Pr DIVIGEL®

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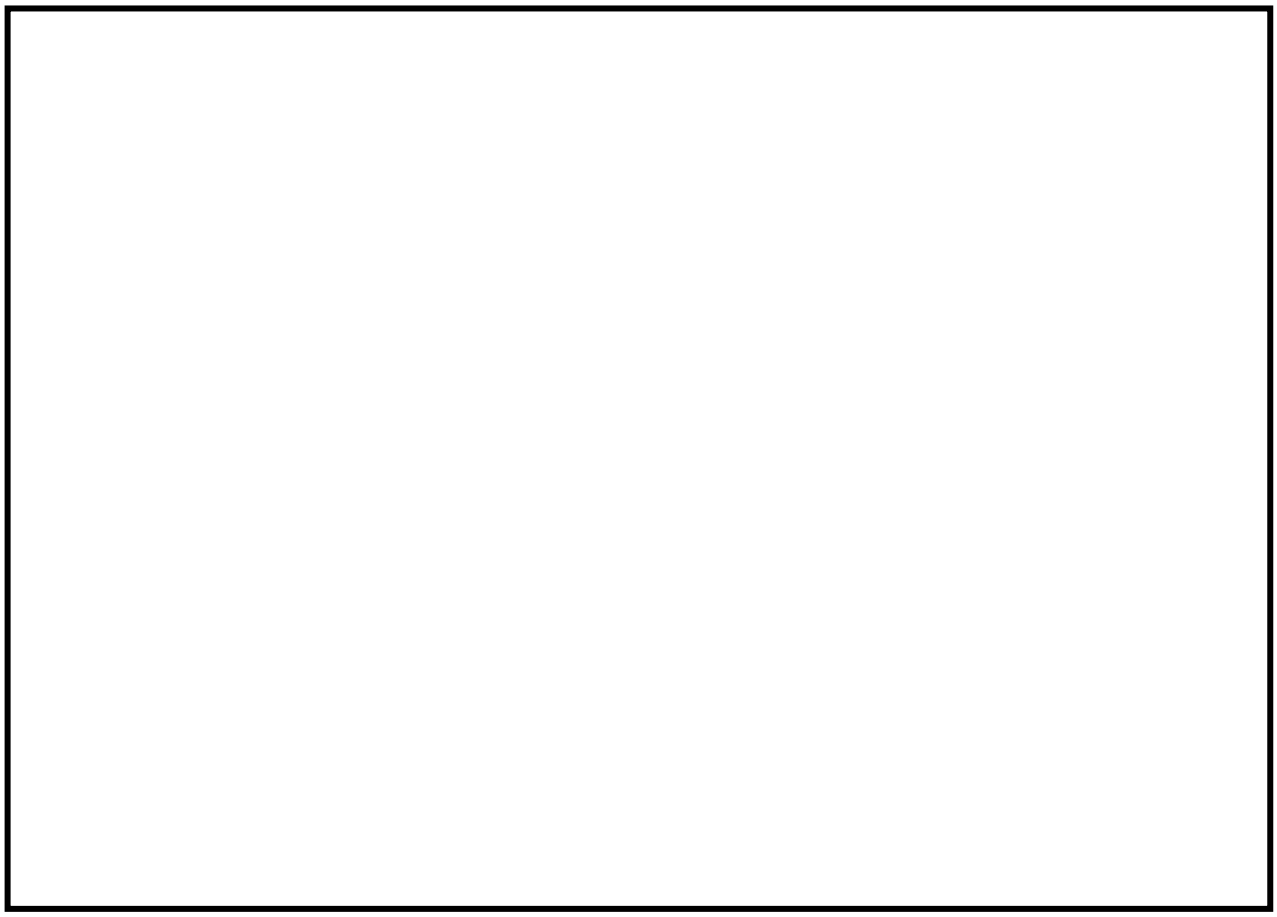


Carcinogenesis and Mutagenesis

Breast cancer

estrogen plus progestin

estrogen plus progestin

estrogen plus progestin

estrogen-alone

Contraindications

Ovarian cancer:

Some recent epidemiological studies have found that the use of hormone replacement therapy (estrogen-

HERS and HERS II Findings

Blood Pressure

Endocrine and Metabolism

Glucose and lipid metabolism

Geritourinary

Vaginal bleeding

Hepatic/Biliary/Pancreatic

Gallbladder diseases

Jaundice

Liver function tests

Monitoring and Laboratory Tests

Neurologic

Cerebrovascular insufficiency

Dementia

estrogen plus progestin

estrogen plus progestin *estrogen-alone*

estrogen

estrogen plus progestin

estrogen-alone

estrogen-alone

Nervous system disorders

Psychiatric disorders

Renal and urinary disorders

Reproductive system and breast disorders

Skin a0 g0 G[* EMC /P <</MCI]

Table 1: Number (%) of Subjects with Common Adverse Events* in a 12-Week Placebo-Controlled Study of Divigel®

	Divigel®			Placebo
SYSTEM ORGAN CLASS *Preferred Term*	**0.25 g/day N=122 n (%)**	**0.5 g/day N=123 n (%)**	**1.0 g/day N=125 n (%)**	**N=125 n (%)**
INFECTIONS & INFESTATIONS				

Table 2 Number (%) of Subjects with AEs Occurring in 1% of Subjects in A 12-Week Placebo Controlled Study of Divigel

AE[a] System Organ Class Preferred Term	Placebo Gel (N=125)	USL-221			
		0.25 g/day (N=122)	0.5 g/day (N=123)	1.0 g/day (N=125)	Combined (N=370)
	n (%)[b]	n (%)[b]	n (%)[b]	n (%)[b]	n (%)[b]
Any AE		[redacted]			

AE[a]
System Organ Class

DRUG INTERACTIONS

Overview

Drug-Drug Interactions

Drug-Food Interactions

Drug-Herb Interactions

Drug-Laboratory Test Interactions

Treatment of Overdosage:

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Pharmacokinetics

A. Absorption

Table 5: Mean (%CV) Pharmacokinetic Parameters for Estradiol (uncorrected for baseline) on Day 14 Following Multiple Daily Doses of Divigel® 0.1%

Parameter (units)	Divigel® 0.25 g	Divigel® 0.5 g	Divigel®

B. Distribution

C. Metabolism

D. Excretion

E. Special Populations

F.

**Evu2-3(lation)-4(s)] TJETQ0.00000912 0 612 792 reW* nBT/F4 12 1f10 0 1 e1W* 0 0 612 790 g0 G[( )] TJETQ0.00000912 0

G. Potential for Estradiol Transfer and Effects of Washing

STORAGE AND STABILITY

DOSAGE FORMS, COMPOSITION AND PACKAGING

CLINICAL TRIALS

Effects on Vasomotor Symptoms

Figure 2 Change from Baseline in Mean Daily Frequency of MSVS by Week Using LOCF (ITT Population) – USL Study P04-001

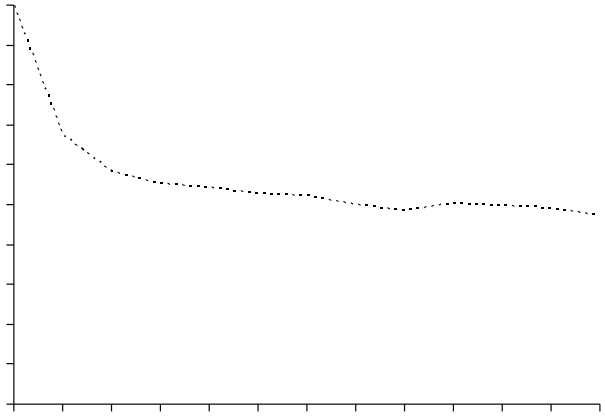


Figure 3 Change from Baseline in Mean Daily Severity of MSVS by Week Using LOCF (ITT Population) – USL Study P04-001

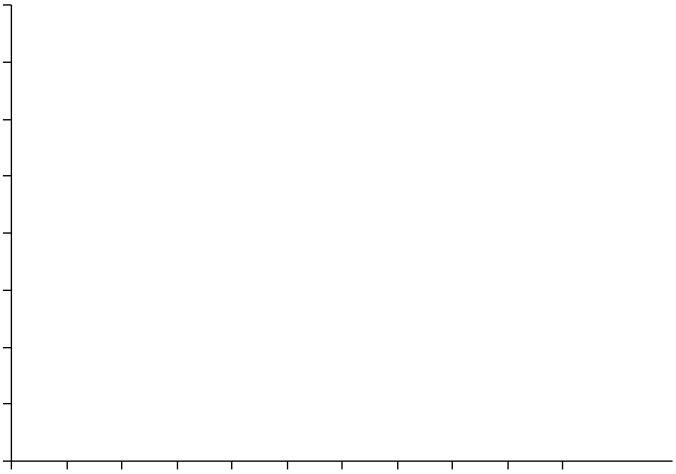


Table 8: Relative and Absolute Risk Seen in the Estrogen-Plus Progestin Substudy of WHI at an Average of 5.6 Years[a]

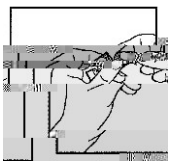
Gallbladder Disease

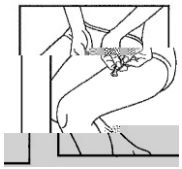
Dementia

estrogen plus progestin

estrogen-alone

BEFORE you use DIVIGEL, talk to your doctor or pharmacist if you:





HOW TO STORE IT

REPORTING SUSPECTED SIDE EFFECTS