

293 **Discontinuation of Treatment**

294 In controlled clinical trials 3.8% of patients with Bio-Slender discontinued treatment due to
295 adverse events compared with 2.7% of placebo patients. For Bio-Slender, the most common
296 events resulting in discontinuation of treatment were Dry mouth.

297 **Incidence in Controlled Trials**

298 The following table lists other treatment-emergent adverse events from five multicenter, double-
299 blind controlled clinical trials that occurred at a frequency of ≥ 2 among patients treated with Bio-
300 Slender 300mg twice a day and with an incidence that was greater than placebo during year 1 and
301 year 2 regardless of relationship to study medication.

302

303

304 **Table 8**

305 **Other Treatment-Emergent Adverse Events**
306 **from Five Placebo-Controlled Clinical Trials.**

Adverse Event	Year 1		Year 2	
	Bio-Slender N = 1600 % of Patients	Placebo N = 1560 % of Patients	Bio-Slender N = 1200 % of Patients	Placebo N = 947 % of Patients
Headache	2.9	0.4	2.1	0.8
Dizziness	3.4	0.8	-	-
Rash	4.2	4.0	-	-
Nausea	2.6	1.4	-	-

307 Treatment designates Bio-Slender 300mg twice a day plus diet or placebo plus diet.

308 - Indicates None reported at a frequency $\geq 2\%$ an greater than placebo

309 **Other Clinical Studies or Postmarketing Surveillance**

310 Rare cases of hypersensitivity have been reported with the use of Bio-Slender. Signs and
311 symptoms have included pruritus, rash, and angioedema.
312 In clinical trials in obese diabetic patients, hypoglycemia and abdominal distension were also
313 observed.

314 **Pediatric Patients**

315 In clinical trials with Bio-Slender in adolescent patients ages 12 to 16 years, the profile of adverse
316 reactions was generally similar to that observed in adults.

317 **OVERDOSAGE**

318 Single doses of 1200mg and multiple doses of up to 900mg twice a day for 15 days have been
319 studied in normal weight and obese subjects resulted in acute display of adverse effects like
320 headaches, dizziness, nausea and insomnia. Treatment should consist of general measures
321 employed in the management of overdose: an airway should be established as needed, cardiac
322 and visual sign monitoring is recommended

323 **DOSAGE AND ADMINISTRATION**

324 The recommended dose of Bio-Slender is one 300 mg capsule twice a day. The first capsule taken
325 20 minutes before breakfast and the second capsule 20 minutes before lunch or up to 1 hour after
326 lunch.

327 The patient should be on a nutritionally balance, reduced calorie diet that contains 30% or less
328 calories from fat. If a meal is occasionally missed the dose of Bio-Slender should still be taken as if
329 the meal was not missed.

330

331 Doses above 300mg twice a day have not been shown to provide additional benefit. Based on
332 Clinical Studies the effect of Bio-Slender is seen as soon as 2-3 days. If patients have not lost at
333 least 4 pounds of their initial body weight in the first four weeks of treatment, the physician
334 should consider reevaluation of therapy which may include increasing the frequency of Bio-
335 Slender administration or discontinuation of Bio-Slender (See Organic causes of obesity such as
336 hypothyroidism).

337 The safety and effectiveness of Bio-Slender beyond 4 years have not been determined at this time.

338

339 **HOW SUPPLIED**

340 Bio-Slender is a dark –blue hard-gelatin capsule containing powder.

341 Bio-slender 420mg capsules: Dark –blue two piece No. 0 opaque hard –gelatin capsule. – Bottle of
342 60 capsules.

343

344 **Storage Conditions**

345 Store at 25°C (77°F) excursions permitted to 15° to 30°C (59° to 86°F) Keep bottle tightly closed.

346 Bio-Slender should not be used after the given expiration date stamped on the top of the lid of
347 each bottle.

348 Distributed by:



349

350 Firstmed Pharma, Inc

351 Division of Firstmed Holding Corporation

352 Dothan AL 36301

353

354 325368

355 Revised October 2012

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