



Clinical trial results:

A Phase III, Randomized, Open-Label, Parallel-Group, Dose-Ranging Clinical Trial to Study the Safety and Efficacy of MK-0954/Losartan Potassium in Pediatric Patients With Hypertension

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2008-004732-20 |
| Trial protocol | HU LT GB ES Outside EU/EEA |
| Global end of trial date | 14 August 2012 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 01 March 2016 |
| First version publication date | 15 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 0954-337 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00756938 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDiscosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDiscosure@merck.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000008-PIP01-07 |
| 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:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 14 August 2012 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 August 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

(1) To define a dose-response relationship for losartan in hypertensive children aged 6 months to 6 years, after a 21-day open-label treatment period (response assessed by change from baseline in mean trough systolic blood pressure [SBP]).

(2) To investigate the safety and tolerability of losartan at doses up to 1.4 mg/kg/day in hypertensive children aged 6 months to 6 years after 12 weeks of treatment.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 10 June 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Romania: 2 |
| Country: Number of subjects enrolled | Spain: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Lithuania: 15 |
| Country: Number of subjects enrolled | Chile: 3 |
| Country: Number of subjects enrolled | India: 8 |
| Country: Number of subjects enrolled | Philippines: 10 |
| Country: Number of subjects enrolled | Argentina: 3 |
| Country: Number of subjects enrolled | Colombia: 2 |
| Country: Number of subjects enrolled | Guatemala: 22 |
| Country: Number of subjects enrolled | Brazil: 24 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 101 |
| EEA total number of subjects | 22 |

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) | 27 |
| Children (2-11 years) | 74 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants met 1 of the following: 6 months to < 1 year old - mean SBP \geq 95th percentile ; \geq 1 year old -mean systolic and/or diastolic blood pressure (DBP) \geq 95th percentile; had co-morbidities with: mean SBP \geq 90th percentile (6 months to < 1 year old) or mean SBP and/or DBP \geq 90th percentile (\geq 1 year old).

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | 12-week Base Study |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-------------------------------------|
| Arm title | Losartan potassium 0.1 to 1.4 mg/kg |
|------------------|-------------------------------------|

Arm description:

Open-label losartan at starting dose of 0.1 mg/kg/day with uptitration at Weeks 3, 6 or 9 to the next highest dose level if blood pressure goal not achieved

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | losartan potassium |
| Investigational medicinal product code | |
| Other name | MK-0954, Cozaar® |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

losartan potassium, dry powder, to be suspended in liquid and given orally, once daily; doses will start at 0.1 mg/kg and can be escalated up to 1.4 mg/kg (maximum dose 100 mg) until target blood pressure is reached.

| | |
|------------------|-------------------------------------|
| Arm title | Losartan potassium 0.3 to 1.4 mg/kg |
|------------------|-------------------------------------|

Arm description:

Open-label losartan at starting dose of 0.3 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved.

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | losartan potassium |
| Investigational medicinal product code | |
| Other name | MK-0954, Cozaar® |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

losartan potassium, dry powder, to be suspended in liquid and given orally, once daily; doses will start at 0.3 mg/kg and can be escalated up to 1.4 mg/kg (maximum dose 100 mg) until target blood pressure is reached.

| | |
|------------------|-------------------------------------|
| Arm title | Losartan potassium 0.7 to 1.4 mg/kg |
|------------------|-------------------------------------|

Arm description:

Open-label losartan at starting dose of 0.7 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved

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

| | |
|--|----------------------------|
| Investigational medicinal product name | losartan potassium |
| Investigational medicinal product code | |
| Other name | MK-0954, Cozaar® |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

losartan potassium, dry powder, to be suspended in liquid and given orally, once daily; doses will start at 0.7 mg/kg and can be escalated up to 1.4 mg/kg (maximum dose 100 mg) until target blood pressure is reached.

| Number of subjects in period 1 | Losartan potassium 0.1 to 1.4 mg/kg | Losartan potassium 0.3 to 1.4 mg/kg | Losartan potassium 0.7 to 1.4 mg/kg |
|---------------------------------------|--|--|--|
| Started | 33 | 34 | 34 |
| Completed | 31 | 34 | 32 |
| Not completed | 2 | 0 | 2 |
| Protocol-specific Criteria Met | 1 | - | 1 |
| Lost to follow-up | 1 | - | - |
| Protocol deviation | - | - | 1 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Extension |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------|------------------------------|
| Arm title | Losartan potassium-Extension |
|------------------|------------------------------|

Arm description:

Participants who elected to enter extension; dose level of Losartan was that which was being administered at end of base study.

| | |
|--|----------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | losartan potassium |
| Investigational medicinal product code | |
| Other name | MK-0954, Cozaar® |
| Pharmaceutical forms | Powder for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

losartan potassium, dry powder, to be suspended in liquid and given orally, once daily; doses will start at 0.1 mg/kg, 0.3 mg/kg, and 0.7 mg/kg, respectively, in the three study arms and can be escalated up to 1.4 mg/kg (maximum dose 100 mg) until target blood pressure is reached.

| Number of subjects in period 2^[1] | Losartan potassium-Extension |
|---|-------------------------------------|
| Started | 90 |
| Completed | 53 |
| Not completed | 37 |
| Physician decision | 3 |
| Consent withdrawn by subject | 10 |
| End of Study | 11 |
| Adverse event, non-fatal | 1 |
| Protocol-specific Criteria Met | 9 |
| Lost to follow-up | 1 |
| Lack of efficacy | 1 |
| Protocol deviation | 1 |

Notes:

[1] - 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: Not all participants who completed the base study elected to enter extension study.

Baseline characteristics

Reporting groups

| | |
|---|-------------------------------------|
| Reporting group title | Losartan potassium 0.1 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.1 mg/kg/day with uptitration at Weeks 3, 6 or 9 to the next highest dose level if blood pressure goal not achieved | |
| Reporting group title | Losartan potassium 0.3 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.3 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved. | |
| Reporting group title | Losartan potassium 0.7 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.7 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved | |

| Reporting group values | Losartan potassium 0.1 to 1.4 mg/kg | Losartan potassium 0.3 to 1.4 mg/kg | Losartan potassium 0.7 to 1.4 mg/kg |
|------------------------------------|--|--|--|
| Number of subjects | 33 | 34 | 34 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|----------------|--------------|----------------|
| Age continuous Units: months arithmetic mean standard deviation | 40.2 ± 24.4 | 45 ± 21.5 | 40.6 ± 21.2 |
| Gender categorical Units: Subjects | | | |
| Female | 13 | 16 | 14 |
| Male | 20 | 18 | 20 |

| Reporting group values | Total | | |
|------------------------------------|-------|--|--|
| Number of subjects | 101 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|--|----|--|--|
| Age continuous Units: months arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 43 | | |
| Male | 58 | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Losartan potassium 0.1 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.1 mg/kg/day with uptitration at Weeks 3, 6 or 9 to the next highest dose level if blood pressure goal not achieved | |
| Reporting group title | Losartan potassium 0.3 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.3 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved. | |
| Reporting group title | Losartan potassium 0.7 to 1.4 mg/kg |
| Reporting group description: Open-label losartan at starting dose of 0.7 mg/kg/day with uptitration at Week 3, 6, or 9 to the next highest dose level if blood pressure goal not achieved | |
| Reporting group title | Losartan potassium-Extension |
| Reporting group description: Participants who elected to enter extension; dose level of Losartan was that which was being administered at end of base study. | |
| Subject analysis set title | Base Study-Losartan potassium 0.1 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All Patients as Treated Population, which consisted of all randomized participants who received at least 1 dose of study drug. Adverse events for the base study were reported by the dose taken at the time of the event and not the study group to which they were randomly assigned. Adverse events for the study extension were reported as 1 arm. | |
| Subject analysis set title | Base Study-Losartan potassium 0.3 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All Patients as Treated Population, which consisted of all randomized participants who received at least 1 dose of study drug. Adverse events for the base study were reported by the dose taken at the time of the event and not the study group to which they were randomly assigned. Adverse events for the study extension were reported as 1 arm. | |
| Subject analysis set title | Base Study-Losartan potassium 0.7 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All Patients as Treated Population, which consisted of all randomized participants who received at least 1 dose of study drug. Adverse events for the base study were reported by the dose taken at the time of the event and not the study group to which they were randomly assigned. Adverse events for the study extension were reported as 1 arm. | |
| Subject analysis set title | Base Study-Losartan potassium 1.4 mg/kg |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All Patients as Treated Population, which consisted of all randomized participants who received at least 1 dose of study drug. Adverse events for the base study were reported by the dose taken at the time of the event and not the study group to which they were randomly assigned. Adverse events for the study extension were reported as 1 arm. | |
| Subject analysis set title | Extension-Losartan potassium |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All Patients as Treated Population, which consisted of all randomized participants who received at least 1 dose of study drug. Adverse events for the base study were reported by the dose taken at the time of the event and not the study group to which they were randomly assigned. Adverse events for the study extension were reported as 1 arm. | |

Primary: Mean Change from Baseline in Systolic Blood Pressure (SBP)

| | |
|-----------------|--|
| End point title | Mean Change from Baseline in Systolic Blood Pressure (SBP) |
|-----------------|--|

End point description:

Sitting blood pressure ([BP] or supine if child could not sit) was measured after the participant had been seated for 5 minutes with back supported, feet on the floor and right arm (or left arm if it was the customary side for BP measurement for the participant) supported at heart level. Systolic BP was determined by averaging 3 replicate measurements obtained at least 1 minute apart.

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

End point timeframe:

Baseline and Day 21

| End point values | Losartan potassium 0.1 to 1.4 mg/kg | Losartan potassium 0.3 to 1.4 mg/kg | Losartan potassium 0.7 to 1.4 mg/kg | |
|--------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 32 | 34 | 33 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | -7.31 (± 12.53) | -7.65 (± 7.49) | -6.67 (± 7.86) | |

Statistical analyses

| | |
|----------------------------|-------------------------------------|
| Statistical analysis title | Comparision of Change from Baseline |
|----------------------------|-------------------------------------|

Statistical analysis description:

The slope of change in SBP after 21 days treatment as compared to baseline as a function of dose was assessed using an analysis of covariance (ANCOVA) model with terms for dose (as a continuous covariate: 0.1, 0.3 or 0.7 mg/kg/day), weight (as a continuous covariate) and presence of co-morbidities/end organ damage (yes/no). The primary hypothesis was assessed by testing whether the slope for dose in the above regression model was zero or not.

| | |
|---|---|
| Comparison groups | Losartan potassium 0.3 to 1.4 mg/kg v Losartan potassium 0.7 to 1.4 mg/kg v Losartan potassium 0.1 to 1.4 mg/kg |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.753 |
| Method | ANCOVA |
| Parameter estimate | Slope |
| Point estimate | 1.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.45 |
| upper limit | 8.9 |

Primary: Number of Participants Who Reported 1 or more Clinical and/or Laboratory Adverse Event(s)

| | |
|-----------------|---|
| End point title | Number of Participants Who Reported 1 or more Clinical and/or |
|-----------------|---|

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE.

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

End point timeframe:

up to 12 weeks (Base Study); up to 24 months (Extension)

Notes:

[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.

Justification: No statistical analyses was planned for this endpoint.

| End point values | Base Study- Losartan potassium 0.1 mg/kg | Base Study- Losartan potassium 0.3 mg/kg | Base Study- Losartan potassium 0.7 mg/kg | Base Study- Losartan potassium 1.4 mg/kg |
|-----------------------------|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 34 | 54 | 63 | 33 |
| Units: Participants | | | | |
| Clinical Adverse Event | 21 | 30 | 36 | 22 |
| Laboratory Adverse Event | 1 | 1 | 0 | 0 |

| End point values | Extension- Losartan potassium | | | |
|-----------------------------|-------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 90 | | | |
| Units: Participants | | | | |
| Clinical Adverse Event | 75 | | | |
| Laboratory Adverse Event | 5 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants Who Were Discontinued From Study Due to a Clinical and/or Laboratory Adverse Event

| | |
|-----------------|--|
| End point title | Number of Participants Who Were Discontinued From Study Due to a Clinical and/or Laboratory Adverse Event ^[2] |
|-----------------|--|

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the drug. Any worsening of a preexisting condition which is temporally associated with the use of the study drug is also an AE. The number of participants who were discontinued from the study due to an AE regardless of relatedness to the study drug were recorded.

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

End point timeframe:

up to 12 weeks (Base Study); up to 24 months (Extension)

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: No statistical analyses was planned for this endpoint.

| End point values | Base Study- Losartan potassium 0.1 mg/kg | Base Study- Losartan potassium 0.3 mg/kg | Base Study- Losartan potassium 0.7 mg/kg | Base Study- Losartan potassium 1.4 mg/kg |
|-----------------------------|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 34 | 54 | 63 | 33 |
| Units: Participants | | | | |
| Clinical Adverse Events | 0 | 0 | 0 | 0 |
| Laboratory Adverse Events | 0 | 0 | 0 | 0 |

| End point values | Extension- Losartan potassium | | | |
|-----------------------------|-------------------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 90 | | | |
| Units: Participants | | | | |
| Clinical Adverse Events | 1 | | | |
| Laboratory Adverse Events | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline in Diastolic Blood Pressure

| | |
|-----------------|---|
| End point title | Mean Change from Baseline in Diastolic Blood Pressure |
|-----------------|---|

End point description:

Sitting BP (or supine if child could not sit) was measured after the participant had been seated for 5 minutes with back supported, feet on the floor and right arm (or left arm if it was the customary side for BP measurement for the patient) supported at heart level. Diastolic BP was determined by averaging 3 replicate measurements obtained at least 1 minute apart.

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

End point timeframe:

Baseline and Day 21

| End point values | Losartan potassium 0.1 to 1.4 mg/kg | Losartan potassium 0.3 to 1.4 mg/kg | Losartan potassium 0.7 to 1.4 mg/kg | |
|--------------------------------------|---|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 32 | 34 | 33 | |
| Units: mmHg | | | | |
| arithmetic mean (standard deviation) | -8.25 (± 11.76) | -5.15 (± 8.06) | -6.73 (± 8.59) | |

Statistical analyses

| | |
|--|---|
| Statistical analysis title | Comparison of Change from Baseline |
| Statistical analysis description: | |
| The slope of change in DBP after 21 days treatment as compared to baseline as a function of dose was assessed using an analysis of covariance (ANCOVA) model with terms for dose (as a continuous covariate: 0.1, 0.3 or 0.7 mg/kg/day), weight (as a continuous covariate) and presence of co-morbidities/end organ damage (yes/no). The primary hypothesis was assessed by testing whether the slope for dose in the above regression model was zero or not. | |
| Comparison groups | Losartan potassium 0.1 to 1.4 mg/kg v Losartan potassium 0.3 to 1.4 mg/kg v Losartan potassium 0.7 to 1.4 mg/kg |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.643 |
| Method | ANCOVA |
| Parameter estimate | Slope |
| Point estimate | 1.81 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.9 |
| upper limit | 9.51 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 12 weeks (Base Study); up to 24 months (Extension)

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug. Adverse events are reported by the dose taken at the time of the event and not the study group to which they were randomized. A participant may have reported an adverse event when taking different dose levels and therefore may have been counted more than once.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Base Study-Losartan potassium 0.1 mg/kg |
|-----------------------|---|

Reporting group description:

Participants who received 0.1 mg/kg losartan during base study.

| | |
|-----------------------|---|
| Reporting group title | Base Study-Losartan potassium 0.3 mg/kg |
|-----------------------|---|

Reporting group description:

Participants who received 0.3 mg/kg losartan during base study

| | |
|-----------------------|---|
| Reporting group title | Base Study-Losartan potassium 0.7 mg/kg |
|-----------------------|---|

Reporting group description:

Participants who received 0.7 mg/kg losartan during base study

| | |
|-----------------------|---|
| Reporting group title | Base Study-Losartan potassium 1.4 mg/kg |
|-----------------------|---|

Reporting group description:

Participants who received 1.4 mg/kg losartan during base study.

| | |
|-----------------------|--|
| Reporting group title | Extension Study-Losartan potassium 0.1 mg/kg |
|-----------------------|--|

Reporting group description:

Participants who received 0.1 mg/kg losartan during extension study

| | |
|-----------------------|--|
| Reporting group title | Extension Study-Losartan potassium 0.3 mg/kg |
|-----------------------|--|

Reporting group description:

Participants who received 0.3 mg/kg losartan during extension study

| | |
|-----------------------|--|
| Reporting group title | Extension Study-Losartan potassium 0.7 mg/kg |
|-----------------------|--|

Reporting group description:

Participants who received 0.7 mg/kg losartan during extension study

| | |
|-----------------------|--|
| Reporting group title | Extension Study-Losartan potassium 1.4 mg/kg |
|-----------------------|--|

Reporting group description:

