



## Clinical trial results:

### A Phase 2 Multicenter, 36-Week Study to Assess the Safety and Effectiveness of Daily Oral Administration of Dexlansoprazole Delayed-Release Capsules for Healing of Erosive Esophagitis and Maintenance of Healed Erosive Esophagitis and Relief of Heartburn, in Adolescent Subjects Aged 12 to 17 Years

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2012-001681-15   |
| Trial protocol           | HU BE PT IT      |
| Global end of trial date | 10 November 2014 |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 04 March 2016 |
| First version publication date | 17 June 2015  |

#### Trial information

##### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | TAK-390MR_207 |
|-----------------------|---------------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT01642615     |
| WHO universal trial number (UTN)   | U1111-1128-6117 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Takeda Development Center Americas, Inc.   |
| Sponsor organisation address | One Takeda Parkway, Deerfield, United States, 60015  |
| Public contact               | Study Registration Call Centre, Takeda Global Research & Development Center, Inc., 001 877-825-3327, medicalinformation@tpna.com |
| Scientific contact           | Study Registration Call Centre, Takeda Global Research & Development Center, Inc., 001 877-825-3327, medicalinformation@tpna.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? | Yes |

Notes:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 13 March 2015    |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 10 November 2014 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 10 November 2014 |
| Was the trial ended prematurely?                     | No               |

Notes:

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**General information about the trial**

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Main objective of the trial:

The purpose of this study was to assess the safety and effectiveness of treatment with once daily oral administration of dexlansoprazole delayed-release capsules in adolescents with erosive esophagitis (EE) and for maintenance of healed EE and relief of heartburn.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 22 June 2012 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | No           |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 22 |
| Country: Number of subjects enrolled | Mexico: 2         |
| Country: Number of subjects enrolled | Poland: 34        |
| Country: Number of subjects enrolled | Portugal: 4       |
| Worldwide total number of subjects   | 62                |
| EEA total number of subjects         | 38                |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                 | 62 |
| Adults (18-64 years)                      | 0  |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at 18 investigative sites in Mexico, Poland, Portugal and the United States from 22 June 2012 (first participant to sign the informed consent) to 10 November 2014.

### Pre-assignment

Screening details:

63 adolescents with a diagnosis of erosive esophagitis (EE) were enrolled in the dexamethasone delayed release 60 mg capsules open label phase. One participant did not take study drug. Participants with healed EE were randomized into one of 2 treatment groups: dexamethasone delayed release 30 mg capsules or placebo in the maintenance phase

### Pre-assignment period milestones

|                              |                   |
|------------------------------|-------------------|
| Number of subjects started   | 63 <sup>[1]</sup> |
| Number of subjects completed | 62                |

### Pre-assignment subject non-completion reasons

|                            |                              |
|----------------------------|------------------------------|
| Reason: Number of subjects | Did not receive treatment: 1 |
|----------------------------|------------------------------|

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 participant did not receive study medication and therefore was not accounted for in the worldwide number enrolled.

### Period 1

|                              |                          |
|------------------------------|--------------------------|
| Period 1 title               | Open Label Healing Phase |
| Is this the baseline period? | Yes                      |
| Allocation method            | Not applicable           |
| Blinding used                | Not blinded              |

### Arms

|           |                                    |
|-----------|------------------------------------|
| Arm title | Healing Phase: Dexamethasone 60 mg |
|-----------|------------------------------------|

Arm description:

Dexamethasone 60 mg delayed-release capsules, orally, once daily for up to 8 weeks.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | dexamethasone |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Capsule       |
| Routes of administration               | Oral use      |

Dosage and administration details:

60 mg delayed release capsules

| Number of subjects in period 1   | Healing Phase:<br>Dexlansoprazole 60 mg |
|----------------------------------|---|
| Started                          | 62                                      |
| Safety Analysis Set              | 62                                      |
| Completed                        | 58                                      |
| Not completed                    | 4                                       |
| Pretreatment Event/Adverse Event | 1                                       |
| Major Protocol Deviation         | 1                                       |
| Voluntary Withdrawal             | 1                                       |
| Lost to follow-up                | 1                                       |

## Period 2

|                              |   |
|------------------------------|---|
| Period 2 title               | Double Blind Maintenance Phase                      |
| Is this the baseline period? | No  |
| Allocation method            | Randomised - controlled                             |
| Blinding used                | Double blind  |
| Roles blinded                | Subject, Investigator, Monitor, Data analyst, Carer |

## Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | Yes                                      |
| <b>Arm title</b>             | Maintenance Phase: Dexlansoprazole 30 mg |

### Arm description:

Participants who are healed at Week 8 will be randomized to receive 30 mg dexlansoprazole delayed-release capsules, orally, once daily for up to 16 weeks.

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | dexlansoprazole |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Capsule         |
| Routes of administration               | Oral use        |

### Dosage and administration details:

delayed release capsules

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Maintenance Phase: Placebo |
|------------------|----------------------------|

### Arm description:

Participants who are healed at Week 8 will be randomized to receive dexlansoprazole placebo-matching capsules, orally, once daily for up to 16 weeks.

|  |                                  |
|--|----------------------------------|
| Arm type                               | Placebo                          |
| Investigational medicinal product name | placebo-matching dexlansoprazole |
| Investigational medicinal product code |                                  |
| Other name                             |                                  |
| Pharmaceutical forms                   | Capsule                          |
| Routes of administration               | Oral use                         |

### Dosage and administration details:

dexlansoprazole placebo-matching capsules

| <b>Number of subjects in period 2<sup>[2]</sup></b> | Maintenance Phase: Dexlansoprazole 30 mg | Maintenance Phase: Placebo |
|---|--|----------------------------|
| Started   | 25                                       | 26                         |
| Completed   | 18                                       | 20                         |
| Not completed                                       | 7  | 6                          |
| Pretreatment Event/Adverse Event                    | 1  | -                          |
| Voluntary Withdrawal                                | 5  | 2                          |
| Requires Treatment with Another Drug                | -  | 1                          |
| Lack of efficacy                                    | 1  | 3                          |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants with healing of EE at the end of the Open-Label Phase were eligible to participate in the Maintenance Phase.

## Baseline characteristics

### Reporting groups

|   |                                      |
|---|--------------------------------------|
| Reporting group title   | Healing Phase: Dexlansoprazole 60 mg |
| Reporting group description:  |                                      |
| Dexlansoprazole 60 mg delayed-release capsules, orally, once daily for up to 8 weeks. |                                      |

| Reporting group values   | Healing Phase:<br>Dexlansoprazole 60<br>mg | Total |  |
|--|--|-------|--|
| Number of subjects   | 62   | 62    |  |
| Age categorical  |  |       |  |
| Units: Subjects  |  |       |  |
| 12 to 14 years   | 24   | 24    |  |
| 15 to 17 years   | 38   | 38    |  |
| Age continuous   |  |       |  |
| Units: years   |  |       |  |
| arithmetic mean  | 14.8                                       |       |  |
| standard deviation   | ± 1.64                                     | -     |  |
| Gender categorical   |  |       |  |
| Units: Subjects  |  |       |  |
| Female   | 24   | 24    |  |
| Male   | 38   | 38    |  |
| Race/Ethnicity, Customized   |  |       |  |
| Units: Subjects  |  |       |  |
| Not Hispanic or Latino   | 16   | 16    |  |
| Hispanic or Latino   | 6  | 6     |  |
| Not Collected outside the United States  | 40   | 40    |  |
| Race/Ethnicity, Customized   |  |       |  |
| Units: Subjects  |  |       |  |
| Black or African American  | 1  | 1     |  |
| White  | 61   | 61    |  |
| Smoking Classification   |  |       |  |
| Units: Subjects  |  |       |  |
| Never smoked   | 61   | 61    |  |
| Current smoker   | 1  | 1     |  |
| Ex-smoker  | 0  | 0     |  |
| Helicobacter pylori (H. pylori) Status   |  |       |  |
| Units: Subjects  |  |       |  |
| Positive   | 0  | 0     |  |
| Negative   | 61   | 61    |  |
| Unknown  | 1  | 1     |  |
| Erosive Esophagitis Present  |  |       |  |
| Units: Subjects  |  |       |  |
| Yes  | 62   | 62    |  |
| No   | 0  | 0     |  |
| [Baseline EE Grade (LA Classification)]  |  |       |  |
| A=1 (or more) mucosal break 5 mm or less that does not extend between the tops of two mucosal folds,<br>B=1 (or more) mucosal break more than 5 mm-long that does not extend between the tops of two |  |       |  |

|  |         |    |  |
|--|---------|----|--|
| mucosal folds, C=1 (or more) mucosal break that is continuous between the tops of two or more mucosal folds but that involves less than 75% of the circumference and D=1 (or more) mucosal break that involves at least 75% of the esophageal circumference. |         |    |  |
| Units: Subjects  |         |    |  |
| Grade A  | 34      | 34 |  |
| Grade B  | 26      | 26 |  |
| Grade C  | 1       | 1  |  |
| Grade D  | 1       | 1  |  |
| Region of Enrollment   |         |    |  |
| Units: Subjects  |         |    |  |
| United States  | 22      | 22 |  |
| Portugal   | 4       | 4  |  |
| Poland   | 34      | 34 |  |
| Mexico   | 2       | 2  |  |
| Height   |         |    |  |
| Units: cm  |         |    |  |
| arithmetic mean  | 165.5   |    |  |
| standard deviation   | ± 9.68  | -  |  |
| Weight   |         |    |  |
| Units: kg  |         |    |  |
| arithmetic mean  | 61.86   |    |  |
| standard deviation   | ± 17.06 | -  |  |
| Body Mass index (BMI)  |         |    |  |
| BMI is calculated using the weight and height.   |         |    |  |
| Units: kg/m <sup>2</sup>   |         |    |  |
| arithmetic mean  | 22.34   |    |  |
| standard deviation   | ± 5.086 | -  |  |



## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | Healing Phase: Dexlansoprazole 60 mg     |
| Reporting group description:<br>Dexlansoprazole 60 mg delayed-release capsules, orally, once daily for up to 8 weeks.  |  |
| Reporting group title  | Maintenance Phase: Dexlansoprazole 30 mg |
| Reporting group description:<br>Participants who are healed at Week 8 will be randomized to receive 30 mg dexlansoprazole delayed-release capsules, orally, once daily for up to 16 weeks. |  |
| Reporting group title  | Maintenance Phase: Placebo               |
| Reporting group description:<br>Participants who are healed at Week 8 will be randomized to receive dexlansoprazole placebo-matching capsules, orally, once daily for up to 16 weeks.      |  |

### Primary: Percentage of Participants Who Experience Each Treatment Emergent Adverse Event Experienced by $\geq 5\%$ of Participants During the 8-week Healing Treatment Period

|  |   |
|--|---|
| End point title  | Percentage of Participants Who Experience Each Treatment Emergent Adverse Event Experienced by $\geq 5\%$ of Participants During the 8-week Healing Treatment Period <sup>[1]</sup> |
| End point description:<br>An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (eg, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. A Treatment Emergent Adverse Event (TEAE) is defined as an Adverse Event (AE) that starts or worsens on or after Study Day 1, and no more than 30 days after the last dose. |   |
| End point type   | Primary   |
| End point timeframe:<br>8 weeks  |   |
| Notes:<br>[1] - 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.<br>Justification: Statistical analysis not done.   |   |

| End point values                  | Healing Phase: Dexlansoprazole 60 mg |  |  |  |
|-----------------------------------|--------------------------------------|--|--|--|
| Subject group type                | Reporting group                      |  |  |  |
| Number of subjects analysed       | 62                                   |  |  |  |
| Units: percentage of participants |                                      |  |  |  |
| number (not applicable)           |                                      |  |  |  |
| Diarrhoea                         | 6.5                                  |  |  |  |
| Nasopharyngitis                   | 6.5                                  |  |  |  |
| Headache                          | 12.9                                 |  |  |  |
| Oropharyngeal pain                | 8.1                                  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percent of Participants Who Experience Each Treatment Emergent Adverse Event Experienced by $\geq 5\%$ of Participants During the 16-week Maintenance Treatment Period

|                 |   |
|-----------------|---|
| End point title | Percent of Participants Who Experience Each Treatment Emergent Adverse Event Experienced by $\geq 5\%$ of Participants During the 16-week Maintenance Treatment Period <sup>[2]</sup> |
|-----------------|---|

End point description:

An Adverse Event (AE) is defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (eg, a clinically significant abnormal laboratory finding), symptom, or disease temporally associated with the use of a drug, whether or not it is considered related to the drug. A Treatment Emergent Adverse Event (TEAE) is defined as an Adverse Event (AE) that starts or worsens on or after Study Day 1, and no more than 30 days after the last dose.

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

End point timeframe:

From Week 8 to Week 24

Notes:

[2] - 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: Statistical analysis not done.

| End point values                  | Maintenance Phase: Dexamethasone 30 mg | Maintenance Phase: Placebo |  |  |
|-----------------------------------|--|----------------------------|--|--|
| Subject group type                | Reporting group                        | Reporting group            |  |  |
| Number of subjects analysed       | 25                                     | 26                         |  |  |
| Units: percentage of participants |  |                            |  |  |
| number (not applicable)           |  |                            |  |  |
| Abdominal pain                    | 12                                     | 11.5                       |  |  |
| Abdominal pain upper              | 4                                      | 7.7                        |  |  |
| Erosive oesophagitis              | 4                                      | 7.7                        |  |  |
| Diarrhoea                         | 0                                      | 7.7                        |  |  |
| Pyrexia                           | 0                                      | 7.7                        |  |  |
| Nasopharyngitis                   | 12                                     | 15.4                       |  |  |
| Pharyngitis                       | 12                                     | 0                          |  |  |
| Sinusitis                         | 12                                     | 0                          |  |  |
| Upper respiratory tract infection | 8                                      | 0                          |  |  |
| Bronchitis                        | 8                                      | 3.8                        |  |  |
| Headache                          | 24                                     | 15.4                       |  |  |
| Insomnia                          | 8                                      | 0                          |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants With Healing of Erosive Esophagitis (EE) by Week 8

|  |   |
|--|---|
| End point title  | Percentage of Participants With Healing of Erosive Esophagitis (EE) by Week 8 |
| End point description:<br>Healing of EE was assessed by endoscopy. |   |
| End point type   | Secondary   |
| End point timeframe:<br>8 weeks                                    |   |

|                                   |   |  |  |  |
|-----------------------------------|---|--|--|--|
| <b>End point values</b>           | Healing Phase:<br>Dexlansoprazole 60 mg |  |  |  |
| Subject group type                | Reporting group                         |  |  |  |
| Number of subjects analysed       | 58                                      |  |  |  |
| Units: percentage of participants |   |  |  |  |
| number (confidence interval 95%)  | 87.9 (76.7 to 95)                       |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Participants Who Maintain Healing of EE From Week 8 to Week 24

|   |  |
|---|--|
| End point title   | Percentage of Participants Who Maintain Healing of EE From Week 8 to Week 24 |
| End point description:<br>Percentage of participants who maintain healing of EE from Week 8 to Week 24 among the patients who were healed at Week 8 as assessed by endoscopy. |  |
| End point type  | Secondary  |
| End point timeframe:<br>From Week 8 to Week 24  |  |

|                                   |   |                            |  |  |
|-----------------------------------|---|----------------------------|--|--|
| <b>End point values</b>           | Maintenance Phase:<br>Dexlansoprazole 30 mg | Maintenance Phase: Placebo |  |  |
| Subject group type                | Reporting group                             | Reporting group            |  |  |
| Number of subjects analysed       | 22  | 24                         |  |  |
| Units: percentage of participants |   |                            |  |  |
| number (confidence interval 95%)  | 81.8 (59.7 to 94.8)                         | 58.3 (36.6 to 77.9)        |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent of Days With Neither Daytime Nor Nighttime Heartburn Over the First 8 Weeks of Treatment

|                 |  |
|-----------------|--|
| End point title | Percent of Days With Neither Daytime Nor Nighttime Heartburn Over the First 8 Weeks of Treatment |
|-----------------|--|

End point description:

Percent of days with neither daytime nor nighttime heartburn over the first 8 weeks of treatment as assessed by electronic daily diary. The percent of days with neither daytime or nighttime heartburn = (total number of days that are heartburn free)/(total number of days for which either a daytime or nighttime result is marked) x 100%.

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

End point timeframe:

8 weeks

|                                      |   |  |  |  |
|--------------------------------------|---|--|--|--|
| <b>End point values</b>              | Healing Phase:<br>Dexlansoprazole 60 mg |  |  |  |
| Subject group type                   | Reporting group                         |  |  |  |
| Number of subjects analysed          | 62                                      |  |  |  |
| Units: percent of days               |   |  |  |  |
| arithmetic mean (standard deviation) | 59.6 (± 30.46)                          |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percent of Days With Neither Daytime Nor Nighttime Heartburn Over Weeks 8 to 24

|                 |   |
|-----------------|---|
| End point title | Percent of Days With Neither Daytime Nor Nighttime Heartburn Over Weeks 8 to 24 |
|-----------------|---|

End point description:

The percent of days with neither daytime nor nighttime heartburn over Weeks 8 to 24 as assessed by electronic daily diary among the participants who were healed at Week 8. The percent of days with neither daytime or nighttime heartburn = (total number of days that are heartburn free)/(total number of days for which either a daytime or nighttime result is marked) x 100%.

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

End point timeframe:

Weeks 8 to 24

|                             |   |                            |  |  |
|-----------------------------|---|----------------------------|--|--|
| <b>End point values</b>     | Maintenance Phase:<br>Dexlansoprazole 30 mg | Maintenance Phase: Placebo |  |  |
| Subject group type          | Reporting group                             | Reporting group            |  |  |
| Number of subjects analysed | 24  | 26                         |  |  |
| Units: percent of days      |   |                            |  |  |

|                                      |                     |                     |  |  |
|--------------------------------------|---------------------|---------------------|--|--|
| arithmetic mean (standard deviation) | 76.7 ( $\pm$ 29.82) | 68.9 ( $\pm$ 26.04) |  |  |
|--------------------------------------|---------------------|---------------------|--|--|

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 24 Weeks

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                                      |
|-----------------------|--------------------------------------|
| Reporting group title | Healing Phase: Dexlansoprazole 60 mg |
|-----------------------|--------------------------------------|

Reporting group description:

Dexlansoprazole 60 mg delayed-release capsules, orally, once daily for up to 8 weeks.

|                       |  |
|-----------------------|--|
| Reporting group title | Maintenance Phase: Dexlansoprazole 30 mg |
|-----------------------|--|

Reporting group description:

Participants who are healed at Week 8 will be randomized to receive 30 mg dexlansoprazole delayed-release capsules, orally, once daily for up to 16 weeks.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Maintenance Phase: Placebo |
|-----------------------|----------------------------|

Reporting group description:

Participants who are healed at Week 8 will be randomized to receive dexlansoprazole placebo-matching capsules, orally, once daily for up to 16 weeks.

| Serious adverse events                            | Healing Phase:<br>Dexlansoprazole 60<br>mg | Maintenance Phase:<br>Dexlansoprazole 30<br>mg | Maintenance Phase:<br>Placebo |
|---|--|--|-------------------------------|
| Total subjects affected by serious adverse events |  |  |                               |
| subjects affected / exposed                       | 1 / 62 (1.61%)                             | 2 / 25 (8.00%)                                 | 1 / 26 (3.85%)                |
| number of deaths (all causes)                     | 0  | 0  | 0                             |
| number of deaths resulting from adverse events    | 0  | 0  | 0                             |
| Nervous system disorders                          |  |  |                               |
| Convulsion  |  |  |                               |
| subjects affected / exposed                       | 0 / 62 (0.00%)                             | 1 / 25 (4.00%)                                 | 0 / 26 (0.00%)                |
| occurrences causally related to treatment / all   | 0 / 0                                      | 0 / 1  | 0 / 0                         |
| deaths causally related to treatment / all        | 0 / 0                                      | 0 / 0  | 0 / 0                         |
| Gastrointestinal disorders                        |  |  |                               |
| Erosive oesophagitis                              |  |  |                               |
| subjects affected / exposed                       | 0 / 62 (0.00%)                             | 1 / 25 (4.00%)                                 | 0 / 26 (0.00%)                |
| occurrences causally related to treatment / all   | 0 / 0                                      | 1 / 1  | 0 / 0                         |
| deaths causally related to treatment / all        | 0 / 0                                      | 0 / 0  | 0 / 0                         |
| Psychiatric disorders                             |  |  |                               |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Substance abuse                                 |                |                |                |
| subjects affected / exposed                     | 1 / 62 (1.61%) | 0 / 25 (0.00%) | 0 / 26 (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          |
| Infections and infestations                     |                |                |                |
| H1N1 influenza                                  |                |                |                |
| subjects affected / exposed                     | 0 / 62 (0.00%) | 0 / 25 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | Healing Phase:<br>Dexlansoprazole 60<br>mg | Maintenance Phase:<br>Dexlansoprazole 30<br>mg | Maintenance Phase:<br>Placebo |
|---|--|--|-------------------------------|
| Total subjects affected by non-serious adverse events |  |  |                               |
| subjects affected / exposed                           | 24 / 62 (38.71%)                           | 14 / 25 (56.00%)                               | 11 / 26 (42.31%)              |
| Nervous system disorders                              |  |  |                               |
| Headache  |  |  |                               |
| subjects affected / exposed                           | 8 / 62 (12.90%)                            | 6 / 25 (24.00%)                                | 4 / 26 (15.38%)               |
| occurrences (all)                                     | 9  | 9  | 7                             |
| General disorders and administration site conditions  |  |  |                               |
| Pyrexia   |  |  |                               |
| subjects affected / exposed                           | 0 / 62 (0.00%)                             | 0 / 25 (0.00%)                                 | 2 / 26 (7.69%)                |
| occurrences (all)                                     | 0  | 0  | 2                             |
| Gastrointestinal disorders                            |  |  |                               |
| Abdominal pain  |  |  |                               |
| subjects affected / exposed                           | 3 / 62 (4.84%)                             | 3 / 25 (12.00%)                                | 3 / 26 (11.54%)               |
| occurrences (all)                                     | 4  | 3  | 3                             |
| Abdominal pain upper                                  |  |  |                               |
| subjects affected / exposed                           | 1 / 62 (1.61%)                             | 1 / 25 (4.00%)                                 | 2 / 26 (7.69%)                |
| occurrences (all)                                     | 1  | 1  | 2                             |
| Diarrhoea   |  |  |                               |
| subjects affected / exposed                           | 4 / 62 (6.45%)                             | 0 / 25 (0.00%)                                 | 2 / 26 (7.69%)                |
| occurrences (all)                                     | 5  | 0  | 2                             |
| Erosive oesophagitis                                  |  |  |                               |

|   |   |  |  |
|---|---|--|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 62 (0.00%)<br>0   | 0 / 25 (0.00%)<br>0  | 2 / 26 (7.69%)<br>2  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)   | 5 / 62 (8.06%)<br>5   | 1 / 25 (4.00%)<br>1  | 1 / 26 (3.85%)<br>1  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 62 (1.61%)<br>2   | 2 / 25 (8.00%)<br>3  | 0 / 26 (0.00%)<br>0  |
| Infections and infestations<br>Bronchitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pharyngitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Sinusitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 1 / 62 (1.61%)<br>1<br><br>4 / 62 (6.45%)<br>5<br><br>3 / 62 (4.84%)<br>3<br><br>1 / 62 (1.61%)<br>1<br><br>2 / 62 (3.23%)<br>2 | 2 / 25 (8.00%)<br>2<br><br>3 / 25 (12.00%)<br>3<br><br>3 / 25 (12.00%)<br>3<br><br>3 / 25 (12.00%)<br>3<br><br>2 / 25 (8.00%)<br>2 | 1 / 26 (3.85%)<br>1<br><br>4 / 26 (15.38%)<br>4<br><br>0 / 26 (0.00%)<br>0<br><br>0 / 26 (0.00%)<br>0<br><br>0 / 26 (0.00%)<br>0 |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 19 April 2012 | <ol style="list-style-type: none"><li>1. In order to decrease the number of required biopsies and to allow flexibility for standard of care, the duodenal biopsies were removed and a serologic test was specified for use to screen for celiac disease.</li><li>2. To ensure compliance with local ethical and regulatory requirements, P450 CYP2C19 genotype testing was not required when local regulations prohibited it. Storage and use of samples were also clarified.</li></ol>   |
| 25 April 2013 | <ol style="list-style-type: none"><li>1. In order to allow for a pre-screening endoscopy to be used for eligibility if all other protocol requirements were met, an allowance was made for the screening endoscopy to have been performed within 1 week prior to signing the informed consent/assent form.</li><li>2. In order to add flexibility for the time allowed for screening, a window of 5 days was added to the Screening Period.</li><li>3. The number of biopsies required at Screening was reduced in order to increase flexibility and to be aligned with standard of care for biopsy collection.</li><li>4. H. pylori test procedures were clarified, particularly for instances in which pre-screening endoscopy results were used to determine eligibility.</li><li>5. Exclusion criterion was updated regarding HIV status.</li><li>6. Exclusion criterion regarding alcohol use was updated to account for regional differences.</li><li>7. Inclusion and exclusion criterion were updated to account for allowance of endoscopies done prior to Screening and other H. pylori test methods.</li><li>8. Alternate dosing options were added to accommodate children who could not swallow the capsule.</li></ol> |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported