



Clinical trial results:

Prospective, open-label, multicenter, multinational, randomized trial to investigate the non-inferiority of treatment with Vagisan® Moisturising Cream in comparison to an Estriol containing cream in a panel of post-menopausal women suffering from the symptoms of "vulvovaginal dryness" in a parallel group design

Summary

EudraCT number	2016-002199-28
Trial protocol	DE
Global end of trial date	19 June 2017

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	VFCr-12/2015
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03044652
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dr. August Wolff GmbH & Co. KG Arzneimittel
Sponsor organisation address	Sudbrackstr. 56, Bielefeld, Germany, 33611
Public contact	Clinical Trial Disclosure Office, Dr. August Wolff GmbH & Co. KG Arzneimittel, AW-ClinicalTrialDisclosures@drwolffgroup.com
Scientific contact	Clinical Trial Disclosure Office, Dr. August Wolff GmbH & Co. KG Arzneimittel, AW-ClinicalTrialDisclosures@drwolffgroup.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 January 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2017
Global end of trial reached?	Yes
Global end of trial date	19 June 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to investigate the non-inferiority of the treatment of "vulvovaginal dryness" with Vagisan® Moisturising Cream in comparison to an Estriol containing cream. The comparison will be based on the subjective assessment of the symptoms of "vulvovaginal dryness" (Total Severity Score: sum score of the single subjective symptom parameters dryness, itching, burning and pain unrelated to sexual intercourse).

Protection of trial subjects:

This study was in compliance with the ethical principles of current applicable regulations, International Council for Harmonisation (ICH) of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements. All regulatory requirements relevant to the safety of the study participants were followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 162
Country: Number of subjects enrolled	Switzerland: 10
Worldwide total number of subjects	172
EEA total number of subjects	162

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	130
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

199 women were screened. 24 women failed to comply with the in- and exclusion criteria while 3 women withdrew from the trial. Hence, 172 of 199 women (86.4 %) had been eligible to be randomized to one of the two treatment arms.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Vagisan® Moisturising Cream
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Vagisan® Moisturising Cream
Investigational medicinal product code	
Other name	Vagisan® FeuchtCreme
Pharmaceutical forms	Cream
Routes of administration	Vaginal use

Dosage and administration details:

2.5 g of the investigational product Vagisan® Moisturising Cream was applied intravaginally, once daily in the evening. After improvement of the symptoms the frequency could be reduced by the patient as needed. In addition, a 0.5 cm strand of cream (1 fingertip unit) could be applied to the outer genital area as needed (also several times per day). All applications were performed by the patients themselves at home for 6 weeks.

Arm title	Ovestin® 1 mg Creme
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Ovestin® 1 mg Creme
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Vaginal use

Dosage and administration details:

0.5 g of the reference product Ovestin® was applied intravaginally once daily in the evening for the first 3 weeks. Subsequently, the frequency was reduced to twice a week for the last 3 weeks for all patients in this treatment group. All applications were performed by the patients themselves at home for 6 weeks.

Number of subjects in period 1	Vagisan® Moisturising Cream	Ovestin® 1 mg Creme
Started	87	85
Completed	84	78
Not completed	3	7
Consent withdrawn by subject	1	2
Adverse event, non-fatal	-	4
The husband did not like her vaginal changes	1	-
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Vagisan® Moisturising Cream
Reporting group description: -	
Reporting group title	Ovestin® 1 mg Creme
Reporting group description: -	

Reporting group values	Vagisan® Moisturising Cream	Ovestin® 1 mg Creme	Total
Number of subjects	87	85	172
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	59.4 ± 7.3	61.7 ± 7.1	-
Gender categorical Units: Subjects			
Female	87	85	172

End points

End points reporting groups

Reporting group title	Vagisan® Moisturising Cream
Reporting group description: -	
Reporting group title	Ovestin® 1 mg Creme
Reporting group description: -	
Subject analysis set title	Vagisan (SP)
Subject analysis set type	Safety analysis
Subject analysis set description: Safety population (SP) for Vagisan® Moisturising Cream. The safety population (SP) includes all patients who were included to the trial and who received at least one application of the test products, regardless of the number of further assessments.	
Subject analysis set title	Ovestin (SP)
Subject analysis set type	Safety analysis
Subject analysis set description: Safety population (SP) for Ovestin® 1 mg Creme. The safety population (SP) includes all patients who were included to the trial and who received at least one application of the test products, regardless of the number of further assessments.	
Subject analysis set title	Vagisan (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intention to treat population (ITT) for Vagisan® Moisturising Cream. The intention to treat population (ITT) includes all patients of the safety population (SP) with at least one post-baseline assessment.	
Subject analysis set title	Ovestin (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intention to treat population (ITT) for Ovestin® 1 mg Creme. The intention to treat population (ITT) includes all patients of the safety population (SP) with at least one post-baseline assessment.	
Subject analysis set title	Vagisan (PP)
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol population (PP) for Vagisan® Moisturising Cream. The per protocol population (PP) includes all patients of the intention to treat population (ITT) who finished the trial in accordance with the trial protocol without major protocol deviations.	
Subject analysis set title	Ovestin (PP)
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol population (PP) for Ovestin® 1 mg Creme. The per protocol population (PP) includes all patients of the intention to treat population (ITT) who finished the trial in accordance with the trial protocol without major protocol deviations.	
Subject analysis set title	Vagisan subgroup (PP): mild overall impairment daily life
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol population for Vagisan® Moisturising Cream subgroup with mild overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1	
Subject analysis set title	Vagisan subgroup (PP): moderate overall impairment daily life
Subject analysis set type	Per protocol
Subject analysis set description: Per protocol population for Vagisan® Moisturising Cream subgroup with moderate overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1	
Subject analysis set title	Vagisan subgroup (PP): severe overall impairment daily life
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol population for Vagisan® Moisturising Cream subgroup with severe overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1

Subject analysis set title	Ovestin subgroup (PP): mild overall impairment daily life
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol population for Ovestin® 1 mg Creme subgroup with mild overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1

Subject analysis set title	Ovestin subgroup (PP): moderate overall impairment daily life
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol population for Ovestin® 1 mg Creme subgroup with moderate overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1

Subject analysis set title	Ovestin subgroup (PP): severe overall impairment daily life
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol population for Ovestin® 1 mg Creme subgroup with severe overall impairment of daily life due to the condition "vaginal dryness" on Study Day 1

Subject analysis set title	Vagisan (PP) Day 1
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Vagisan® Moisturising Cream on Day 1.

Subject analysis set title	Vagisan (PP) Day 43
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Vagisan® Moisturising Cream on Day 43.

Subject analysis set title	Ovestin (PP) Day 1
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Ovestin® 1 mg Creme on Day 1.

Subject analysis set title	Ovestin (PP) Day 43
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Ovestin® 1 mg Creme on Day 43.

Subject analysis set title	Vagisan (PP) Day 22
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Vagisan® Moisturising Cream on Day 22.

Subject analysis set title	Ovestin (PP) Day 22
Subject analysis set type	Per protocol

Subject analysis set description:

Per protocol (PP) population for Ovestin® 1 mg Creme on Day 22.

Primary: Non inferiority, assessed by the difference of the Total Severity Score between baseline and after six weeks of treatment

End point title	Non inferiority, assessed by the difference of the Total Severity Score between baseline and after six weeks of treatment
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End point description:

Main analysis based on per protocol population (PP). In accordance with the recommendations of the FDA for non-inferiority trials (2010), a second analysis was performed on the ITT population. The Total Severity Score is defined as the sum of the single parameters dryness, itching, burning and pain unrelated to sexual intercourse, each scored from 0 = none to 4 = very severe. In total a range of 0 = no complaints to 16 = very severe complaints is possible.

End point type	Primary
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End point timeframe:

Visit 1 (Day 1) to Visit 3 (Day 43)

End point values	Vagisan (ITT)	Ovestin (ITT)	Vagisan (PP)	Ovestin (PP)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	85	81	80	71
Units: Difference of the Total Severity Score				
arithmetic mean (standard deviation)	-5.0 (± 2.2)	-5.3 (± 2.4)	-5.0 (± 2.2)	-5.4 (± 2.1)

Statistical analyses

Statistical analysis title	Test of non-inferiority (PP)
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Statistical analysis description:

Mann-Whitney-Wilcoxon Test was utilized to evaluate non-inferiority of the treatment Vagisan® in comparison to Ovestin® based on the differences of the Total Severity Score between Baseline and Day 43

Comparison groups	Vagisan (PP) v Ovestin (PP)
Number of subjects included in analysis	151
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
P-value	= 0.0002
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - Non-inferiority margin of 1.5 units

Statistical analysis title	Test of non-inferiority (ITT)
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Statistical analysis description:

One-sided Independent t-Test was utilized to evaluate non-inferiority of the treatment Vagisan® in comparison to Ovestin® based on the differences of the Total Severity Score between Baseline and Day 43

Comparison groups	Ovestin (ITT) v Vagisan (ITT)
Number of subjects included in analysis	166
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
P-value	= 0.0006
Method	t-test, 1-sided

Notes:

[2] - Non-inferiority margin of 1.5 units

Secondary: Severity scoring for dryness

End point title	Severity scoring for dryness
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End point description:

Severity scored from 0 = none to 4 = very severe.

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[3]	71 ^[4]		
Units: Severity scoring				
arithmetic mean (standard deviation)				
Day 1	2.3 (± 0.8)	2.3 (± 0.9)		
Day 7	1.1 (± 0.9)	1.0 (± 0.8)		
Day 14	0.8 (± 0.9)	0.6 (± 0.7)		
Day 21	0.7 (± 0.7)	0.4 (± 0.6)		
Day 22	0.7 (± 0.7)	0.5 (± 0.7)		
Day 28	0.5 (± 0.6)	0.3 (± 0.5)		
Day 35	0.5 (± 0.6)	0.3 (± 0.5)		
Day 42	0.4 (± 0.6)	0.2 (± 0.4)		
Day 43	0.4 (± 0.6)	0.2 (± 0.4)		

Notes:

[3] - n = 80 (D1); 78 (D7); 78 (D14); 79 (D21); 80 (D22); 76 (D28); 77 (D35); 75 (D42); 80 (D43)

[4] - n = 71 (D1); 71 (D7); 67 (D14); 70 (D21); 70 (D22); 70 (D28); 71 (D35); 70 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Severity scoring for itching

End point title	Severity scoring for itching
End point description: Severity scored from 0 = none to 4 = very severe.	
End point type	Secondary
End point timeframe: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[5]	71 ^[6]		
Units: Severity scoring				
arithmetic mean (standard deviation)				
Day 1	1.4 (± 1.0)	1.4 (± 0.9)		
Day 7	0.8 (± 0.8)	0.8 (± 0.8)		
Day 14	0.7 (± 0.8)	0.7 (± 0.8)		
Day 21	0.5 (± 0.6)	0.4 (± 0.7)		
Day 22	0.5 (± 0.7)	0.5 (± 0.7)		
Day 28	0.4 (± 0.5)	0.4 (± 0.5)		
Day 35	0.3 (± 0.6)	0.3 (± 0.6)		
Day 42	0.2 (± 0.5)	0.2 (± 0.4)		

Day 43	0.3 (\pm 0.5)	0.2 (\pm 0.4)		
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Notes:

[5] - n = 80 (D1); 78 (D7); 78 (D14); 78 (D21); 80 (D22); 75 (D28); 77 (D35); 75 (D42); 80 (D43)

[6] - n = 71 (D1); 70 (D7); 67 (D14); 69 (D21); 71 (D22); 71 (D28); 71 (D35); 70 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Severity scoring for burning

End point title	Severity scoring for burning
End point description: Severity scored from 0 = none to 4 = very severe.	
End point type	Secondary
End point timeframe: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[7]	71 ^[8]		
Units: Severity scoring				
arithmetic mean (standard deviation)				
Day 1	1.4 (\pm 1.0)	1.5 (\pm 1.0)		
Day 7	0.7 (\pm 0.8)	0.6 (\pm 0.8)		
Day 14	0.6 (\pm 0.7)	0.5 (\pm 0.7)		
Day 21	0.4 (\pm 0.6)	0.4 (\pm 0.6)		
Day 22	0.6 (\pm 0.7)	0.4 (\pm 0.6)		
Day 28	0.4 (\pm 0.6)	0.3 (\pm 0.5)		
Day 35	0.3 (\pm 0.6)	0.2 (\pm 0.5)		
Day 42	0.3 (\pm 0.5)	0.1 (\pm 0.3)		
Day 43	0.3 (\pm 0.6)	0.1 (\pm 0.3)		

Notes:

[7] - n = 80 (D1); 78 (D7); 78 (D14); 79 (D21); 80 (D22); 76 (D28); 77 (D35); 75 (D42); 80 (D43)

[8] - n = 71 (D1); 70 (D7); 67 (D14); 70 (D21); 71 (D22); 71 (D28); 71 (D35); 69 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Severity scoring for pain unrelated to sexual intercourse

End point title	Severity scoring for pain unrelated to sexual intercourse
End point description: Severity scored from 0 = none to 4 = very severe.	
End point type	Secondary
End point timeframe: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[9]	71 ^[10]		
Units: Severity scoring				
arithmetic mean (standard deviation)				
Day 1	1.1 (± 0.9)	0.8 (± 1.0)		
Day 7	0.5 (± 0.8)	0.4 (± 0.7)		
Day 14	0.4 (± 0.7)	0.2 (± 0.6)		
Day 21	0.3 (± 0.5)	0.2 (± 0.5)		
Day 22	0.4 (± 0.6)	0.2 (± 0.5)		
Day 28	0.3 (± 0.5)	0.1 (± 0.4)		
Day 35	0.2 (± 0.0)	0.1 (± 0.3)		
Day 42	0.1 (± 0.0)	0.0 (± 0.2)		
Day 43	0.2 (± 0.0)	0.1 (± 0.2)		

Notes:

[9] - n = 80 (D1); 77 (D7); 78 (D14); 78 (D21); 80 (D22); 76 (D28); 76 (D35); 75 (D42); 80 (D43)

[10] - n = 71 (D1); 69 (D7); 67 (D14); 70 (D21); 71 (D22); 70 (D28); 71 (D35); 69 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for severity scoring for dryness

End point title	AUC for severity scoring for dryness
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	64		
Units: Severity score * days				
arithmetic mean (standard deviation)	34.6 (± 24.9)	27.5 (± 18.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for severity scoring for itching

End point title	AUC for severity scoring for itching
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	65		
Units: Severity score * days				
arithmetic mean (standard deviation)	25.1 (± 22.6)	21.9 (± 20.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for severity scoring for burning

End point title	AUC for severity scoring for burning
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	65		
Units: Severity score * days				
arithmetic mean (standard deviation)	23.2 (± 22.8)	18.3 (± 17.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for severity scoring for pain unrelated to sexual intercourse

End point title	AUC for severity scoring for pain unrelated to sexual intercourse
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	65		
Units: Severity score * days				
arithmetic mean (standard deviation)	15.6 (± 19.4)	9.5 (± 14.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impairment of daily life due to dryness

End point title	Impairment of daily life due to dryness
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End point description:

Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[11]	71 ^[12]		
Units: cm				
arithmetic mean (standard deviation)				
Day 1	5.62 (± 2.34)	5.22 (± 2.81)		
Day 7	2.30 (± 2.52)	1.90 (± 1.98)		
Day 14	1.60 (± 2.13)	1.02 (± 1.60)		
Day 21	1.05 (± 1.60)	0.67 (± 1.36)		
Day 22	1.17 (± 1.53)	0.75 (± 1.37)		
Day 28	0.76 (± 1.28)	0.36 (± 0.89)		
Day 35	0.59 (± 1.15)	0.34 (± 0.88)		
Day 42	0.47 (± 1.08)	0.20 (± 0.59)		
Day 43	0.54 (± 1.17)	0.21 (± 0.56)		

Notes:

[11] - n = 80 (D1); 80 (D7); 80 (D14); 79 (D21); 79 (D22); 77 (D28); 78 (D35); 75 (D42); 80 (D43)

[12] - n = 71 (D1); 71 (D7); 69 (D14); 71 (D21); 71 (D22); 71 (D28); 71 (D35); 70 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Impairment of daily life due to itching

End point title	Impairment of daily life due to itching
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End point description:

Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[13]	71 ^[14]		
Units: cm				
arithmetic mean (standard deviation)				
Day 1	3.90 (± 2.89)	3.79 (± 2.73)		
Day 7	1.66 (± 1.90)	1.48 (± 1.77)		
Day 14	1.16 (± 1.85)	1.03 (± 1.56)		
Day 21	0.65 (± 1.26)	0.68 (± 1.50)		
Day 22	0.72 (± 1.33)	0.80 (± 1.61)		
Day 28	0.46 (± 0.92)	0.36 (± 0.86)		
Day 35	0.34 (± 1.05)	0.36 (± 1.25)		
Day 42	0.30 (± 1.07)	0.15 (± 0.52)		
Day 43	0.34 (± 1.07)	0.20 (± 0.60)		

Notes:

[13] - n = 80 (D1); 80 (D7); 80 (D14); 79 (D21); 79 (D22); 76 (D28); 77 (D35); 76 (D42); 80 (D43)

[14] - n = 71 (D1); 70 (D7); 69 (D14); 71 (D21); 71 (D22); 70 (D28); 70 (D35); 69 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Impairment of daily life due to burning

End point title	Impairment of daily life due to burning
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End point description:

Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[15]	71 ^[16]		
Units: cm				
arithmetic mean (standard deviation)				
Day 1	3.73 (± 3.01)	3.66 (± 3.08)		
Day 7	1.43 (± 1.96)	1.14 (± 1.72)		
Day 14	1.09 (± 1.66)	0.64 (± 1.36)		
Day 21	0.66 (± 1.18)	0.49 (± 1.94)		
Day 22	0.86 (± 1.39)	0.52 (± 1.08)		
Day 28	0.61 (± 1.22)	0.26 (± 0.77)		
Day 35	0.47 (± 1.20)	0.24 (± 0.86)		
Day 42	0.42 (± 1.17)	0.12 (± 0.49)		
Day 43	0.41 (± 1.23)	0.23 (± 1.24)		

Notes:

[15] - n = 79 (D1); 80 (D7); 80 (D14); 79 (D21); 80 (D22); 77 (D28); 78 (D35); 76 (D42); 79 (D43)

[16] - n = 70 (D1); 70 (D7); 69 (D14); 71 (D21); 71 (D22); 70 (D28); 70 (D35); 70 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: Impairment of daily life due to pain unrelated to sexual intercourse

End point title	Impairment of daily life due to pain unrelated to sexual intercourse
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End point description:

Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[17]	71 ^[18]		
Units: cm				
arithmetic mean (standard deviation)				
Day 1	2.50 (± 2.62)	1.83 (± 2.66)		
Day 7	1.00 (± 1.85)	0.77 (± 1.68)		
Day 14	0.81 (± 1.58)	0.42 (± 1.14)		
Day 21	0.47 (± 1.02)	0.36 (± 1.00)		
Day 28	0.35 (± 0.91)	0.21 (± 0.80)		
Day 35	0.23 (± 0.73)	0.09 (± 0.40)		
Day 42	0.18 (± 0.72)	0.05 (± 0.37)		
Day 43	0.18 (± 0.69)	0.05 (± 0.28)		

Notes:

[17] - n = 79 (D1); 79 (D7); 79 (D14); 78 (D21); 80 (D22); 77 (D28); 78 (D35); 76 (D42); 80 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for impairment of daily life due to dryness

End point title	AUC for impairment of daily life due to dryness
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	73	68		
Units: cm * days				
arithmetic mean (standard deviation)	61.94 (± 59.35)	46.77 (± 40.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for impairment of daily life due to itching

End point title	AUC for impairment of daily life due to itching
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	73	66		
Units: cm * days				
arithmetic mean (standard deviation)	43.87 (± 47.97)	40.12 (± 42.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for impairment of daily life due to burning

End point title	AUC for impairment of daily life due to burning
End point description:	
End point type	Secondary
End point timeframe:	
Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	73	66		
Units: cm * days				
arithmetic mean (standard deviation)	43.87 (± 50.53)	31.13 (± 36.30)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for impairment of daily life due to pain unrelated to sexual intercourse

End point title	AUC for impairment of daily life due to pain unrelated to sexual intercourse
End point description:	
End point type	Secondary
End point timeframe:	
Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	72	65		
Units: cm * days				
arithmetic mean (standard deviation)	26.90 (± 41.06)	18.52 (± 32.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Weighted Impairment of Daily Life

End point title	Weighted Impairment of Daily Life
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End point description:

Represents the impairment of daily life due to each subjective symptom (dryness, itching, burning and pain unrelated to sexual intercourse) weighted by the severity of the subjective symptoms.

Weighted Impairment of Daily Life = (Severity Scoring (Dryness) * Impairment of Daily Life (Dryness) + Severity Scoring (Itching) * Impairment of Daily Life (Itching) + Severity Scoring (Burning) * Impairment of Daily Life (Burning) + Severity Scoring (Pain) * Impairment of Daily Life (Pain)) / 16

Range: 1-10

End point type	Secondary
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End point timeframe:

At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	79 ^[19]	71 ^[20]		
Units: Score				
arithmetic mean (standard deviation)				
Day 1	2.11 (± 1.44)	2.02 (± 1.59)		
Day 7	0.66 (± 0.89)	0.56 (± 0.68)		
Day 14	0.47 (± 0.78)	0.32 (± 0.59)		
Day 21	0.25 (± 0.44)	0.21 (± 0.43)		
Day 22	0.31 (± 0.51)	0.22 (± 0.42)		
Day 28	0.19 (± 0.36)	0.09 (± 0.21)		
Day 35	0.16 (± 0.43)	0.11 (± 0.41)		
Day 42	0.14 (± 0.43)	0.03 (± 0.11)		
Day 43	0.14 (± 0.44)	0.05 (± 0.18)		

Notes:

[19] - n = 79 (D1); 77 (D7); 76 (D14); 78 (D21); 79 (D22); 74 (D28); 76 (D35); 74 (D42); 79 (D43)

[20] - n = 70 (D1); 69 (D7); 67 (D14); 69 (D21); 69 (D22); 70 (D28); 69 (D35); 69 (D42); 71 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for Weighted Total Severity Score

End point title AUC for Weighted Total Severity Score

End point description:

End point type Secondary

End point timeframe:

Over all assessment time points: At each visit and once weekly (Days 1, 7, 14, 21, 22, 28, 35, 42, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	60		
Units: Severity Score * cm * days				
arithmetic mean (standard deviation)	19.8 (± 21.09)	14.48 (± 14.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Severity scoring for dyspareunia (if sexually active)

End point title Severity scoring for dyspareunia (if sexually active)

End point description:

Severity scored from 0 = none to 4 = very severe

End point type Secondary

End point timeframe:

Visit 1 (Day 1) and visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64 ^[21]	42 ^[22]		
Units: Severity Score				
arithmetic mean (standard deviation)				
Day 1	2.6 (± 1.2)	2.7 (± 1.2)		
Day 43	0.9 (± 1.0)	0.5 (± 0.7)		

Notes:

[21] - n = 64 (D1); 56 (D43);

[22] - n = 42 (D1); 38 (D43);

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for severity scoring for dyspareunia (if sexually active)

End point title AUC for severity scoring for dyspareunia (if sexually active)

End point description:

End point type Secondary

End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	56	37		
Units: Severity Score * Days				
arithmetic mean (standard deviation)	73.1 (± 36.3)	67.0 (± 30.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Impairment of daily life due to dyspareunia (if sexually active)

End point title Impairment of daily life due to dyspareunia (if sexually active)

End point description:

Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type Secondary

End point timeframe:

At each visit: Visit 1 (Day 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64 ^[23]	42 ^[24]		
Units: cm				
arithmetic mean (standard deviation)				
Day 1	7.03 (± 2.73)	6.66 (± 2.94)		
Day 22	2.64 (± 2.69)	1.43 (± 2.18)		
Day 43	1.56 (± 2.42)	0.65 (± 1.63)		

Notes:

[23] - n = 64 (D1); 57 (D22); 57 (D43);

[24] - n = 42 (D1); 37 (D22); 37 (D43);

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for impairment of daily life due to dyspareunia (if sexually active)

End point title	AUC for impairment of daily life due to dyspareunia (if sexually active)
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	52	34		
Units: cm * days				
arithmetic mean (standard deviation)	139.91 (\pm 87.04)	107.47 (\pm 73.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall impairment of daily life due to the condition "vaginal dryness"

End point title	Overall impairment of daily life due to the condition "vaginal dryness"
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End point description:

Overall impairment of daily life due to the condition "vaginal dryness", including a subgroup analysis of patients with mild, moderate and severe overall impairment at each visit. Evaluation on a visual analogue scale (VAS): 0 = no impairment; 10 = very pronounced impairment

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)	Vagisan subgroup (PP): mild overall impairment daily life	Vagisan subgroup (PP): moderate overall impairment daily life
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80 ^[25]	71 ^[26]	21 ^[27]	27 ^[28]
Units: cm				
arithmetic mean (standard deviation)				
Day 1	5.54 (\pm 2.63)	4.82 (\pm 2.56)	2.13 (\pm 0.95)	4.98 (\pm 0.86)
Day 22	1.61 (\pm 0.23)	1.02 (\pm 1.64)	0.57 (\pm 0.84)	1.16 (\pm 1.64)
Day 43	0.92 (\pm 1.76)	0.40 (\pm 0.99)	0.83 (\pm 1.78)	0.96 (\pm 1.76)

Notes:

[25] - n = 80 (D1); 78 (D22); 78 (D43)

[26] - n = 71 (D1); 70 (D22); 71 (D43)

[27] - n = 21 (D1); 21 (D22); 20 (D43)

[28] - n = 27 (D1); 25 (D22); 26 (D43)

End point values	Vagisan subgroup (PP): severe overall impairment daily life	Ovestin subgroup (PP): mild overall impairment daily life	Ovestin subgroup (PP): moderate overall impairment daily life	Ovestin subgroup (PP): severe overall impairment daily life
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32 ^[29]	19 ^[30]	31 ^[31]	21 ^[32]
Units: cm				
arithmetic mean (standard deviation)				
Day 1	8.26 (± 0.83)	1.71 (± 0.93)	4.57 (± 0.94)	8.00 (± 0.94)
Day 22	2.63 (± 2.42)	0.82 (± 1.30)	1.02 (± 1.71)	1.19 (± 1.86)
Day 43	0.94 (± 1.79)	0.28 (± 0.86)	0.39 (± 0.72)	0.52 (± 1.39)

Notes:

[29] - n = 32 (D1); 32 (D22); 32 (D43)

[30] - n = 19 (D1); 19 (D22); 19 (D43)

[31] - n = 31 (D1); 30 (D22); 31 (D43)

[32] - n = 21 (D1); 21 (D22); 21 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for overall impairment of daily life

End point title	AUC for overall impairment of daily life
End point description:	
End point type	Secondary
End point timeframe:	
Over all assessment time points: At each visit (Days 1, 22, 43)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	76	70		
Units: cm * Days				
arithmetic mean (standard deviation)	102.79 (± 67.21)	75.93 (± 50.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index parameter elasticity

End point title	Vaginal health index parameter elasticity
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End point description:

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
None	1	0	2	0
Poor	33	3	26	1
Fair	25	14	30	1
Good	19	50	12	26
Excellent	2	11	1	42
Missing	0	2	0	1

End point values	Vagisan (PP) Day 22	Ovestin (PP) Day 22		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
None	0	0		
Poor	3	1		
Fair	15	6		
Good	51	30		
Excellent	7	33		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index parameter fluid secretion

End point title	Vaginal health index parameter fluid secretion
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End point description:

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
None	8	0	11	1
Scant, thin yellow	27	1	20	0
Superficial, thin white	29	20	23	4
Moderate, thin white	10	43	15	22
Normal (white flocculent)	6	14	2	43
Missing	0	2	0	1

End point values	Vagisan (PP) Day 22	Ovestin (PP) Day 22		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
None	0	0		
Scant, thin yellow	4	1		
Superficial, thin white	14	4		
Moderate, thin white	44	22		
Normal (white flocculent)	14	43		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index parameter pH

End point title	Vaginal health index parameter pH
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End point description:

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
>=6.1	29	18	28	1
5.6 - 6.0	15	16	11	1
5.1 - 5.5	7	13	7	4
4.7 - 5.0	14	17	19	22
<= 5.6	15	14	7	42
Missing	0	2	0	1

End point values	Vagisan (PP) Day 22	Ovestin (PP) Day 22		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
>=6.1	13	1		
5.6 - 6.0	16	2		
5.1 - 5.5	10	3		
4.7 - 5.0	22	14		
<= 5.6	15	50		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index parameter epithelial mucosa

End point title Vaginal health index parameter epithelial mucosa

End point description:

End point type Secondary

End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
Petechiae noted before contact	0	0	3	0
Bleeds with light contact	12	3	7	0
Bleeds with scraping	10	5	4	0
Not friable, thin mucosa	48	56	52	20

Not friable, normal mucosa	10	14	5	50
Missing	0	2	0	1

End point values	Vagisan (PP) Day 22	Ovestin (PP) Day 22		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
Petechiae noted before contact	0	0		
Bleeds with light contact	0	0		
Bleeds with scraping	7	1		
Not friable, thin mucosa	44	21		
Not friable, normal mucosa	25	48		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index parameter moisture

End point title	Vaginal health index parameter moisture
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End point description:

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
None, mucosa inflamed	4	0	6	0
None, mucosa not inflamed	17	2	13	0
Minimal	37	11	29	3
Moderate	16	40	21	16
Normal	6	25	2	51
Missing	0	2	0	1

End point values	Vagisan (PP) Day 22	Ovestin (PP) Day 22		
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Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
None, mucosa inflamed	1	1		
None, mucosa not inflamed	0	0		
Minimal	10	1		
Moderate	40	21		
Normal	25	47		
Missing	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal health index sum score

End point title	Vaginal health index sum score
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End point description:

Scores of VHI subparameters:

Overall Elasticity: None - 1, Poor - 2, Fair - 3, Good - 4, Excellent - 5

Fluid secretion type and consistency: None - 1, Scant, thin yellow - 2, Superficial, thin white - 3, Moderate, thin white - 4, Normal (white flocculent) - 5

pH: ≥ 6.1 - 1, 5.6–6.0 - 2, 5.1–5.5 - 3, 4.7–5.0 - 4, ≤ 4.6 - 5

Epithelial mucosa: Petechiae noted before contact - 1, Bleeds with light contact - 2, Bleeds with scraping - 3, Not friable, thin mucosa - 4, Not friable, normal mucosa - 5

Moisture: None, mucosa inflamed - 1, None, mucosa not inflamed - 2, Minimal - 3, Moderate - 4, Normal - 5

Each of the five criteria was graded from 1 (worst) to 5 (best) and then summed up.

Range of VHI sum score: 5 - 25

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Days 1), visit 2 (Day 22), visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80 ^[33]	71 ^[34]		
Units: VHI Score				
arithmetic mean (standard deviation)				
Day 1	15.0 (± 4.4)	14.7 (± 4.1)		
Day 22	9.2 (± 3.2)	22.7 (± 2.6)		
Day 43	18.9 (± 0.3)	22.9 (± 2.5)		

Notes:

[33] - n = 80 (D1); 76 (D22); 78 (D43)

[34] - n = 71 (D1); 70 (D22); 70 (D43)

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index parameter elasticity

End point title	AUC for vaginal health index parameter elasticity
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	151.0 (± 23.4)	168.6 (± 22.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index parameter fluid secretion

End point title	AUC for vaginal health index parameter fluid secretion
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	152.1 (± 27.4)	170.4 (± 25.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index parameter pH

End point title	AUC for vaginal health index parameter pH
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	122.2 (± 53.2)	169.2 (± 29.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index parameter epithelial mucosa

End point title	AUC for vaginal health index parameter epithelial mucosa
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	169.4 (± 23.3)	186.1 (± 19.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index parameter moisture

End point title	AUC for vaginal health index parameter moisture
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	163.3 (± 25.1)	177.6 (± 22.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC for vaginal health index sum score

End point title	AUC for vaginal health index sum score
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End point description:

End point type	Secondary
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End point timeframe:

Over all assessment time points: At each visit (Days 1, 22, 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	74	69		
Units: Days				
arithmetic mean (standard deviation)	758.0 (± 128.7)	872.0 (± 94.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Vaginal status of Lactobacillus flora

End point title	Vaginal status of Lactobacillus flora
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 (Visit 1) and Day 43 (Visit 3)

End point values	Vagisan (PP) Day 1	Vagisan (PP) Day 43	Ovestin (PP) Day 1	Ovestin (PP) Day 43
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	80	80	71	71
Units: Number of patients				
Increased	0	1	0	0
Normal	22	18	16	34
Decreased	58	61	55	37

Statistical analyses

No statistical analyses for this end point

Secondary: Global judgment of the efficacy by the Investigator

End point title	Global judgment of the efficacy by the Investigator
End point description:	
End point type	Secondary
End point timeframe:	
On Visit 3 (Day 43, after 6 weeks of treatment)	

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
Very good	19	53		
Good	48	14		
Moderate	10	3		
Poor	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Global judgment of the efficacy by the patient

End point title	Global judgment of the efficacy by the patient
End point description:	
End point type	Secondary

End point timeframe:

On Visit 3 (Day 43, after 6 weeks of treatment)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
Very good	40	55		
Good	29	12		
Moderate	9	4		
Poor	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Global judgment of the tolerability by the Investigator

End point title Global judgment of the tolerability by the Investigator

End point description:

End point type Secondary

End point timeframe:

On Visit 3 (Day 43, after 6 weeks of treatment)

End point values	Vagisan (SP)	Ovestin (SP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	84	78		
Units: Number of patients				
Very good	58	65		
Good	21	9		
Moderate	3	4		
Poor	1	0		
Missing	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Global judgment of the tolerability by the patient

End point title Global judgment of the tolerability by the patient

End point description:

End point type	Secondary
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End point timeframe:

On Visit 3 (Day 43, after 6 weeks of treatment)

End point values	Vagisan (SP)	Ovestin (SP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	84	78		
Units: Number of patients				
Very good	56	63		
Good	17	10		
Moderate	7	3		
Poor	3	2		
Missing	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of concomitant therapies at screening

End point title	Number of concomitant therapies at screening
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End point description:

End point type	Secondary
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End point timeframe:

At screening

End point values	Vagisan (SP)	Ovestin (SP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	85		
Units: Count				
Therapies	72	84		
Patients with any therapy	44	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of study participants that used any treatment for vulvovaginal

dryness before study participation

End point title	Number of study participants that used any treatment for vulvovaginal dryness before study participation
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End point description:

End point type	Secondary
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End point timeframe:

Visit 1 (Day 1)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
Yes	16	14		
No	64	57		

Statistical analyses

No statistical analyses for this end point

Secondary: Satisfaction with treatment for vulvovaginal dryness before study participation

End point title	Satisfaction with treatment for vulvovaginal dryness before study participation
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End point description:

Satisfaction with previous treatment in subgroup of patients that used treatment for vulvovaginal dryness before study participation

End point type	Secondary
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End point timeframe:

Visit 1 (Day 1)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	16	14		
Units: Number of patients				
Very good	1	2		
Good	5	5		
Moderate	6	6		
Poor	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Urinary incontinence

End point title	Urinary incontinence
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End point description:

The urinary incontinence was assessed by the patient:

Visit 1: yes/no-question

Visit 2 and Visit 3: improvement/worsening/no change

Data reported for the subgroup of women suffering from urinary incontinence on Visit 1.