Participants who received 1.4 mg/kg losartan during extension study

| Serious adverse events | Base Study-Losartan potassium 0.1 mg/kg | Base Study-Losartan potassium 0.3 mg/kg | Base Study-Losartan potassium 0.7 mg/kg |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 2 / 54 (3.70%) | 2 / 63 (3.17%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nephroblastoma | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Injury, poisoning and procedural complications | | | |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Gastrointestinal disorders | | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Psychiatric disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Psychomotor retardation | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Ureteric stenosis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Infections and infestations | | | |
| Adenoiditis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Laryngitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 54 (1.85%) | 0 / 63 (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 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 54 (0.00%) | 1 / 63 (1.59%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Upper respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 1 / 54 (1.85%) | 0 / 63 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (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 |

| Serious adverse events | Base Study-Losartan potassium 1.4 mg/kg | Extension Study-Losartan potassium 0.1 mg/kg | Extension Study-Losartan potassium 0.3 mg/kg |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 3 / 15 (20.00%) | 5 / 28 (17.86%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nephroblastoma | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Thermal burn | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Gastrointestinal disorders | | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Psychiatric disorders | | | |
| Psychomotor retardation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ureteric stenosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Adenoiditis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 2 / 28 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Nasopharyngitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Upper respiratory tract infection bacterial | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Extension Study- Losartan potassium 0.7 mg/kg | Extension Study- Losartan potassium 1.4 mg/kg | |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 42 (11.90%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nephroblastoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |

| | | | |
|--|----------------|----------------|--|
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Psychomotor retardation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal impairment | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ureteric stenosis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Adenoiditis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Salmonellosis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 42 (2.38%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Base Study-Losartan potassium 0.1 mg/kg | Base Study-Losartan potassium 0.3 mg/kg | Base Study-Losartan potassium 0.7 mg/kg |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 34 (47.06%) | 26 / 54 (48.15%) | 26 / 63 (41.27%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lip and/or oral cavity cancer stage III | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 54 (1.85%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 4 / 54 (7.41%) | 3 / 63 (4.76%) |
| occurrences (all) | 3 | 6 | 3 |
| Immune system disorders | | | |

| | | | |
|--|--|--|--|
| Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 0 / 34 (0.00%) 0 | 2 / 54 (3.70%) 3 0 / 54 (0.00%) 0 | 2 / 63 (3.17%) 2 1 / 63 (1.59%) 1 |
| Investigations Protein urine present subjects affected / exposed occurrences (all) Red blood cell count decreased subjects affected / exposed occurrences (all) Urine leukocyte esterase positive subjects affected / exposed occurrences (all) White blood cells urine positive subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 0 / 54 (0.00%) 0 1 / 54 (1.85%) 1 1 / 54 (1.85%) 1 | 0 / 63 (0.00%) 0 0 / 63 (0.00%) 0 0 / 63 (0.00%) 0 0 / 63 (0.00%) 0 |
| Injury, poisoning and procedural complications Animal bite subjects affected / exposed occurrences (all) Ligament rupture subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 0 / 63 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 1 / 54 (1.85%) 1 | 1 / 63 (1.59%) 1 |
| Eye disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 54 (3.70%) 2 | 1 / 63 (1.59%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 1 / 54 (1.85%) 1 | 0 / 63 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 34 (5.88%) 2 | 3 / 54 (5.56%) 3 | 4 / 63 (6.35%) 4 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 34 (2.94%) 1 | 1 / 54 (1.85%) 1 | 1 / 63 (1.59%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 54 (3.70%) 2 | 1 / 63 (1.59%) 1 |
| Renal and urinary disorders | | | |
| Enuresis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Nephrocalcinosis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Infections and infestations | | | |
| Acute sinusitis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Acute tonsillitis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 0 / 54 (0.00%) 0 | 0 / 63 (0.00%) 0 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 34 (0.00%) 0 | 2 / 54 (3.70%) 2 | 0 / 63 (0.00%) 0 |

| | | | |
|-----------------------------------|----------------|-----------------|----------------|
| Ear infection | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 54 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 54 (1.85%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 54 (1.85%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 7 / 54 (12.96%) | 3 / 63 (4.76%) |
| occurrences (all) | 2 | 7 | 3 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 1 / 54 (1.85%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 34 (8.82%) | 2 / 54 (3.70%) | 1 / 63 (1.59%) |
| occurrences (all) | 3 | 2 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 1 / 54 (1.85%) | 5 / 63 (7.94%) |
| occurrences (all) | 2 | 1 | 6 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 3 / 54 (5.56%) | 0 / 63 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 1 / 63 (1.59%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 34 (2.94%) | 3 / 54 (5.56%) | 2 / 63 (3.17%) |
| occurrences (all) | 1 | 3 | 3 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 34 (5.88%) | 2 / 54 (3.70%) | 4 / 63 (6.35%) |
| occurrences (all) | 3 | 2 | 4 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 34 (0.00%) | 0 / 54 (0.00%) | 0 / 63 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Base Study-Losartan potassium 1.4 mg/kg | Extension Study- Losartan potassium 0.1 mg/kg | Extension Study- Losartan potassium 0.3 mg/kg |
|--|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 33 (60.61%) | 12 / 15 (80.00%) | 20 / 28 (71.43%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lip and/or oral cavity cancer stage III | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 15 (6.67%) | 4 / 28 (14.29%) |
| occurrences (all) | 1 | 1 | 5 |
| Immune system disorders | | | |

| | | | |
|--|--|--|--|
| Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 28 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) | 5 / 33 (15.15%) 5 1 / 33 (3.03%) 1 | 1 / 15 (6.67%) 1 1 / 15 (6.67%) 1 | 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0 |
| Investigations Protein urine present subjects affected / exposed occurrences (all) Red blood cell count decreased subjects affected / exposed occurrences (all) Urine leukocyte esterase positive subjects affected / exposed occurrences (all) White blood cells urine positive subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 | 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 0 / 15 (0.00%) 0 | 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0 1 / 28 (3.57%) 1 0 / 28 (0.00%) 0 |
| Injury, poisoning and procedural complications Animal bite subjects affected / exposed occurrences (all) Ligament rupture subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 | 0 / 15 (0.00%) 0 1 / 15 (6.67%) 1 | 2 / 28 (7.14%) 3 0 / 28 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 0 / 15 (0.00%) 0 | 3 / 28 (10.71%) 3 |
| Eye disorders | | | |

| | | | |
|---|---------------------|----------------------|----------------------|
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 15 (13.33%) 2 | 0 / 28 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 1 / 28 (3.57%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 1 / 28 (3.57%) 1 |
| Diarrhoea subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 3 / 15 (20.00%) 4 | 3 / 28 (10.71%) 5 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 0 / 15 (0.00%) 0 | 1 / 28 (3.57%) 7 |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 5 | 2 / 15 (13.33%) 2 | 1 / 28 (3.57%) 1 |
| Renal and urinary disorders | | | |
| Enuresis subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 28 (0.00%) 0 |
| Nephrocalcinosis subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 0 / 28 (0.00%) 0 |
| Infections and infestations | | | |
| Acute sinusitis subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 15 (6.67%) 1 | 1 / 28 (3.57%) 1 |
| Acute tonsillitis subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 2 / 15 (13.33%) 2 | 1 / 28 (3.57%) 1 |
| Bronchitis subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 0 / 15 (0.00%) 0 | 2 / 28 (7.14%) 3 |

| | | | |
|-----------------------------------|----------------|-----------------|-----------------|
| Ear infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 2 / 28 (7.14%) |
| occurrences (all) | 0 | 0 | 2 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 1 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 2 / 15 (13.33%) | 4 / 28 (14.29%) |
| occurrences (all) | 3 | 3 | 6 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 1 | 1 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 4 / 15 (26.67%) | 1 / 28 (3.57%) |
| occurrences (all) | 1 | 5 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 2 / 15 (13.33%) | 3 / 28 (10.71%) |
| occurrences (all) | 3 | 2 | 3 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 0 | 0 | 4 |

| | | | |
|-----------------------------------|-----------------|-----------------|-----------------|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 15 (0.00%) | 0 / 28 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 2 / 15 (13.33%) | 1 / 28 (3.57%) |
| occurrences (all) | 1 | 2 | 2 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 15 (6.67%) | 4 / 28 (14.29%) |
| occurrences (all) | 0 | 1 | 4 |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 33 (12.12%) | 0 / 15 (0.00%) | 1 / 28 (3.57%) |
| occurrences (all) | 4 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 15 (0.00%) | 2 / 28 (7.14%) |
| occurrences (all) | 1 | 0 | 2 |

| Non-serious adverse events | Extension Study- Losartan potassium 0.7 mg/kg | Extension Study- Losartan potassium 1.4 mg/kg | |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 20 / 31 (64.52%) | 28 / 42 (66.67%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lip and/or oral cavity cancer stage III | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 4 / 42 (9.52%) | |
| occurrences (all) | 2 | 10 | |
| Immune system disorders | | | |

| | | | |
|--|--|--|--|
| Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinitis allergic subjects affected / exposed occurrences (all) | 3 / 31 (9.68%) 3 0 / 31 (0.00%) 0 | 5 / 42 (11.90%) 9 0 / 42 (0.00%) 0 | |
| Investigations Protein urine present subjects affected / exposed occurrences (all) Red blood cell count decreased subjects affected / exposed occurrences (all) Urine leukocyte esterase positive subjects affected / exposed occurrences (all) White blood cells urine positive subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 2 / 31 (6.45%) 2 | 1 / 42 (2.38%) 1 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0 | |
| Injury, poisoning and procedural complications Animal bite subjects affected / exposed occurrences (all) Ligament rupture subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 0 / 42 (0.00%) 0 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 1 / 42 (2.38%) 1 | |
| Eye disorders | | | |

| | | | |
|---|----------------------|----------------------|--|
| Conjunctivitis subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | 1 / 42 (2.38%) 2 | |
| Gastrointestinal disorders | | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 1 / 42 (2.38%) 1 | |
| Constipation subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 5 / 31 (16.13%) 5 | 6 / 42 (14.29%) 8 | |
| Vomiting subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | 3 / 42 (7.14%) 3 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 4 / 42 (9.52%) 4 | |
| Renal and urinary disorders | | | |
| Enuresis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 | |
| Nephrocalcinosis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 | |
| Infections and infestations | | | |
| Acute sinusitis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 0 / 42 (0.00%) 0 | |
| Acute tonsillitis subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | 0 / 42 (0.00%) 0 | |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | 2 / 42 (4.76%) 2 | |

| | | |
|-----------------------------------|-----------------|-----------------|
| Ear infection | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 1 / 42 (2.38%) |
| occurrences (all) | 1 | 1 |
| Gastroenteritis | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 3 / 42 (7.14%) |
| occurrences (all) | 0 | 3 |
| Gastroenteritis viral | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 0 / 42 (0.00%) |
| occurrences (all) | 0 | 0 |
| Impetigo | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 0 / 42 (0.00%) |
| occurrences (all) | 2 | 0 |
| Laryngitis | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 1 |
| Lower respiratory tract infection | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 1 |
| Nasopharyngitis | | |
| subjects affected / exposed | 5 / 31 (16.13%) | 2 / 42 (4.76%) |
| occurrences (all) | 6 | 2 |
| Oral herpes | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 0 |
| Otitis media acute | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 2 / 42 (4.76%) |
| occurrences (all) | 2 | 3 |
| Pharyngitis | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) |
| occurrences (all) | 0 | 1 |
| Respiratory tract infection | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 5 / 42 (11.90%) |
| occurrences (all) | 6 | 13 |
| Rhinitis | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|-----------------------------------|----------------|-----------------|--|
| Sinusitis | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | 5 / 42 (11.90%) | |
| occurrences (all) | 2 | 6 | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | 2 / 42 (4.76%) | |
| occurrences (all) | 1 | 2 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 4 / 42 (9.52%) | |
| occurrences (all) | 8 | 4 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | 7 / 42 (16.67%) | |
| occurrences (all) | 12 | 13 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | 1 / 42 (2.38%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|--|
| 13 March 2009 | AM1: The primary reason for protocol amendment 337-01 was to remove the COZAAR™ (losartan potassium) Worldwide Product Circular and replace with the COZAAR® (losartan potassium) United States Product Circular |
| 17 June 2010 | AM2: The primary reason for protocol amendment was to add language clarifying that Visit 1 screening procedures could be completed over more than 1 day if needed. |
| 20 May 2011 | AM3: The primary reason for protocol amendment was to clarify the duration of follow-up in the open-label extension. |
| 21 March 2012 | AM5: The primary reason for protocol amendment was to revert the lower age limit for inclusion into the study from 3 months to 6 months of age. The eligibility of children as young as 3 months was proposed in protocol amendment 337-04 but was not implemented due to regulatory concerns. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported