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*APPLICATION NUMBER:*

**21-543**

**CLINICAL PHARMACOLOGY AND  
BIOPHARMACEUTICS REVIEW(S)**

**OFFICE OF CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW**

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NDA: 21-543	Submission Date(s): 08/07/02, 09/03/02, 12/03/02, 06/17/03
Brand Name	Striant™ (testosterone buccal system) mucoadhesive
Generic Name	Testosterone
Reviewer	Venkat Jarugula, Ph.D.
Team Leader	Ameeta Parekh, Ph.D.
OCPB Division	Division of Pharmaceutical Evaluation II
ORM division	Division of Reproductive & Urologic Drug Products
Sponsor	Columbia Research Laboratories
Relevant IND(s)	60,906
Submission Type; Code	3S
Formulation; Strength(s)	Buccal mucoadhesive tablets, 30 mg
Dosing regimen	Twice daily
Indication	

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**1. Executive Summary**

Striant™ (testosterone buccal system) is a controlled and sustained release buccal mucoadhesive tablet containing 30 mg testosterone in a matrix of bioadhesive polymers, corbomer and polycarbophil. Striant™ is applied to gum tissue above the incisors twice daily (morning and evening). Each tablet is supposed to be kept in place for 12 hour dosing interval. Striant™ is indicated for replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone i.e., primary hypogonadism and hypogonadotropic hypogonadism.

The NDA is organized according to the common technical document format. In Module 2.7 Clinical pharmacology and Biopharmaceutics section, four phase I pharmacokinetic studies investigating the single and multiple dose pharmacokinetics of Striant were submitted. In addition, since serum testosterone is the primary endpoint for this indication, the testosterone pharmacokinetic results from a phase III pivotal safety and efficacy study of 12 weeks duration is also reviewed from the clinical section of the NDA.

**2. Recommendation**

NDA 21543 for Striant™ (mucoadhesive buccal tablets) is acceptable from Clinical Pharmacology and Biopharmaceutics perspective. The labeling comments outlined in the Clinical pharmacology section of the labeling should be communicated to the sponsor as appropriate.

### 3. Phase IV studies:

No phase IV studies are recommended from Clinical Pharmacology and Biopharmaceutics perspective.

### 4. Summary of Clinical Pharmacology and Biopharmaceutics findings

Following single application of Striant, mean serum testosterone (T) levels increased from baseline to within normal physiologic range in young healthy men (300 to 1050 ng/dl) within 3 to 4 hours and the T levels are consistently maintained within normal range for 12 hours after application. T levels declined to below normal range by two hours after removal of the buccal tablet.

Following multiple dosing, the steady state T levels were reached by the second day of application and there was no significant accumulation.

The serum T profile of Striant has been shown to be consistent across the multiple clinical studies in the NDA.

Based on the phase III study of 12 weeks duration, serum T levels were replaced within normal range in 72% of the evaluable patients according to the pre-specified primary endpoint ( $C_{avg(0-12h)}$  and  $C_{avg(12-24)}$  between 300 to 1050 ng/dl and average trough (of  $C_{12h}$  and  $C_{24h}$ ) > 300 ng/dl). About 87% of the patients had their average steady state serum T levels within the normal range.

There were 5 patients who had their  $C_{max}$  >20 ng/ml and 9 patients with  $C_{max}$  >15ng/ml out of a total of 82 patients who completed the study. The label should recommend that the patient's serum T levels should be measured at about four weeks after initiation of Striant.

The average serum T concentrations are 12.7% higher in patients with age group  $\geq 65$  years compared to those with <65 years of age. Correspondingly the T/DHT ratio was about 16% lower with  $\geq 65$  years age group. However, these differences don't seem to be of any clinical relevance because the average serum T levels were still within normal physiological range

Although no specific food effect study was conducted with Striant, the data from Phase 3 studies showed that the intake of food or beverages did not affect the serum testosterone concentrations.

The effect of toothbrushing, mouthwash, chewing gum and alcoholic beverages on the use and absorption of Striant was not specifically investigated in controlled studies. However, Phase 3 studies permitted patients to do these activities indicating the use of Striant was not significantly affected by these activities.

Based on the *in vitro* dissolution, Striant buccal mucoadhesive tablets release testosterone slowly and continuously for 12 hours. The following *in vitro* dissolution method and release specifications are found acceptable:

Method:

Apparatus: USP II paddle

Medium: \_\_\_\_\_

Rotation: \_\_\_\_\_

Sampling: \_\_\_\_\_

Release specifications: \_\_\_\_\_ at \_\_\_\_\_, at \_\_\_\_\_, at \_\_\_\_\_ and not less than \_\_\_\_\_ at \_\_\_\_\_. Sponsor agreed to implement these specifications.

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## **Question Based Review**

### **5.1. General Attributes**

**What are the highlights of the chemistry and physico-chemical properties of the drug substance, and the formulation of the drug product?**

Testosterone is an endogenous sex steroid hormone responsible for normal growth and development of the male sex organs and for the maintenance of secondary sex characteristics. It is practically insoluble in water and fatty oils, but is freely soluble in alcohol and methylene chloride.

Striant is a buccal mucoadhesive tablet formulated to slowly release testosterone in the buccal cavity. (see details in Formulation section on page 17).

**What is the proposed mechanism of action?**

Male hypogonadism results from insufficient production of testosterone and is characterized by low serum testosterone concentrations. Symptoms reported to be associated with hypogonadism include impotence and decreased sexual desire, fatigue and loss of energy, mood depression, regression of secondary sexual characteristics and osteoporosis.

The aim of the testosterone replacement products such as Striant is to replace the serum testosterone in hypogonadal men into normal physiological range seen in young adult healthy males leading to the presumed benefit of relieving the symptoms associated with deficiency testosterone.

### **5.2. Clinical Pharmacology**

**What is the basis for selecting the response endpoints, i.e., clinical or surrogate endpoints, or biomarkers and how are they measured in clinical pharmacology and clinical studies?**

Since the indication is testosterone replacement in hypogonadal men who are deficient in testosterone levels, the primary endpoint for clinical studies is the replacement of plasma concentration of testosterone in the normal physiologic range for young healthy adult men.

**Are the active moieties in the plasma (or other biological fluid) appropriately identified and measured to assess pharmacokinetic parameters and exposure response relationships?**

Yes. The active moiety, testosterone and the active metabolite dihydrotestosterone (DHT) were measured following administration of Striant (refer to analytical methods section).

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## 5.2.1. Pharmacokinetics

What are the pharmacokinetic characteristics of Striant after single and multiple dosing?

### Single dose pharmacokinetics

Single dose pharmacokinetics of Striant buccal bioadhesive tablets was studied following application period of 12 h (Study COL-1621-02) and 24 h (Study COL-1621-06).

The mean serum concentration profiles of total testosterone are illustrated in the following two figures:

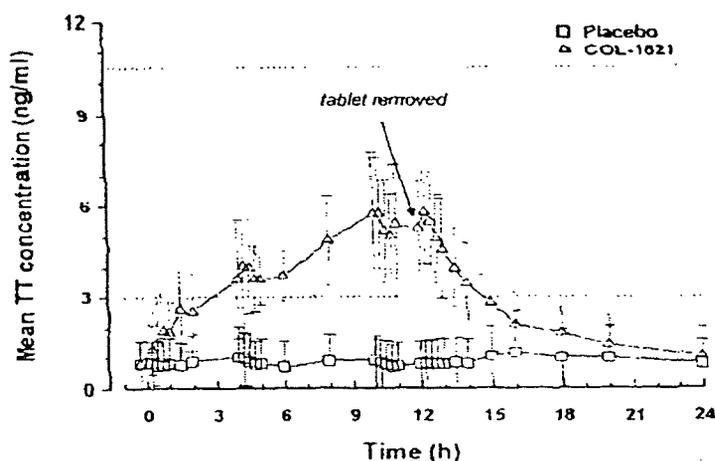


Figure 1. Mean (SD) serum total testosterone concentrations following single application Striant 30 mg buccal bioadhesive or placebo tablets to testosterone-deficient men (n=12) (Study COL-1621-02). (Horizontal dotted lines represent lower and upper normal physiologic range of 3 to 10.5 ng/ml in this and other graphs).

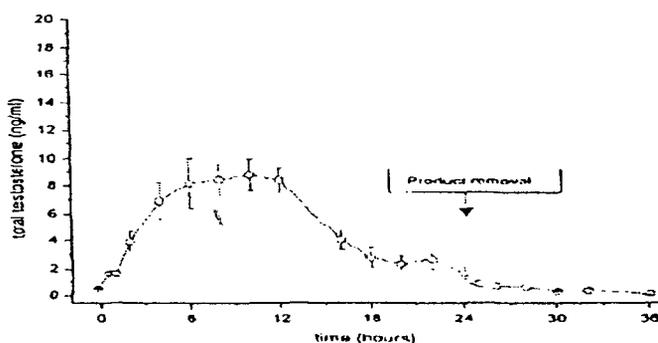


Figure 2. Mean serum total testosterone levels with single application of Striant 30 mg for 24 hours to healthy premenopausal women (n=8) (Study COL-1621-06).

The above two single dose studies have shown that following single application of Striant buccal mucoadhesive tablet, serum testosterone levels increased gradually after initial application of Striant tablet and reached maximum concentration after 10 to 12 hours. The mean serum total testosterone levels rise above the baseline levels to normal physiological levels of healthy young men (3 to 10.5 ng/ml) within 3 to 4 hours after initiation of dosing. The serum T levels were maintained up to 14 hours with either 12 or 24 hour application. Therefore, the dosing interval of 12 hr is justified for Striant.

### Multiple dose pharmacokinetics

A multiple dose study for seven days in twelve testosterone deficient men investigated the steady state pharmacokinetics of Striant.

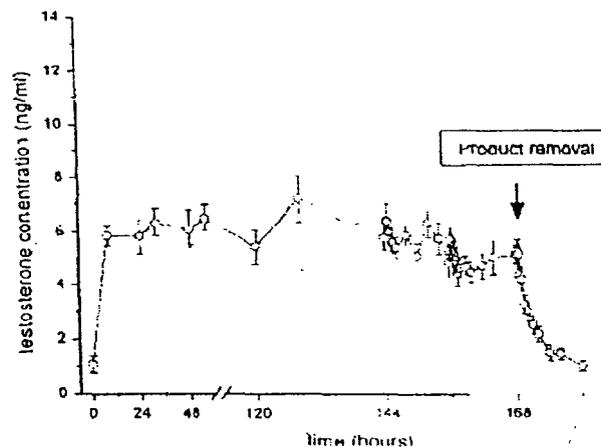


Figure 3. Mean ( $\pm$ SEM) serum total testosterone levels during repeated twice daily dosing (7 days) of Striant 30 mg. (Study COL-1621-03).

Following the application of first dose of Striant 30 mg, in the first sampling time of 8 hours on Day 1, the mean serum T levels increased from the baseline level of 1.08 ng/ml to 5.85 ng/ml. Mean serum T levels were consistently maintained within normal physiologic limits of you healthy males (3 to 10.5 ng/ml) throughout the 7-day dosing period. The serum T levels declined below normal levels at about 2 hours after removal of the last dose.

The average serum T levels were within normal range for all 12 patients. Cmax during the entire 7-day dosing period was higher or equal to the upper normal range ( $\geq 10.5$  ng/ml) in 5 patients and was within normal reference range for 7 patients.

Following multiple dosing, steady state T levels were reached by the second day of dosing and there is no significant accumulation of concentrations.

### 5.2.2. Pivotal efficacy study (COL-1621-05):

This open-label, single arm study with enrollment of 98 testosterone deficient male patients receiving study treatment of testosterone buccal adhesive 30 mg twice a day for 12 consecutive weeks. A total of nine investigative sites in the USA participated in this study.

The primary efficacy endpoint was defined as the percentage of treatment responders, defined as patients having time-averaged steady-state total testosterone serum concentrations ( $C_{avg(0-12)}$  and  $C_{avg(12-24)}$ ) within physiologic range for healthy adult males (300 to 1050 ng/dl) and the average of the total serum T concentrations at the end of each of the last two consecutive 12-hour dosing interval at Week 12 ( $C_{12/24(avg)} \geq 300$  ng/dl).

Sponsor proposed a supplemental primary efficacy endpoint as percentage of the treatment responders, defined as patients having time-averaged steady-state total serum T concentration over the last two consecutive 12-hour dosing intervals ( $C_{avg(0-24)}$ ) within the physiologic range (300 to 1050 ng/dl).

The study enrolled 98 patients with testosterone deficiency (<2.5 ng/ml) and 84 completed the study. A total 14 patients discontinued from the study due to: patient desire to withdraw (10 patients; 10.2%); protocol violation (2 patients; 2.0%); missed appointments (investigator-initiated withdrawal) (1 patient; 1.0%); and death from motor vehicle accident (1 patient; 1.0%)

In addition, sponsor reported that two patients were excluded from the PK analysis because these patients were non-compliant with the treatment schedule at Visit 6 (week 12, when PK sampling was done)

Table 1. Percentage of treatment responders at week 12 of buccal testosterone treatment

Treatment responders	%(N)	95% CI
Primary efficacy responders	72.0% (59)	60.9% - 81.3%
$C_{avg(0-12)}$ within physiologic range	84.1% (69)	
$C_{avg(12-24)}$ within physiologic range	80.5% (66)	
$C_{12/24(avg)}$ within physiologic range (Trough)	90.2% (74)	
Supplemental efficacy responders ( $C_{avg(0-24)}$ ) within physiologic range	86.6% (71)	77.3% - 93.1%

Table 2. Mean (SD) serum total testosterone pharmacokinetic parameters

PK parameter	All patients (n=82)	Primary efficacy	
		Responders N=59	Non-responders (n=11)
$C_{avg(0-12)}$ (ng/ml)	5.41 (2.36)	5.58 (1.61)	4.97 (3.66)
$C_{avg(12-24)}$ (ng/ml)	4.99 (2.10)	5.34 (1.68)	4.08 (2.78)
$C_{avg(0-24)}$ (ng/ml)	5.20 (2.05)	5.46 (1.44)	4.53 (3.07)
$C_{min(0-24)}$ (ng/ml)	2.91 (1.30)	3.15 (1.20)	2.30 (1.37)
$C_{max(0-24)}$ (ng/ml)	9.69 (4.42)	9.96 (3.41)	9.02 (6.37)
%T <sub>24(dur)</sub>	75.45 (27.77)	88.90 (14.18)	40.96 (23.82)

Based on the primary efficacy analysis at week 12 of the treatment with Striant buccal T mucoadhesive, the percentage of primary efficacy responders (patients who have  $C_{avg(0-12)}$  and  $C_{avg(12-24)}$  within 300 to 1050 ng/dl and  $C_{12/24(avg)} \geq 300$  ng/dl) was 72% (95 CI: 60.9% - 81.3%) and the percentage of responders who have their  $C_{avg(0-24)}$  was 86.6% (95 CI: 77.3% - 93.1%).

The mean percentage of time over the 24-hour sampling interval that serum T concentrations were within the normal range (%T<sub>24(dur)</sub>) or above 300 ng/dl (%T<sub>24(above)</sub>) was at 89% and 91% in responders compared with 41% and 51%, respectively, in non-responders (Table 2).

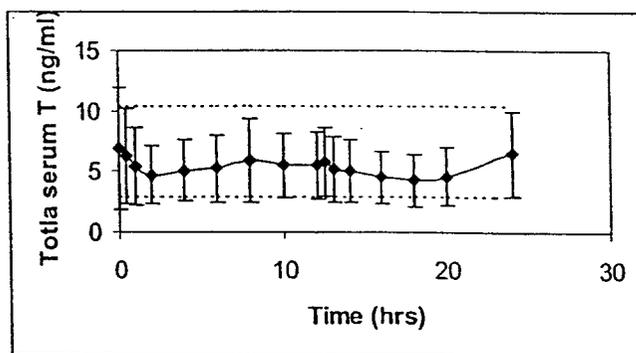


Figure 4. Mean serum (SD) total testosterone concentrations at week 12 of Striant buccal mucoadhesive treatment (Horizontal dotted lines represent lower and upper normal physiologic range of 3 to 10.5 ng/ml in this and other graphs).

Mean serum testosterone levels (Figure 4) for two consecutive dosing intervals at week 12 were within the normal physiologic range.

Overall, Striant buccal T mucoadhesive formulation provides serum T levels for the majority of the patients within the normal physiologic range for adult males.

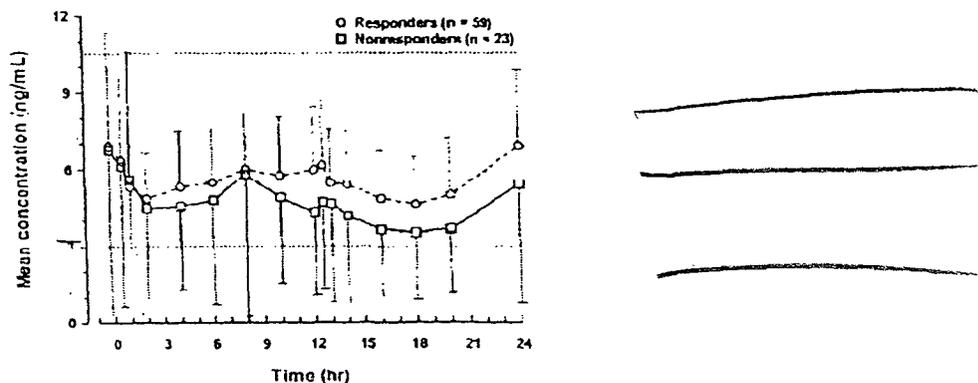


Figure 5. Mean serum T levels in treatment responders vs non-responders (Left panel); and individual average serum T levels for non responders (right panel).

Based on the above figures, it can be noted that majority of the patients who did not meet the primary endpoint criterion had their average serum T concentrations near the low normal range as opposed to 5 patients who had their  $C_{avg}$  above the upper normal limit.

The following table lists the individual patients who have experienced  $C_{max}$  values that are higher than the upper normal limit of 10.5 ng/ml.

Table 3. List of patients with  $C_{max}$  (either 0-12 or 12-24 hr) higher than the upper normal limit (10.5 ng/ml):

Pt No.	$C_{max}012$	$C_{max}1224h$	$c12h$ (trough)	$c24h$ (trough)	$C_{avg}024h$
1002					7.76
1005					16.91
1007					8.33
1009					11.83
2016					8.39
2018					8.86
2021					4.07
4001					6.58
5007					5.09
5032					9.08
6007					6.06
7003					3.97
8002					5.45
8005					7.41

8007					6.52
8020					10.34
8022					7.83
8024					9.77
9002					10.68
9003					5.16

There were 5 patients who had their  $C_{max} > 20$  ng/ml and 9 patients with  $C_{max} > 15$  ng/ml out of a total of 82 patients that completed the study. In most of these patients the high peak concentrations were transient and did not stay for the entire dosing interval. However, as a precaution, the labeling should recommend that serum T levels should be checked after four weeks of therapy to make an informed decision about the performance of the product.

#### Serum dihydrotestosterone (DHT) concentrations:

Serum DHT concentrations were measured at week 12, at predose, 4, 8, 12 and 24 hrs time points.

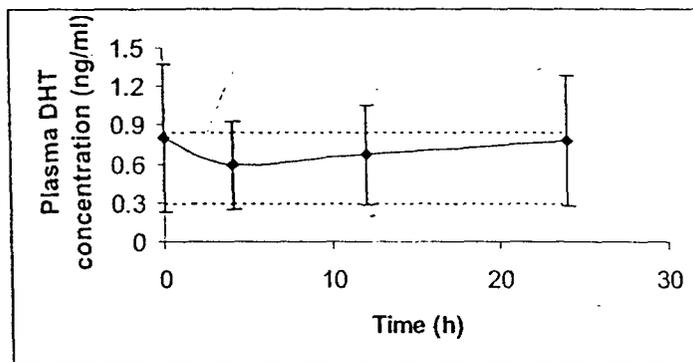


Figure 6. Mean (SD) serum DHT concentrations over two consecutive 12 hr dosing intervals at week 12

The normal physiologic limit of DHT is 0.3 to 0.85 ng/ml. The mean DHT levels, as shown in Figure 6 are within normal limits and the ratio of T/DHT was in the range of 9 to 12. However, there are some individuals with concentrations above the upper normal limit.

#### *In vivo* adhesion performance of Striant:

The frequency of swallowed, missed, dislodged/non-adhering and replaced tablets were summarized in the phase III study (COL-1621-05) using patient comments recorded on their diary. Twenty one (21) patients reported a total of 78 swallowing events, resulting in an incidence of swallowed tablets of 0.49% (78/15,890).

Forty-nine patients reported 362 events of dislodged or non-adhering tablets with an incidence of 2.3%. The number of replaced tablets was initially high at study start (160 tablets /week) and decreased over the course of study to 33 tablets/week at week 12.

Assuming all tablet replacements were due adhesion problems, the incidence of adhesion problems over the course of the 12 week study was low at 4.8%.

#### Consistency of serum T levels across clinical studies:

To see whether Striant is able to provide serum T levels consistently within normal range, the following figure compares the serum levels obtained from three different clinical studies:

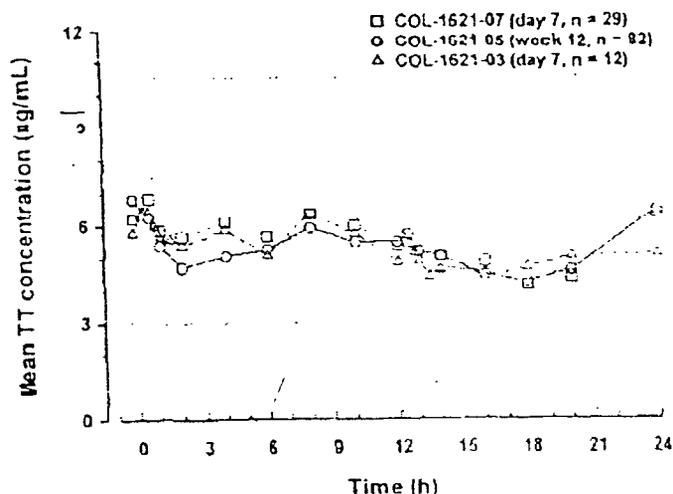


Figure 6. Comparison of mean serum total testosterone concentrations across three clinical studies.

It is evident from the above figure that Striant is able to provide mean serum T levels consistently within normal range of 300 to 1050 ng/dl in different studies.

#### Effects of concomitant medications potentially causing dry mouth on serum testosterone profile:

Sponsor did an exploratory analysis of patients who were on concomitant medications that may cause dry mouth in Study -05 at week 12. In total 36 of 82 patients took medications at week 12 that may potentially cause dry mouth. The exploratory analysis showed that concomitant medications that potentially cause dry mouth did not significantly affect the serum testosterone levels following Striant administration. However, sponsor reported that data regarding the incidence of dry mouth was not collected. So, dry mouth may or may not have occurred with these medications. These data should be interpreted with caution.

#### Effects of age on pharmacokinetic profile of serum testosterone

Pharmacokinetic parameters by age groups of <65 years and ≥65 years are summarized in the Table below:

Table 4. PK parameters by age group (Study COL-1621-05)

PK Parameter	<65 years N=62	≥65 years N=20
Total testosterone $C_{avg(0-24h)}$ (ng/ml)		
Mean (SD)	5.04 (1.89)	5.68 (2.49)
Median	4.67	5.32
Range		
Total testosterone/DHT $AUC_{last}$ ratio		
Mean (SD)	9.72 (3.13)	8.20 (2.21)
Median	8.89	7.43
Range		

The average serum T concentrations are 12.7% higher in patients with age group ≥65 years compared to those with <65 years of age. Correspondingly the T/DHT ratio was about 16% lower with age group. However, these differences don't seem to be of no clinical relevance because the average serum T levels were still within normal physiological range (see figure below).

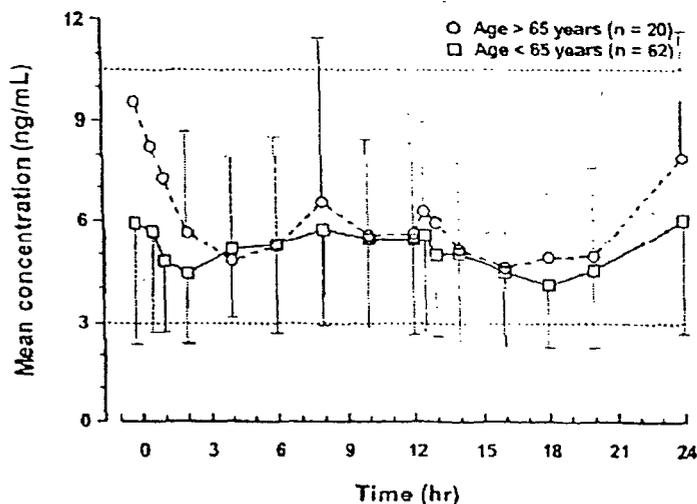


Figure 7. Effect of age on Serum T concentrations following Striant administration at week 12.

Sponsor also explored the effect of gum abnormalities on the pharmacokinetic profiles of serum T and there was no significant difference noted in patients with (n=11) and without (n=71) gum abnormalities

Sponsor reported a small negative correlation between BMI and  $C_{avg(0-24)}$  values ( $r = -0.166$ ). However, there was substantial variability in the data and the small degree of correlation is not clinical significant.

**Comparison to Androgel:**

The serum T profile of Striant was compared with that from Androgel in a randomized, open label, parallel arm study (COL-1621-10 (US)). Thirteen (13) testosterone deficient men received Striant buccal tablets twice daily for two weeks and another group of 13 hypogonadal patients received Androgel (5 mg, lowest approved dose) once a day for two weeks.

The primary endpoint of this study was percentage of patients who have the time averaged steady state serum T levels ( $C_{avg}(0-24h)$ ) within the normal range of 3 to 10.5 ng/ml.

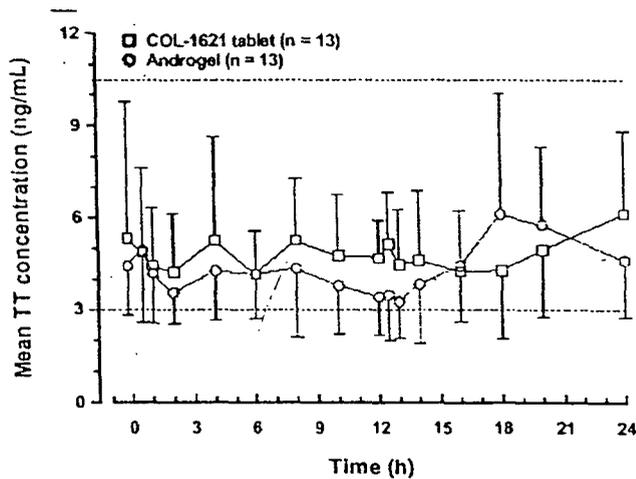


Figure 8. Mean (SD) serum total testosterone concentrations for Striant (COL-1621 tablet) and Androgel groups on Day 14.

	COL-1621 N= 13		Androgel* N= 15		Ratio of LS Means (95% CI)	(p-value)*
	Mean (SD)	%CV	Mean (SD)	% CV		
$C_{avg}(0-24)$ (ng/mL)	4.8 (1.4)	28.1	4.4 (1.4)	31.6	0.904 (0.705, 1.159)	0.406
$C_{avg}(0-12)$ (ng/mL)	4.7 (1.7)	36.2	4.0 (1.4)	34.7	0.836 (0.636, 1.101)	0.190
$C_{avg}(12-24)$ (ng/mL)	4.8 (1.8)	37.7	4.9 (1.9)	39.4	0.983 (0.727, 1.329)	0.906

Reference: Appendix A, Table 3.2.1, Appendix J, Tables 1 and 2

\* Differences in treatment groups are provided via ANOVA on log-transformed data including the effects of treatment group and center

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The mean serum testosterone levels for both Striant and AndroGel were within normal limits at all time points, although based on SD deviation some subjects may have T levels out of the normal range.

Based on the primary endpoint, of the 25 patients in the PP population, there are 92% responders (12 out of 13) in Striant group and 83% (10 out of 12) in AndroGel group who had their average serum T levels within normal physiologic range. It should be noted that AndroGel (5 mg) used in this study was the lowest approved dose has different approved doses and can be titrated based on the serum T levels.

### 5.3. Biopharmaceutics

**How does the intake of food or beverage affect the pharmacokinetics of testosterone following administration Striant buccal tablets?**

#### 5.3.1. Food effect

No specific food effect study was conducted with Striant. However, an exploratory analysis was conducted in the pivotal Phase III study (COL-1621-05) to investigate if the intake food and beverage affected the absorption of testosterone from the buccal tablet. Because meals were ingested during the morning, but not during the evening dosing interval, an exploratory analysis conducted to compare the PK parameters of the morning (with food) versus evening doses (without food) for each patient. The Cavg parameter calculated from partial AUC from the time of breakfast, lunch or dinner to the end of the dosing interval in the AM dosing is compared to the Cavg from corresponding time period from the PM dosing. Cavg calculated from 1 h before and after breakfast and 2 h before and after lunch and dinner are compared within the dosing interval.

Table 5. Mean ratios of Cavg from the AM and PM dosing intervals at week 12

PK parameter	N	Mean	% CV
$C_{avg}(B'-RT)_{12-24}/C_{avg}(B-RT)_{0-12}$	75	0.98	32.9
$C_{avg}(L'-RT)_{12-24}/C_{avg}(L-RT)_{0-12}$	75	1.01	43.1
$C_{avg}(D'-RT)_{12-24}/C_{avg}(D-RT)_{0-12}$	67	1.33	75.6
$C_{avg}(B+1h)/C_{avg}(B-1h)$	26	0.94	21.1
$C_{avg}(L+2h)/C_{avg}(L-2h)$	67	1.05	21.7
$C_{avg}(D+2h)/C_{avg}(D-2h)$	66	0.98	24.3

B, L and D = Time of Breakfast, Lunch and Dinner respectively (AM dosing). B', L' and D' = Relative time (at PM dosing) that corresponds to Breakfast, Lunch and Dinner, respectively.

All comparisons except for the comparison of dinner effect showed minor changes (<7%) in total T concentrations. The Cavg was 33% higher in the evening dose compared to the morning dose at the time of dinner.

These results should be interpreted with caution because of the limited number of samples collected around the time of meal and the potential for other sources of variability.

Since all the meals were taken during the morning dosing interval and no food was given in the evening dosing interval, serum T concentrations are compared in the following figure from the two consecutive dosing intervals.

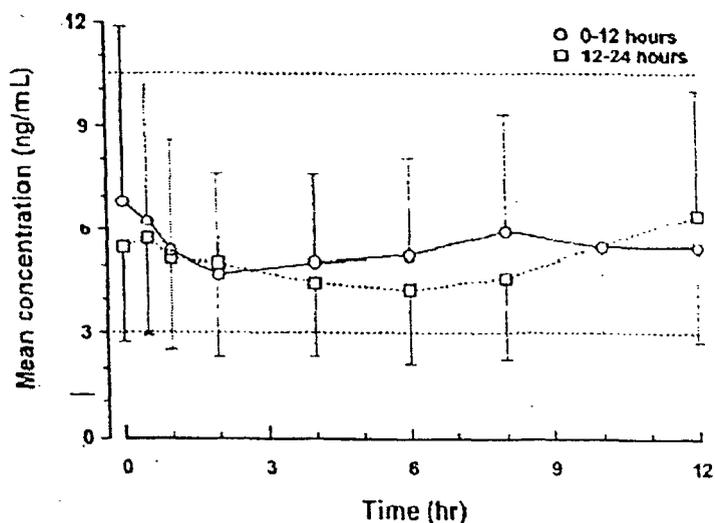


Figure 9. Comparison of mean (SD) serum total testosterone concentration following Striant application in the morning (0-12h, with food) and in the evening (12-24 h, without food)

Based on the above figure and also the pharmacokinetic parameters (see Table 2), the intake of food or beverage did not seem to significantly affect the serum T concentration.

**What is the formulation of Striant buccal mucoadhesive tablets? How is the to be marketed formulation different from the clinical trials formulation?**

### 5.3.2. Formulation

Striant Tablet is a bioadhesive formulation for buccal administration and contains 30 mg of testosterone in a bioadhesive matrix. Testosterone is dispersed in the tablet matrix and diffuses as the matrix hydrates following buccal application, allowing controlled release over at least 12 hours. The buccal bioadhesive is manufactured using conventional tableting technology and is designed with a convex side to sit against the gum and a flat side to sit against cheek.

The bioadhesive properties of the tablet are provided by two polymers, carbomer 934P and polycarbophil. These pharmacopeal polymers are present in the two approved products in the US and throughout Europe: Replens Gel (vaginal moisturizer) and Crinone Progesterone Vaginal Gel (both are products of Columbia Laboratories, Inc).

Table 6. Composition of the to be marketed formulation

Ingredient	Amount (mg) per tablet	%W/W
Active ingredient		
Testosterone	30.000	
Excipients		
Magnesium stearate		



Table 8. *In vitro* dissolution of Striant ( mean and range) (clinical) and commercial batches

Batch No.				
scale batches				
0119910				
0.139910				
0010003				
0040010				
Commercial scale batches				
020105				
0030105				
0040105				

Figure 9. *In vitro* dissolution profiles of Striant (batch 0010003, n=6 tablets)

The *in vitro* release from the drug product is slow and consistent for (clinical) Based on the release data from the clinical trial batches; the following specifications are recommended: (clinical) and not less than (clinical) at (clinical)

Are the analytical methods used to determine testosterone and dihydrotestosterone adequate to characterize the pharmacokinetics of Striant?

#### 5.3.4. Analytical Methods

Serum samples from the pivotal phase III clinical study (COL-1621-05) were analyzed at Serum concentrations of total testosterone and dihydrotestosterone (DHT) were measured by radioimmunoassay (RIA) Free (unbound) testosterone is measured by

Table 7. Assay validation parameters

Analyte	Method	LOQ	Precision	Accuracy (%difference from nominal)
Total Testosterone	RIA	— ng/ml	<10%	-0.3 to 7.5%
DHT	RIA	— ng/ml	<11.45%	-7.5 to 0.4%

For testosterone RIA method, L

The assay methods for serum T and DHT are acceptable for characterizing the pharmacokinetics of Striant.

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