End point type	Secondary
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End point timeframe:

At each visit: Visit 1 (Day 1), Visit 2 (Day 22) and Visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	15		
Units: Number of patients				
No change until visit 2, improvement until visit 3	0	1		
No change until visit 2, no change until visit 3	14	14		
No change until visit 2, worsening until visit 3	1	0		
Worsening until visit 2, improvement until visit 3	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Questionnaire about satisfaction with the test product

End point title	Questionnaire about satisfaction with the test product
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End point description:

Question: "Were you satisfied with the preparation you used?"

End point type	Secondary
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End point timeframe:

Visit 3 (Day 43)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Number of patients				
Yes	71	67		
No	5	2		
I don't know	4	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose of the treatment with the test product (Vagisan only)

End point title	Dose of the treatment with the test product (Vagisan only)
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End point description:

End point type	Secondary
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End point timeframe:

Day 1 (Visit 1) to Day 43 (Visit 3)

End point values	Vagisan (PP)			
Subject group type	Subject analysis set			
Number of subjects analysed	80			
Units: Sum of product applications during trial				
arithmetic mean (standard deviation)				
1/2 applicator	35 (± 11)			
More	1 (± 4)			
Less	5 (± 10)			
Missing	0 (± 1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of the treatment with the test product

End point title	Frequency of the treatment with the test product
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End point description:

End point type	Secondary
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End point timeframe:

From Day 1 (Visit 1) to Day 43 (Visit 3)

End point values	Vagisan (PP)	Ovestin (PP)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	80	71		
Units: Sum of product applications during trial				
arithmetic mean (standard deviation)				
Vaginal application	41 (± 2.7)	26.5 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 - 43

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Vagisan (SP)
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Reporting group description: -

Reporting group title	Ovestin (SP)
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Reporting group description: -

Serious adverse events	Vagisan (SP)	Ovestin (SP)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 87 (0.00%)	0 / 85 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Vagisan (SP)	Ovestin (SP)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 87 (37.93%)	46 / 85 (54.12%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 87 (0.00%)	2 / 85 (2.35%)	
occurrences (all)	0	3	
Hypertension			
subjects affected / exposed	2 / 87 (2.30%)	3 / 85 (3.53%)	
occurrences (all)	2	3	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 87 (0.00%)	2 / 85 (2.35%)	
occurrences (all)	0	2	
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 87 (1.15%)	1 / 85 (1.18%)	
occurrences (all)	1	1	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	5	0	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 87 (0.00%)	3 / 85 (3.53%)	
occurrences (all)	0	5	
Female sexual arousal disorder			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Genital burning sensation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Genital haemorrhage			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Uterine spasm			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	2 / 87 (2.30%)	4 / 85 (4.71%)	
occurrences (all)	2	7	
Vaginal haemorrhage			
subjects affected / exposed	1 / 87 (1.15%)	1 / 85 (1.18%)	
occurrences (all)	2	1	

Vulvovaginal burning sensation subjects affected / exposed occurrences (all)	5 / 87 (5.75%) 7	9 / 85 (10.59%) 9	
Vulvovaginal discomfort subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	0 / 85 (0.00%) 0	
Vulvovaginal erythema subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Vulvovaginal pain subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	0 / 85 (0.00%) 0	
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	2 / 87 (2.30%) 5	5 / 85 (5.88%) 5	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 87 (2.30%) 2	2 / 85 (2.35%) 2	
Dysphonia subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Psychiatric disorders Sleep disorder subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	2 / 87 (2.30%) 2	0 / 85 (0.00%) 0	
Foot fracture subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Tooth fracture subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Cardiovascular insufficiency			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	2	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	8 / 87 (9.20%)	8 / 85 (9.41%)	
occurrences (all)	11	14	
Migraine			
subjects affected / exposed	1 / 87 (1.15%)	1 / 85 (1.18%)	
occurrences (all)	1	3	
Neuralgia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	3	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Macular degeneration			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	3 / 87 (3.45%) 4	1 / 85 (1.18%) 1	
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	5 / 85 (5.88%) 5	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Constipation subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	0 / 85 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	2 / 85 (2.35%) 2	
Dry mouth subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	1 / 85 (1.18%) 1	
Nausea subjects affected / exposed occurrences (all)	2 / 87 (2.30%) 3	0 / 85 (0.00%) 0	
Toothache subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	1 / 85 (1.18%) 1	
Skin and subcutaneous tissue disorders			
Dermatitis allergic subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	1 / 85 (1.18%) 1	
Pruritus subjects affected / exposed occurrences (all)	1 / 87 (1.15%) 1	0 / 85 (0.00%) 0	
Rash			

subjects affected / exposed occurrences (all)	0 / 87 (0.00%) 0	1 / 85 (1.18%) 1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 87 (2.30%)	1 / 85 (1.18%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	2 / 87 (2.30%)	3 / 85 (3.53%)	
occurrences (all)	2	3	
Limb discomfort			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 87 (0.00%)	3 / 85 (3.53%)	
occurrences (all)	0	3	
Musculoskeletal pain			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Infections and infestations			
Anal fungal infection			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Candida infection			

subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	7 / 87 (8.05%)	12 / 85 (14.12%)	
occurrences (all)	7	12	
Sinusitis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 85 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	
Vulvitis			
subjects affected / exposed	0 / 87 (0.00%)	1 / 85 (1.18%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported