



Clinical trial results:

Multi-center, randomized, comparator-controlled, single-blind, parallel-group study to investigate the pharmacodynamics, pharmacokinetics and safety of an intrauterine system releasing BAY 1007626, as compared with Mirena and Jaydess, in a combined proof-of-concept and dose-finding study in healthy pre-menopausal women treated for 90 days

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2013-003980-74 |
| Trial protocol | DE GB NL |
| Global end of trial date | 22 July 2016 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 07 June 2017 |
| First version publication date | 07 June 2017 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY1007626/15731 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02490774 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany, |
| Public contact | Bayer Clinical Trial Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.com |
| Scientific contact | Bayer Clinical Trial Contact, Bayer HealthCare AG, clinical-trials-contact@bayerhealthcare.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 | 22 July 2016 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 July 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate local and systemic effects of BAY1007626 on:

- Number of bleeding and spotting days,
- Endometrial histology,
- Ovulation (as surrogate for systemic effects).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 22 June 2015 |
| 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 | Netherlands: 59 |
| Country: Number of subjects enrolled | United Kingdom: 32 |
| Country: Number of subjects enrolled | Germany: 110 |
| Worldwide total number of subjects | 201 |
| EEA total number of subjects | 201 |

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) | 201 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 9 study centers in multiple countries: Germany, the Netherlands and the United Kingdom between 22 June 2015 (first subject first visit) and 26 May 2016 (last subject last visit).

Pre-assignment

Screening details:

Overall, 395 subjects were screened, of these 194 subjects were screen failures. A total of 201 subjects were randomized: 19 subjects were never administered study drug and 182 subjects were treated and of them 126 completed the study.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Single blind |
| Roles blinded | Subject |

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | BAY1007626, 5 microgram (mcg) |

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BAY1007626 |
| Investigational medicinal product code | BAY1007626 |
| Other name | |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.

| | |
|------------------|--------------------|
| Arm title | BAY1007626, 15 mcg |
|------------------|--------------------|

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BAY1007626 |
| Investigational medicinal product code | BAY1007626 |
| Other name | |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.

| | |
|------------------|--------------------|
| Arm title | BAY1007626, 30 mcg |
|------------------|--------------------|

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------------|
| Investigational medicinal product name | BAY1007626 |
| Investigational medicinal product code | BAY1007626 |
| Other name | |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.

| | |
|------------------|--------------------|
| Arm title | BAY1007626, 60 mcg |
|------------------|--------------------|

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BAY1007626 |
| Investigational medicinal product code | BAY1007626 |
| Other name | |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.

| | |
|------------------|--------------------------------------|
| Arm title | Levonorgestrel (Jaydess, BAY86-5028) |
|------------------|--------------------------------------|

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.

| | |
|--|------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Levonorgestrel |
| Investigational medicinal product code | BAY86-5028 |
| Other name | Jaydess |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.

| | |
|------------------|-------------------------------------|
| Arm title | Levonorgestrel (Mirena, BAY86-5028) |
|------------------|-------------------------------------|

Arm description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.

| | |
|--|------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Levonorgestrel |
| Investigational medicinal product code | BAY86-5028 |
| Other name | Mirena |
| Pharmaceutical forms | Intrauterine delivery system |
| Routes of administration | Intrauterine use |

Dosage and administration details:

Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.

| Number of subjects in period 1 | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg |
|---------------------------------------|----------------------------------|-----------------------|-----------------------|
| Started | 39 | 36 | 37 |
| Completed | 22 | 24 | 26 |
| Not completed | 17 | 12 | 11 |
| Protocol violation | 2 | 1 | 1 |
| Adverse event | 4 | - | 1 |
| Study terminated by sponsor | 11 | 9 | 8 |
| Withdrawal by subject | - | 2 | 1 |

| Number of subjects in period 1 | BAY1007626, 60 mcg | Levonorgestrel (Jaydess, BAY86- 5028) | Levonorgestrel (Mirena, BAY86- 5028) |
|---------------------------------------|-----------------------|---|--|
| | | | |
| Started | 39 | 12 | 38 |
| Completed | 24 | 10 | 24 |
| Not completed | 15 | 2 | 14 |
| Protocol violation | 2 | 1 | 1 |
| Adverse event | 3 | - | 3 |
| Study terminated by sponsor | 8 | 1 | 9 |
| Withdrawal by subject | 2 | - | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--------------------------------------|
| Reporting group title | BAY1007626, 5 microgram (mcg) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 15 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 30 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 60 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days. | |
| Reporting group title | Levonorgestrel (Jaydess, BAY86-5028) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days. | |
| Reporting group title | Levonorgestrel (Mirena, BAY86-5028) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days. | |

| Reporting group values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg |
|------------------------------------|-------------------------------|--------------------|--------------------|
| Number of subjects | 39 | 36 | 37 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|---------------|---------------|
| Age continuous Units: years arithmetic mean standard deviation | 29.9 ± 6.2 | 27.8 ± 5.4 | 30.7 ± 5.1 |
| Gender categorical Units: Subjects | | | |
| Female | 39 | 36 | 37 |

| Reporting group values | BAY1007626, 60 mcg | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) |
|------------------------------------|--------------------|--------------------------------------|-------------------------------------|
| Number of subjects | 39 | 12 | 38 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------|------|------|
| Age continuous Units: years arithmetic mean | 29.9 | 29.4 | 29.1 |
|---|------|------|------|

| | | | |
|--------------------|-------|-----|-------|
| standard deviation | ± 5.3 | ± 6 | ± 5.3 |
|--------------------|-------|-----|-------|

| | | | |
|---------------------------------------|----|----|----|
| Gender categorical Units: Subjects | | | |
| Female | 39 | 12 | 38 |

| | | | |
|------------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 201 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|---|-----|--|--|
| Age continuous Units: years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 201 | | |

End points

End points reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | BAY1007626, 5 microgram (mcg) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 15 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 30 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days. | |
| Reporting group title | BAY1007626, 60 mcg |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days. | |
| Reporting group title | Levonorgestrel (Jaydess, BAY86-5028) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days. | |
| Reporting group title | Levonorgestrel (Mirena, BAY86-5028) |
| Reporting group description: Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days. | |
| Subject analysis set title | Safety analysis set (SAF) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: SAF (N= 182) included all subjects who received study medication. | |
| Subject analysis set title | Pharmacodynamic analysis set 1 (PDS1) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: PDS1 (N= 134) included all subjects within the safety analysis set without major protocol deviations who were non completers with at least 60 days of treatment, and for whom not more than 9 entries in the bleeding diary were missing during the treatment period. | |
| Subject analysis set title | Pharmacodynamic analysis set 2 (PDS2) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: PDS2 (N= 44) included all subjects who received study medication, without major protocol violations for whom the pharmacodynamics biopsy was evaluated. | |
| Subject analysis set title | Pharmacodynamic analysis set 3 (PDS3) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: PDS3 (N= 167) included all subjects from the safety analysis set without major protocol deviations who were treated for at least 40 days (a time span that would cover at least one menstrual cycle in an untreated woman), and for whom weekly measurements of progesterone were performed as outlined in the protocol. | |

Primary: Number of Bleeding and Spotting Days During the 90 Days Treatment Period

| | |
|--|--|
| End point title | Number of Bleeding and Spotting Days During the 90 Days Treatment Period |
| End point description: The total number of bleeding and spotting days per subject under treatment were determined as the total number of days for which a code greater than (>) 1 had been observed. The following codes 1,2,3,4,5 were given for the below mentioned categories. 1) None: no bleeding 2) Spotting: less than associated with normal menstruation relative to the subject's experience, with no need for sanitary protection (except for panty liners) 3) Light: less than associated with normal menstruation relative to the subject's experience, with need for sanitary protection 4) Normal: like normal menstruation relative to the subject's experience 5) Heavy: more than normal menstruation relative to the subject's experience | |
| End point type | Primary |
| End point timeframe: Day 1 to Day 90 | |

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|--------------------------------------|-------------------------------|---------------------|---------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 ^[1] | 17 ^[2] | 22 ^[3] | 20 ^[4] |
| Units: days | | | | |
| arithmetic mean (standard deviation) | 38.0526 (± 18.0045) | 36.2353 (± 16.1072) | 49.8636 (± 15.3973) | 42.35 (± 19.2826) |

Notes:

[1] - PDS1 with number of subjects evaluable for this specific endpoint

[2] - PDS1 with number of subjects evaluable for this specific endpoint

[3] - PDS1 with number of subjects evaluable for this specific endpoint

[4] - PDS1 with number of subjects evaluable for this specific endpoint

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|--------------------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[5] | 20 ^[6] | | |
| Units: days | | | | |
| arithmetic mean (standard deviation) | 40.1111 (± 15.8623) | 37.3 (± 12.2178) | | |

Notes:

[5] - PDS1 with number of subjects evaluable for this specific endpoint

[6] - PDS1 with number of subjects evaluable for this specific endpoint

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 5 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95 percent (%) confidence interval (CI) estimates were given for the mean difference between Mirena and BAY1007626, 5 mcg arm. Point and CI estimates were determined by using a Bayesian analysis. | |
| Comparison groups | Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 5 |

| | |
|---|-----------------|
| | microgram (mcg) |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference |
| Point estimate | 2.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.7 |
| upper limit | 11.6 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 2 |
|-----------------------------------|------------------------|

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 15 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 15 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

| | |
|---|--|
| Comparison groups | Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 15 mcg |
| Number of subjects included in analysis | 37 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference |
| Point estimate | 0.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.3 |
| upper limit | 9.5 |

| | |
|-----------------------------------|------------------------|
| Statistical analysis title | Statistical analysis 3 |
|-----------------------------------|------------------------|

Statistical analysis description:

Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 30 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 30 mcg arm. Point and CI estimates were determined by using a Bayesian analysis.

| | |
|---|--|
| Comparison groups | Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 30 mcg |
| Number of subjects included in analysis | 42 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference |
| Point estimate | 14.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 6.9 |
| upper limit | 21.6 |

| | |
|--|--|
| Statistical analysis title | Statistical analysis 4 |
| Statistical analysis description: | |
| Number of bleeding and spotting days during the 90 days of treatment were analyzed assuming a normal distribution. BAY1007626, 60 mcg treatment arm was compared with the Mirena arm. Point estimates as well as two-sided 95% CI estimates were given for the mean difference between Mirena and BAY1007626, 60 mcg arm. Point and CI estimates were determined by using a Bayesian analysis. | |
| Comparison groups | Levonorgestrel (Mirena, BAY86-5028) v BAY1007626, 60 mcg |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| Parameter estimate | Mean difference |
| Point estimate | 6.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.8 |
| upper limit | 16.2 |

Primary: Number of Subjects With Endometrium Proliferative

| | |
|---|--|
| End point title | Number of Subjects With Endometrium Proliferative ^[7] |
| End point description: | |
| Endometrial histology was evaluated in endometrial biopsy specimen taken. The histology of the specimen was evaluated by blinded reading. As the study was terminated prematurely, biopsies were only assessed by blinded read assessment in a few subjects. Endometrial biopsies were taken between Days 41 and 90 during treatment and on Day 9 during follow-up. In the below table, "n" indicates the number of subjects analysed for the specified parameter at given time point for each arm, respectively. | |
| End point type | Primary |
| End point timeframe: | |
| Treatment (between Days 41 and 90), post-treatment, follow-up (Day 9 during follow-up) | |

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|---------------------------------|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 ^[8] | 7 ^[9] | 11 ^[10] | 8 ^[11] |
| Units: subjects | | | | |
| Treatment (n= 4,7,11,8,7,6) | 0 | 0 | 0 | 0 |
| Post-treatment (n= 0,1,0,0,0,0) | 0 | 0 | 0 | 0 |
| Follow-up (n= 2,1,4,0,3,2) | 2 | 1 | 4 | 0 |

Notes:

[8] - PDS2

[9] - PDS2

[10] - PDS2

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|---------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 7 ^[12] | 6 ^[13] | | |
| Units: subjects | | | | |
| Treatment (n= 4,7,11,8,7,6) | 0 | 1 | | |
| Post-treatment (n= 0,1,0,0,0,0) | 0 | 0 | | |
| Follow-up (n= 2,1,4,0,3,2) | 3 | 1 | | |

Notes:

[12] - PDS2

[13] - PDS2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Ovulation During Treatment

| | |
|-----------------|--|
| End point title | Number of Subjects With Ovulation During Treatment ^[14] |
|-----------------|--|

End point description:

Ovulation activity is defined as:

In the weekly visit group: frequency of ovulation (based on assessments of progesterone serum levels > 5 nanomoles/liter)

In the dense visit group: frequency of ovulation (based on evaluation of Hoogland score of 6).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 1 to Day 90

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: EudraCT database does not allow to report only one treatment group in statistical analyses section. Due to this format constraint, charts have been uploaded with the accurate details of statistical analyses for this endpoint. Please find the statistical analyses in the attachment below.

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|-----------------------------|-------------------------------------|-----------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 31 ^[15] | 31 ^[16] | 31 ^[17] | 32 ^[18] |
| Units: subjects | 28 | 29 | 29 | 19 |

Notes:

[15] - PDS3

[16] - PDS3

[17] - PDS3

[18] - PDS3

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 ^[19] | 31 ^[20] | | |
| Units: subjects | 10 | 19 | | |

Notes:

[19] - PDS3

[20] - PDS3

| | |
|-----------------------------------|---|
| Attachments (see zip file) | 15731_Statistical Analysis_Primary OM/15731_Statistical |
|-----------------------------------|---|

Statistical analyses

No statistical analyses for this end point

Secondary: Endometrial Thickness

| | |
|---|-----------------------|
| End point title | Endometrial Thickness |
| End point description: Endometrium is the tissue lining the inner cavity of the uterus. Endometrial thickness was measured by transvaginal ultrasound (TVU). TVU examination was performed by a trained qualified member of the investigation team. The endometrial thickness was measured in the medio-sagittal section as double layer in millimetres. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore, endometrial thickness was not measured. | |
| End point type | Secondary |
| End point timeframe: From start of treatment until end of study | |

| | | | | |
|-----------------------------|-------------------------------|--------------------|--------------------|--------------------|
| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[21] | 0 ^[22] | 0 ^[23] | 0 ^[24] |
| Units: subjects | | | | |

Notes:

[21] - As the primary endpoints could not be met, the study was discontinued permanently.

[22] - As the primary endpoints could not be met, the study was discontinued permanently.

[23] - As the primary endpoints could not be met, the study was discontinued permanently.

[24] - As the primary endpoints could not be met, the study was discontinued permanently.

| | | | | |
|-----------------------------|--------------------------------------|-------------------------------------|--|--|
| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[25] | 0 ^[26] | | |
| Units: subjects | | | | |

Notes:

[25] - As the primary endpoints could not be met, the study was discontinued permanently.

[26] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Bleeding Characterization (Intensity and Pattern)

| | |
|-----------------|---|
| End point title | Bleeding Characterization (Intensity and Pattern) |
|-----------------|---|

End point description:

A bleeding/spotting episode is defined as day(s) with bleeding/spotting preceded and followed by at least 2 bleed-free days.

For bleeding pattern the following dichotomous variables were analysed:

- a) Irregular bleeding: 3 to 5 bleeding/spotting episodes and less than 3 bleeding/spotting-free intervals of 14 or more days.
- b) Prolonged bleeding: any bleeding/spotting episode lasting more than 14 days.
- c) Frequent bleeding: more than 5 bleeding/spotting episodes.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 1 to Day 90

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|-----------------------------|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 19 ^[27] | 17 ^[28] | 22 ^[29] | 20 ^[30] |
| Units: subjects | | | | |
| Irregular bleeding | 8 | 8 | 12 | 13 |
| Prolonged bleeding | 9 | 7 | 14 | 13 |
| Frequent bleeding | 4 | 6 | 3 | 2 |

Notes:

[27] - PDS with number of subjects evaluable for this specific endpoint

[28] - PDS with number of subjects evaluable for this specific endpoint

[29] - PDS with number of subjects evaluable for this specific endpoint

[30] - PDS

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|-----------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 ^[31] | 20 ^[32] | | |
| Units: subjects | | | | |
| Irregular bleeding | 7 | 11 | | |
| Prolonged bleeding | 4 | 11 | | |
| Frequent bleeding | 0 | 5 | | |

Notes:

[31] - PDS

[32] - PDS with number of subjects evaluable for this specific endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Levels of Hormones (Estradiol, Progesterone, Luteinizing Hormone, Follicle-Stimulating Hormone)

| | |
|-----------------|---|
| End point title | Serum Levels of Hormones (Estradiol, Progesterone, Luteinizing Hormone, Follicle-Stimulating Hormone) |
|-----------------|---|

End point description:

Blood samples for the determination of estradiol, progesterone, luteinizing hormone, follicle-stimulating

hormone levels in serum were taken during the treatment period and the follow-up period. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore serum levels of hormones in blood were not evaluated.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From start of treatment until end of study | |

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|-----------------------------|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[33] | 0 ^[34] | 0 ^[35] | 0 ^[36] |
| Units: subjects | | | | |

Notes:

[33] - As the primary endpoints could not be met, the study was discontinued permanently.

[34] - As the primary endpoints could not be met, the study was discontinued permanently.

[35] - As the primary endpoints could not be met, the study was discontinued permanently.

[36] - As the primary endpoints could not be met, the study was discontinued permanently.

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|-----------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[37] | 0 ^[38] | | |
| Units: subjects | | | | |

Notes:

[37] - As the primary endpoints could not be met, the study was discontinued permanently.

[38] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

| | |
|-----------------|--|
| End point title | Number of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs) |
|-----------------|--|

End point description:

An adverse event (AE) was any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly and another medical important serious event as judged by investigator. AE/SAEs that started or worsened after study drug treatment were recorded as TEAE/TESAEs.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From start of study treatment until end of study | |

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|-----------------------------|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 36 ^[39] | 33 ^[40] | 33 ^[41] | 34 ^[42] |
| Units: subjects | | | | |
| TEAEs | 32 | 28 | 28 | 32 |
| TESAEs | 2 | 0 | 0 | 0 |

Notes:

[39] - SAF

[40] - SAF

[41] - SAF

[42] - SAF

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|-----------------------------|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 ^[43] | 35 ^[44] | | |
| Units: subjects | | | | |
| TEAEs | 11 | 33 | | |
| TESAEs | 0 | 0 | | |

Notes:

[43] - SAF

[44] - SAF

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Drug Concentration of BAY1007626 After Insertion of Intrauterine System (Cmax) in Plasma

| | |
|-----------------|---|
| End point title | Maximum Observed Drug Concentration of BAY1007626 After Insertion of Intrauterine System (Cmax) in Plasma |
|-----------------|---|

End point description:

Maximum observed drug concentration of BAY1007626 after insertion of intrauterine system in plasma. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|---|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[45] | 0 ^[46] | 0 ^[47] | 0 ^[48] |
| Units: microgram per liter (mcg/L) | | | | |
| geometric mean (geometric coefficient of variation) | () | () | () | () |

Notes:

[45] - As the primary endpoints could not be met, the study was discontinued permanently.

[46] - As the primary endpoints could not be met, the study was discontinued permanently.

[47] - As the primary endpoints could not be met, the study was discontinued permanently.

[48] - As the primary endpoints could not be met, the study was discontinued permanently.

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|---|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[49] | 0 ^[50] | | |
| Units: microgram per liter (mcg/L) | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[49] - As the primary endpoints could not be met, the study was discontinued permanently.

[50] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Versus Time Curve (AUC) of BAY1007626 in Plasma After Insertion of Intrauterine System

| | |
|-----------------|---|
| End point title | Area Under the Concentration Versus Time Curve (AUC) of BAY1007626 in Plasma After Insertion of Intrauterine System |
|-----------------|---|

End point description:

Area under the concentration versus time curve of BAY1007626 in plasma after insertion of intrauterine system. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|---|-------------------------------------|-----------------------|-----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[51] | 0 ^[52] | 0 ^[53] | 0 ^[54] |
| Units: microgram*hour per liter (mcg*h/L) | | | | |
| geometric mean (geometric coefficient of variation) | () | () | () | () |

Notes:

[51] - As the primary endpoints could not be met, the study was discontinued permanently.

[52] - As the primary endpoints could not be met, the study was discontinued permanently.

[53] - As the primary endpoints could not be met, the study was discontinued permanently.

[54] - As the primary endpoints could not be met, the study was discontinued permanently.

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|------------------|--|---|--|--|
|------------------|--|---|--|--|

| | | | | |
|---|-------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[55] | 0 ^[56] | | |
| Units: microgram*hour per liter (mcg*h/L) | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[55] - As the primary endpoints could not be met, the study was discontinued permanently.

[56] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Secondary: Half-life Associated With the Terminal Slope (t_{1/2}) of BAY1007626 in Plasma

| | |
|-----------------|--|
| End point title | Half-life Associated With the Terminal Slope (t _{1/2}) of BAY1007626 in Plasma |
|-----------------|--|

End point description:

Half-life associated with the terminal slope of BAY1007626 in plasma. As an interim analysis had shown that the primary endpoints could not be met, the study was discontinued permanently and therefore pharmacokinetic parameters were not evaluated.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre-dose (30 minutes prior on Day 1) to post-dose on Day 90

| End point values | BAY1007626, 5 microgram (mcg) | BAY1007626, 15 mcg | BAY1007626, 30 mcg | BAY1007626, 60 mcg |
|---|-------------------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[57] | 0 ^[58] | 0 ^[59] | 0 ^[60] |
| Units: hours | | | | |
| geometric mean (geometric coefficient of variation) | () | () | () | () |

Notes:

[57] - As the primary endpoints could not be met, the study was discontinued permanently.

[58] - As the primary endpoints could not be met, the study was discontinued permanently.

[59] - As the primary endpoints could not be met, the study was discontinued permanently.

[60] - As the primary endpoints could not be met, the study was discontinued permanently.

| End point values | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) | | |
|---|--------------------------------------|-------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0 ^[61] | 0 ^[62] | | |
| Units: hours | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[61] - As the primary endpoints could not be met, the study was discontinued permanently.

[62] - As the primary endpoints could not be met, the study was discontinued permanently.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment until end of study

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | BAY1007626, 5 mcg |
|-----------------------|-------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 5 mcg BAY1007626/day for 90 days.

| | |
|-----------------------|--------------------|
| Reporting group title | BAY1007626, 15 mcg |
|-----------------------|--------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 15 mcg BAY1007626/day for 90 days.

| | |
|-----------------------|--------------------|
| Reporting group title | BAY1007626, 30 mcg |
|-----------------------|--------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 30 mcg BAY1007626/day for 90 days.

| | |
|-----------------------|--------------------|
| Reporting group title | BAY1007626, 60 mcg |
|-----------------------|--------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 60 mcg BAY1007626/day for 90 days.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Levonorgestrel (Jaydess, BAY86-5028) |
|-----------------------|--------------------------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 12 mcg levonorgestrel/day for 90 days.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Levonorgestrel (Mirena, BAY86-5028) |
|-----------------------|-------------------------------------|

Reporting group description:

Subjects were treated with an intrauterine system with a nominal in vitro release of 20 mcg levonorgestrel/day for 90 days.

| Serious adverse events | BAY1007626, 5 mcg | BAY1007626, 15 mcg | BAY1007626, 30 mcg |
|---|-------------------|--------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | BAY1007626, 60 mcg | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) |
|---|--------------------|--------------------------------------|-------------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | BAY1007626, 5 mcg | BAY1007626, 15 mcg | BAY1007626, 30 mcg |
|---|-------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 32 / 36 (88.89%) | 28 / 33 (84.85%) | 28 / 33 (84.85%) |
| Surgical and medical procedures | | | |
| Mole excision | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dental care | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 1 | 1 |
| General disorders and administration | | | |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 3 | 1 | 1 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hangover | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Social circumstances | | | |
| Tattoo | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| disorders | | | |
| Breast enlargement | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Breast pain | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 4 | 0 | 1 |
| Breast tenderness | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | 3 / 33 (9.09%) | 1 / 33 (3.03%) |
| occurrences (all) | 11 | 3 | 2 |
| Dyspareunia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Galactorrhoea | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Menorrhagia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metrorrhagia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Nipple pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 33 (6.06%) | 6 / 33 (18.18%) |
| occurrences (all) | 3 | 2 | 8 |
| Ovulation pain | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pelvic pain | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 4 / 36 (11.11%) | 1 / 33 (3.03%) | 3 / 33 (9.09%) |
| occurrences (all) | 13 | 2 | 3 |
| Uterine polyp | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal discharge | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 33 (6.06%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 2 | 1 |
| Vaginal odour | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal discomfort | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 1 | 1 |
| Uterine cyst | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Breast discomfort | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 3 / 33 (9.09%) |
| occurrences (all) | 0 | 1 | 4 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 4 / 33 (12.12%) | 2 / 33 (6.06%) |
| occurrences (all) | 1 | 5 | 2 |
| Vulvovaginal burning sensation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal erythema | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 33 (6.06%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 2 | 1 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 33 (6.06%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 33 (6.06%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 2 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Listless | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Mood swings | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Sleep disorder subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Suicidal ideation subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Affect lability subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Product issues Device expulsion subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Investigations Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 2 / 33 (6.06%) 2 | 2 / 33 (6.06%) 2 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 2 / 33 (6.06%) 2 | 3 / 33 (9.09%) 3 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Blood potassium increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Blood prolactin increased subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Blood triglycerides increased | | | |

| | | | |
|----------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | 4 / 33 (12.12%) | 2 / 33 (6.06%) |
| occurrences (all) | 4 | 4 | 2 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monocyte count increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Red blood cell count decreased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 3 / 33 (9.09%) | 0 / 33 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 1 / 33 (3.03%) | 2 / 33 (6.06%) |
| occurrences (all) | 2 | 1 | 2 |
| Urine bilirubin increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nitrite urine present | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Protein urine present | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 2 | 1 | 1 |
| Lymph node palpable | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Waist circumference increased | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bilirubin urine present | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Traumatic haematoma | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb injury | | | |

| | | | |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 2 / 33 (6.06%) 2 | 0 / 33 (0.00%) 0 |
| Procedural pain subjects affected / exposed occurrences (all) | 4 / 36 (11.11%) 4 | 5 / 33 (15.15%) 7 | 5 / 33 (15.15%) 5 |
| Ligament rupture subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Procedural nausea subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 4 / 33 (12.12%) 4 | 1 / 33 (3.03%) 1 |
| Headache subjects affected / exposed occurrences (all) | 14 / 36 (38.89%) 21 | 14 / 33 (42.42%) 31 | 14 / 33 (42.42%) 35 |
| Hemiparesis subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Muscle contractions involuntary subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Sciatica subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Sinus headache | | | |

| | | | |
|---|-----------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Syncope subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Visual field defect subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Hemianaesthesia subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Microcytic anaemia subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Eye disorders Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | 5 / 33 (15.15%) 13 | 5 / 33 (15.15%) 7 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 8 / 36 (22.22%) 20 | 11 / 33 (33.33%) 29 | 11 / 33 (33.33%) 34 |
| Abdominal pain upper | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 33 (6.06%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 3 / 33 (9.09%) |
| occurrences (all) | 1 | 1 | 4 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | 2 / 33 (6.06%) | 1 / 33 (3.03%) |
| occurrences (all) | 4 | 2 | 1 |
| Toothache | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 0 / 33 (0.00%) | 3 / 33 (9.09%) |
| occurrences (all) | 2 | 0 | 3 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 3 | 1 | 1 |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | 1 / 33 (3.03%) | 4 / 33 (12.12%) |
| occurrences (all) | 3 | 2 | 4 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Alopecia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 1 | 2 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Eczema | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hair texture abnormal | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Hirsutism | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 2 | 1 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| Skin disorder | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 2 / 33 (6.06%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Bilirubinuria | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 2 / 33 (6.06%) |
| occurrences (all) | 1 | 1 | 2 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 2 / 33 (6.06%) |
| occurrences (all) | 1 | 1 | 2 |
| Ketonuria | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 33 (6.06%) | 1 / 33 (3.03%) |
| occurrences (all) | 2 | 2 | 1 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Urobilinuria | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocyturia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Back pain | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | 5 / 33 (15.15%) | 0 / 33 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 33 (6.06%) | 2 / 33 (6.06%) |
| occurrences (all) | 2 | 4 | 2 |
| Myositis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Bacterial vaginosis | | | |

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|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 2 / 33 (6.06%) | 3 / 33 (9.09%) |
| occurrences (all) | 1 | 3 | 4 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Furuncle | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gingivitis | | | |

| | | | |
|-----------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 6 / 36 (16.67%) | 6 / 33 (18.18%) | 3 / 33 (9.09%) |
| occurrences (all) | 8 | 8 | 3 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 14 / 36 (38.89%) | 11 / 33 (33.33%) | 13 / 33 (39.39%) |
| occurrences (all) | 20 | 14 | 18 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 1 / 33 (3.03%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vaginal infection | | | |
| subjects affected / exposed | 0 / 36 (0.00%) | 0 / 33 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal candidiasis | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 2 / 33 (6.06%) 2 |
| Tooth infection subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Vaginitis bacterial subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 1 / 33 (3.03%) 1 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Oral herpes subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 4 | 0 / 33 (0.00%) 0 | 2 / 33 (6.06%) 2 |
| Metabolism and nutrition disorders | | | |
| Increased appetite subjects affected / exposed occurrences (all) | 1 / 36 (2.78%) 1 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 1 / 33 (3.03%) 1 | 0 / 33 (0.00%) 0 |
| Food intolerance subjects affected / exposed occurrences (all) | 0 / 36 (0.00%) 0 | 0 / 33 (0.00%) 0 | 0 / 33 (0.00%) 0 |

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|--|---------------------|--------------------------------------|-------------------------------------|
| Non-serious adverse events | BAY1007626, 60 mcg | Levonorgestrel (Jaydess, BAY86-5028) | Levonorgestrel (Mirena, BAY86-5028) |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 32 / 34 (94.12%) | 11 / 11 (100.00%) | 33 / 35 (94.29%) |
| Surgical and medical procedures | | | |
| Mole excision subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Dental care subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| General disorders and administration site conditions | | | |

| | | | |
|--|----------------|----------------|----------------|
| Asthenia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 1 | 1 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hangover | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Social circumstances | | | |
| Tattoo | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| Breast enlargement | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Breast pain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Breast tenderness | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 4 / 34 (11.76%) | 2 / 11 (18.18%) | 2 / 35 (5.71%) |
| occurrences (all) | 6 | 2 | 2 |
| Dyspareunia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Galactorrhoea | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Metrorrhagia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nipple pain | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ovarian cyst | | | |
| subjects affected / exposed | 17 / 34 (50.00%) | 2 / 11 (18.18%) | 14 / 35 (40.00%) |
| occurrences (all) | 24 | 2 | 21 |
| Ovulation pain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 3 / 11 (27.27%) | 4 / 35 (11.43%) |
| occurrences (all) | 2 | 4 | 5 |

| | | | |
|---|-----------------|-----------------|----------------|
| Uterine polyp | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vaginal discharge | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Vaginal odour | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vulvovaginal discomfort | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Uterine cyst | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breast discomfort | | | |
| subjects affected / exposed | 4 / 34 (11.76%) | 1 / 11 (9.09%) | 3 / 35 (8.57%) |
| occurrences (all) | 4 | 1 | 4 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhagic ovarian cyst | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal burning sensation | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal erythema | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 2 / 11 (18.18%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 3 | 1 |
| Dysphonia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |
| Psychiatric disorders | | | |
| Affective disorder | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Libido decreased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Listless | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 2 |
| Mood swings | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------|-----------------|----------------|
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Affect lability | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Product issues | | | |
| Device expulsion | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 0 | 1 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 2 / 11 (18.18%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 2 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood potassium increased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood prolactin increased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 11 (9.09%) | 1 / 35 (2.86%) |
| occurrences (all) | 3 | 3 | 1 |
| Blood urine present | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 3 / 34 (8.82%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 3 | 0 | 1 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Monocyte count increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Red blood cell count decreased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 1 | 0 | 3 |
| Urine bilirubin increased | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nitrite urine present | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Platelet count increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Protein urine present | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymph node palpable | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Waist circumference increased | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bilirubin urine present | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 3 / 35 (8.57%) |
| occurrences (all) | 0 | 0 | 3 |
| Traumatic haematoma | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |

| | | | |
|---------------------------------|------------------|------------------|------------------|
| subjects affected / exposed | 7 / 34 (20.59%) | 2 / 11 (18.18%) | 12 / 35 (34.29%) |
| occurrences (all) | 10 | 2 | 13 |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural nausea | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 11 (9.09%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 1 | 1 |
| Headache | | | |
| subjects affected / exposed | 15 / 34 (44.12%) | 10 / 11 (90.91%) | 11 / 35 (31.43%) |
| occurrences (all) | 22 | 28 | 12 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle contractions involuntary | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Syncope | | | |

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|---|------------------------|-----------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Visual field defect subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Hemianaesthesia subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Microcytic anaemia subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Eye disorders Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 35 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 3 / 34 (8.82%) 4 | 1 / 11 (9.09%) 1 | 5 / 35 (14.29%) 6 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 17 / 34 (50.00%) 38 | 7 / 11 (63.64%) 18 | 10 / 35 (28.57%) 17 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 1 | 1 / 35 (2.86%) 2 |
| Constipation | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 1 / 11 (9.09%) | 1 / 35 (2.86%) |
| occurrences (all) | 2 | 1 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal pain | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 1 / 11 (9.09%) | 1 / 35 (2.86%) |
| occurrences (all) | 3 | 1 | 2 |
| Toothache | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Chapped lips | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 1 / 11 (9.09%) | 3 / 35 (8.57%) |
| occurrences (all) | 2 | 1 | 4 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Dry skin | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Hair texture abnormal | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hirsutism | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 2 / 35 (5.71%) |
| occurrences (all) | 0 | 0 | 2 |
| Rosacea | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------------|---------------------|----------------------|
| Skin irritation subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Bilirubinuria subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 4 | 1 / 11 (9.09%) 2 | 4 / 35 (11.43%) 6 |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Haematuria subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 1 / 11 (9.09%) 3 | 0 / 35 (0.00%) 0 |
| Ketonuria subjects affected / exposed occurrences (all) | 5 / 34 (14.71%) 5 | 1 / 11 (9.09%) 1 | 1 / 35 (2.86%) 3 |
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 35 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 2 | 0 / 35 (0.00%) 0 |
| Renal pain subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Urobilinuria subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 1 | 0 / 35 (0.00%) 0 |
| Leukocyturia subjects affected / exposed occurrences (all) | 4 / 34 (11.76%) 5 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Back pain | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 34 (8.82%) | 2 / 11 (18.18%) | 4 / 35 (11.43%) |
| occurrences (all) | 3 | 2 | 4 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Myositis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| Cystitis | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Diarrhoea infectious | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Furuncle | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 2 / 11 (18.18%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| Laryngitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 34 (38.24%) | 6 / 11 (54.55%) | 13 / 35 (37.14%) |
| occurrences (all) | 18 | 7 | 19 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 0 | 0 | 1 |
| Paronychia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 11 (0.00%) | 1 / 35 (2.86%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal infection | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vulvovaginal candidiasis | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 1 / 11 (9.09%) | 0 / 35 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 11 (0.00%) | 0 / 35 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Vaginitis bacterial subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 1 |
| Oral herpes subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 2 |
| Metabolism and nutrition disorders | | | |
| Increased appetite subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 11 (9.09%) 1 | 1 / 35 (2.86%) 1 |
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 0 / 35 (0.00%) 0 |
| Food intolerance subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 11 (0.00%) 0 | 1 / 35 (2.86%) 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? Yes

| Date | Interruption | Restart date |
|-------------|--|--------------|
| 26 May 2016 | The underlying clinical development program had been discontinued permanently. An interim analysis had shown that one of the primary endpoints (reduction in number of bleeding and spotting days compared to Mirena during the first 90 days of treatment) could not be met. Without demonstrating superiority of this primary variable a further development of an IUS releasing BAY1007626 intended to reduce initial bleeding/ spotting after IUS insertion did not make sense and the development program was discontinued. | - |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was discontinued permanently as the primary endpoints could not be met. Decimal places were automatically truncated if last decimal equals zero.

Notes: