16.1.9 Documentation of Statistical Methods

STATISTICAL ANALYSIS PLAN

Title: A Randomized, Double-blind, Placebo-controlled Study to Evaluate the Effect of AMG 334 on Exercise Time During a Treadmill Test in Subjects With Stable Angina

AMG 334

Protocol Number:	**20140254**
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Table of Abbreviations

Abbreviation or Term	Definition/Explanation
AFT	Accelerated Failure Time Model
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
CI	Confidence Interval
CRF	Case Report Form
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common Toxicity Criteria for Adverse Events
DMC	Data Monitoring Committee
DMP	Data Management Plan
DRE	Disease Related Event
DTP	Data Transfer Plan
EAS	Efficacy Analysis Set
ECG	Electrocardiograph
EOS	End Of Study
ETT	Exercise Treadmill Test
ETTr	Exercise Treadmill Test post-randomization
FAS	Full Analysis Set
HR	Heart Rate
IP	Investigational Product
MedDRA	Medical Dictionary for Regulatory Activities
NCI	National Cancer Institute
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SBP	Systolic Blood Pressure
TEAE	Treatment Emergent Adverse Event
TET	Total Exercise Time
ULN	Upper Limit of Normal
VHP	Voluntary Harmonization Procedure

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1. Introduction

The purpose of this Statistical Analysis Plan (SAP) is to provide details of the statistical analyses that have been outlined within Protocol Amendments 4 and associated Country Specific Supplement 3 for AMG 334 Study 20140254 dated 28 October 2016 and 14 November 2016, respectively. The scope of this plan includes the primary and final analyses that are planned and will be executed by the Biostatistics department unless otherwise specified.

2. Objectives

2.1 Primary

To evaluate the effect of AMG 334 compared to placebo on exercise capacity in subjects with stable angina as measured by total exercise time (TET) during an exercise treadmill test (ETT).

2.2 Secondary

To evaluate the effect of AMG 334 compared to placebo during an ETT on the time to the onset of:

- Exercise-induced angina
- ST-segment depression

2.3 Safety

To evaluate the safety and tolerability of AMG 334 in a population with stable angina.

3. Study Overview

3.1 Study Design

This is a phase 2a, multicenter, randomized, double-blind, placebo-controlled study in subjects with stable angina. At least 54 subjects will be randomized in a 1:1 ratio to receive either a single dose of AMG 334 140 mg or placebo intravenously prior to completing an ETT. Randomization will be stratified by the TET average of the 2 qualifying screening ETTs (< 7 minutes or ≥ 7 minutes). Treatment group will be blinded to the investigator, subjects, and the Amgen study team.

3.2 Sample Size

The primary endpoint is the change from baseline in TET. Assuming between-subject standard deviation for change from baseline in exercise duration of 130 seconds, with a planned study size of at least 27 subjects in each group and a difference in change from baseline in exercise duration of 0 seconds between AMG 334 group and placebo group, there is an 80% probability (power) that the lower bound of the 90% confidence interval

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(CI) will exceed -90 seconds. A margin larger than -60 seconds between groups was required to accommodate the possibility of more than 60 second (up to 20%) difference allowed in qualifying TETs for individual subjects. Because of this within-subject TET variation, a maximum TET difference of 90 seconds between the AMG 334 group and placebo group was considered reasonable in this study. A margin of -90 seconds was selected, which corresponds to the margin used in previous study testing a comparable hypothesis (Patterson, et.al 2005). Twenty-nine subjects are needed in each group if considering 5% dropout.

When approximately 45 subjects have been enrolled, Amgen may conduct a blinded sample size-estimation and may choose to alter the sample size based on the blinded variance in the pooled treatment groups.

4. Study Endpoints and Covariates

4.1 Study Endpoints

4.1.1 Primary Endpoint

- Change from baseline in TET

4.1.2 Secondary Endpoints

- During the ETT
  - Time to onset of exercise-induced angina
  - Time to onset of ≥ 1 mm ST-segment depression

4.1.3 Safety Endpoints

- Adverse events and disease related events
- Changes in vital signs

For Country Specific Supplement countries only:

  - Maximum change in ST-segment depression (mm) from baseline
  - Maximum heart rate (HR)
  - Maximum change in systolic blood pressure (SBP) from baseline

4.2 Planned Covariates

The stratification factor of baseline TET (< 7 or ≥ 7 minutes) will be included as a covariate in the primary analysis of the efficacy endpoints.

Stratification factor will use the values used for randomization unless otherwise noted.

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5. Hypotheses

The primary endpoint of the study will be tested for AMG 334 compared to placebo, with type I error 0.1

- Null Hypothesis: In subjects with angina, AMG 334 does significantly decrease exercise capacity (by at least 90 seconds), as measured by change from baseline in total exercise time, compared to placebo, and that the true treatment difference in change from baseline in TET is -90 seconds or more (worse).
- Alternative Hypothesis: In subjects with angina, AMG334 does not decrease exercise capacity, as measured by change from baseline in total exercise time, compared to placebo, and that the difference in change from baseline in TET if any, is less than a 90 second decrease.

6. Definitions

6.1 Study Dates

Enrollment Date

Enrollment Date is defined as the randomization date.

Randomization Date

Randomization Date is defined as the date subject was allocated to a treatment group.

First IP Dose Date

First IP Dose Date is the date on which a subject is administered the first dose of IP following randomization. For subjects who are randomized but not dosed with IP, first dose date is missing.

Subject-level End of Study (EOS) Date

End of study for each subject is defined as the last date on which the subject last completed a protocol-specified procedure. The date will be recorded on the End of Study CRF page.

Primary Completion Date

The primary completion date is defined as the date the last subject completes the on study ETT

Study Completion Date

The study completion date is the EOS date of the last subject in the study.

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6.2 Study Points of Reference

Study Day 1

Study Day 1 is defined as the first IP dose date. For subjects who are randomized but not dosed, Study Day 1 is defined as the date of randomization.

Study Day

Study Day is defined as the number of days from Study Day 1.

Before Study Day 1:

Study Day = (Date of Interest – Date of Study Day 1)

On or after Study Day 1:

Study Day = (Date of Interest – Date of Study Day 1) + 1

Therefore the day prior to Study Day 1 is -1.

Post-baseline Study Visit

See Appendix A.

Completing Study

A subject is defined as completing study if the primary reason for ending study is "Completed".

Completing Investigational Product (IP)

A subject is defined as completing IP if the reason for ending IP is "Completed".

6.3 Baseline and Demographics

Age at Enrollment

Subject age at enrollment will be collected in years in the clinical database.

Baseline Values

Baseline TET is the average of the 2 qualifying screening ETTs.

If subject completes Columbia-Suicide Severity Rating Scale (C-SSRS) form on Study Day 1 then all individual items from Study Day 1 visit will be used as baseline. If subject does not complete C-SSRS form on Study Day 1 then the last completed form prior to Study Day 1 will be used.

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For all other variables, unless otherwise specified, baseline values are defined as the last non-missing value before the first dose of IP, or randomization date for subjects who never received IP. In cases where baseline measurements are taken on the same day as the first IP dose date, it will be assumed that these measurements are taken prior to IP being administered.

BMI

Subject's BMI will be derived in kg/m^2 in the clinical database.

6.4 Efficacy Endpoints

Change from baseline in TET

Change from baseline in TET = TET from on-study ETT post-randomization - baseline TET

Time to Event

Time to event (onset of angina, ≥ 1 mm ST-segment depression) is defined as the time subject received IP to the time of event onset.

Time to event = event onset time – time received investigational product

If no event occurs, then subject will be censored at the ETT stop time.

6.5 Safety Endpoints

Treatment-Emergent Adverse Event

Events categorized as adverse events (AEs) starting on or after first dose of IP as determined by the flag indicating if the AEs started prior to the first dose on the Events CRF and up to and including 84 days after the end of IP or end of study, whichever comes first.

Serious adverse events (SAEs) are events categorized as AEs that are starting on or after first dose of IP as determined by the flag indicating if the adverse event started prior to the first dose of the Events CRF and up to and including 84 days after the end of investigational product.

Treatment-emergent Disease-related Event

Events categorized as Disease-related Events (DREs) starting on or after first dose of investigational product as determined by the flag indicated if the event started prior to the first dose on the Events CRF and up to and including 84 days after the end of investigational product.

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Serious disease-related events are events are events categorized as DREs that are starting on or after first dose of investigational product as determined by the flag indicating if the event started prior to the first dose on the Events CRF and up to and including 84 days after the end of investigational product

Maximum Change from Baseline in SBP

The maximum change from baseline in SBP is calculated by the maximum value of (SBP after first dose date– baseline SBP)

Maximum Change from Baseline in HR

The maximum change from baseline in HR is calculated by the maximum value of (HR after first dose date – baseline HR)

Maximum Change from Baseline in ST-Segment Depression

The maximum change from baseline in ST-Segment Depression is calculated by the maximum value of (ST-Segment Depression after first dose– baseline ST-Segment Depression).

Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS is a clinician rating of suicidal behavior and ideation. Two versions depending on the type of visits will be used in this study: Screening and Since Last Visit. The C-SSRS consists of a maximum of 20 items to evaluate suicidal behavior and suicidal ideation.

7. Analysis Subsets

7.1 Full Analysis Set

The Full Analysis Set (FAS) includes all randomized subjects. Subjects will be analyzed according to their randomized treatment, regardless of the treatment received.

7.2 Safety Analysis Set

The Safety Analysis Set (SAS) includes all randomized subjects who received at least one dose of investigational product. For all safety analyses, subjects will be grouped according to the actual treatment received.

7.3 Efficacy Analysis Set

The Efficacy Analysis Set (EAS) utilizes the FAS and includes subjects who received IP and completed the exercise treadmill test post-randomization (ETTr). Subjects will be grouped according to their randomized treatment, regardless of the treatment received.

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7.4 Per Protocol Set

The Per Protocol Set (PPS) utilizes the EAS and includes subjects who completed IP on Study Day 1 and do not have important protocol deviations that will potentially impact primary analysis of efficacy endpoints. Subjects who deviate from key eligibility criteria including currently participating in another investigational device or drug study (exclusion criteria 201) and cardiovascular conditions (exclusion criteria 214, 215, 216, 217, 218) will be excluded from the analysis.

7.5 Subgroup Analyses

Primary and secondary analyses will be performed according to the following subgroups: baseline TET (< 7 minutes or ≥ 7 minutes) randomization strata, age group (<65, ≥65) and sex.

8. Interim Analysis and Early Stopping Guidelines

A Data Monitoring Committee (DMC) will review all available safety data periodically. The DMC will have access to subjects' individual treatment assignments. To minimize the potential introduction of bias to the conduct of the study, members of the DMC will not have any direct contact with study center personnel or subjects. The DMC will communicate major safety concerns and recommendations regarding study modification or termination based on the safety parameters to Amgen in accordance with the DMC charter.

Records of all meetings will be maintained by the DMC for the duration of the study. Records of all meetings will be stored in the Amgen official document management system at the conclusion of the study. Further details are provided in the DMC charter.

No interim analysis is planned for this study except for sample size re-estimation that will be performed on the pooled sample after 45 subjects have been enrolled. Amgen may choose to alter the sample size based on the pooled variance in the overall group.

9. Data Screening and Acceptance

9.1 General Principles

The objective of the data screening is to assess the quantity, quality, and statistical characteristics of the data relative to the requirements of the planned analyses.

9.2 Data Handling and Electronic Transfer of Data

The Amgen Global Study Operations-Data Management (GSO-DM) department will provide all data to be used in the planned analyses. This study will use the RAVE database. The database will be subjected to edit check outlined in the Data

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Management Plan (DMP). Central laboratory, PK, antibody, biomarkers, adjudicated events and ECG data is outside of RAVE database. All the datasets to be used for planned analyses will be received from GSO-DM department. Additional details will be provided in the DMP and Data Transfer Plan (DTP).

9.3 Handling of Missing and Incomplete Data

Subjects may miss specific data points for a variety of causes. In general, data could be missing due to a subject's early withdrawal from study, a missed visit, or inability to evaluate an endpoint at a particular point in time. Missing assessment at baseline or on-study will not be imputed.

9.3.1 Missing and Incomplete Dates

Missing and partially missing dates for the following parameters will be queried. In general, the algorithm for imputing missing dates will use the logic below. Unless otherwise specified, Study Day 1 will be the first dose date or randomization date for subjects who never received IP:

- If the year and month are the same as Study Day 1 but the day part is missing, the day will be set to the 1st of the month of Study Day 1.
- If the year is the same as Study Day 1 but the day and month are missing, the day and month will be set to the 1st of January of Study Day 1.
- If the year and day are the same as Study Day 1 but month is missing, the month will be set to January of Study Day 1.
- If the month and day are the same as Study Day 1 but year is missing, the year will be reset to the year of Study Day 1.
- If any of the resulting dates are prior to reference date, the imputed date will be reset to the reference date.
- If day, month and year are all missing, no imputation will be applied.

Partial/missing AE and concomitant medication start dates will be imputed using the algorithm above, with the Study Day 1 being the first dose date. For subjects who are randomized but not dosed, Study Day 1 is defined as the date of randomization. AEs that occurred before first dose as indicated by "Did event start before first dose of investigational product" is marked 'Y', will not be imputed.

9.4 Detection of Bias

This study has been designed to minimize potential bias by allocating treatment groups randomly, assessing endpoints and handling withdrawals without knowledge of the treatment. Other factors that may bias the results of the study include:

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- important protocol deviations likely to impact the analysis and interpretation of the efficacy endpoints
- inadvertent breaking of the blind before formal unblinding
- investigational product dosing non-compliance
- the timing of and reasons for early withdrawal from treatment and from study

The incidence of these factors may be assessed. Important protocol deviations will be listed and/or tabulated in the clinical study report (CSR). If necessary, the incidence of other factors will be tabulated.

Any breaking of the blind for individual subjects prior to formal unblinding of the study will be documented in the CSR.

9.5 Outliers

Histograms will be examined to identify outliers in any of the continuous variables used in the analyses. Unexpected and/or unexplained values in categorical data will be identified by utilizing frequency tables.

Extreme data points will be identified during blinded review of the data before final database lock. These data points will be reviewed and queried per the data management or clinical listing review plans. Extreme values will not be excluded from the analyses.

9.6 Distributional Characteristics

Statistical assumptions for the primary and secondary endpoint analyses will be assessed. Continuous endpoints of change from baseline in TET will be analyzed under normality assumption. If the assumptions for the primary analysis are not met, then suitable transformation methods (eg, log transform) will be applied.

9.7 Validation of Statistical Analyses

Programs will be developed and maintained, and output will be verified in accordance with current risk-based quality control procedures.

Tables, figures, and listings will be produced with validated standard macro programs where standard macros can produce the specified outputs.

The production environment for statistical analyses consists of Amgen-supported versions of statistical analysis software; for example, the SAS System version 9.3 or later.

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10. Statistical Methods of Analysis

10.1 General Principles

The primary analysis to evaluate the effect of AMG 334 compared to placebo on exercise capacity in subjects with stable angina as measured by TET during an ETT.

The FAS will be used to tabulate demographic data, baseline disease characteristics, and subject disposition. The EAS will include all FAS subjects who received IP and completed the ETTr and will be used to analyze the primary and secondary endpoints including the change from baseline in TET, time to onset of ≥ 1 mm ST-segment depression, and time to onset of exercise-induced angina. The Safety Analysis Set will be used to analyze safety endpoints.

Summary statistics by each treatment group will be tabulated at each visit. For continuous endpoints, descriptive statistics will be provided including number of subjects, mean, median, standard deviation, standard error, lower and upper quartiles, minimum, and maximum. For categorical endpoints, frequency, and percentage will be given. Missing data will not be imputed.

Baseline value for exercise duration is the average value of the two qualifying measurements in the screening period.

10.2 Subject Accountability

The number and percent of subjects who were screened, randomized, received IP, received partial or none, completed study, discontinued study and reasons for discontinuing will be summarized by treatment group.

The number and percent of subjects randomized will be tabulated by study site.

Key study dates for the first subject enrolled, last subject enrolled, last subject's end of study, and last subject's ETT will be presented.

Data analysis will occur at the following time points:

The primary analysis will take place after all subjects have completed the on study ETT.

The final analysis will take place after all subjects have completed the study and after the final database lock.

10.3 Important Protocol Deviations

Important Protocol Deviations (IPDs) categories are defined by the study team before the first subject's visit and updated during the IPD reviews throughout the study prior to database lock. These definitions of IPD categories, sub-category codes, and

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descriptions will be used during the course of the study. Eligibility deviations are defined in the protocol.

10.4 Demographic and Baseline Characteristics

Demographic (ie, age, age group (based on median cut point), geriatric age group [< 65, ≥ 65 and ≥75], sex, race, ethnicity) and baseline disease characteristics will be summarized by treatment group and overall using descriptive statistics.

If multiple races have been reported for a subject, the subject will be categorized as multiple race.

The following baseline characteristics will also be summarized:

- Weight (kg)
- Height (cm)
- Body Mass Index (BMI, kg/m2)
- Systolic BP (mmHg)
- Diastolic BP (mmHg)
- Heart Rate (beats/min)
- Baseline TET (seconds)
- Concomitant medications of interest (beta blockers, nitrates, calcium channel blockers, ranolazine, ACE inhibitors and angiotensin receptor blockers)

10.5 Efficacy Analyses

Detailed primary, secondary and sensitivity analysis methods are summarized in the table below.

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Table 1. Summary of Efficacy Endpoints and Analysis Methods

Endpoint	Primary and Secondary Analysis Methods (EAS)	Sensitivity Analysis Methods
Primary Endpoint		
Change from baseline in TET (seconds)	• Primary analysis: Two-Way ANOVA model with terms of treatment group and randomization strata (< 7 or ≥ 7 minutes)	• Analysis of covariance (ANCOVA) model with terms of treatment group and baseline TET as a continuous measure • Repeat primary analysis using the Per Protocol Analysis Set • Repeat primary analysis by subgroups, including baseline TET randomization strata, age group and sex (if sample size permits.)
Secondary Endpoints		
Time to onset of exercise-induced angina* (seconds) Time to onset of ≥ 1 mm ST-segment depression (seconds)	• Primary analysis: K-M log-rank test stratified by Baseline TET strata (< 7 or ≥ 7 minute) Secondary analysis: Cox proportional hazard model including treatment group and baseline TET as a continuous measure	• Repeat primary and secondary analyses using the Per Protocol Analysis Set • Repeat primary and secondary analyses by subgroups including baseline TET randomization strata, age group and sex (if sample size permits)

*includes angina-related symptoms

10.5.1 Analyses of Primary Efficacy Endpoint

The analysis for the primary endpoint, evaluating change from baseline in TET, will be performed using the EAS. The primary hypothesis is that AMG 334 does not substantially decrease exercise capacity, as measured by change from baseline in exercise duration, compared to placebo (ie, the true treatment difference in change from baseline in exercise duration is -90 seconds or more).

In the primary analysis, the primary endpoint will be analyzed using an ANOVA model with terms for treatment group and baseline TET (< 7 or ≥ 7 minutes) randomization strata. Adjusted group means for each treatment group, standard error, 90% CI, difference of group means compared to placebo and associated 90% CIs will be tabulated. If the lower bound of the 90% CI of the difference is more than -90 seconds, then the hypothesis that AMG 334 does not substantially decrease exercise duration will be supported.

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Statistical assumptions for the primary endpoint method of analysis will be assessed. If the assumptions for the primary analysis are not met, then nonparametric methods or suitable transformation will be utilized.

Sensitivity analyses described below will be performed for the primary endpoint using the EAS:

- An analysis of covariance (ANCOVA) model including treatment group and baseline TET as a continuous measure
- The primary analysis will be repeated using the PPS

To assess if the treatment effect varies across subgroups of interest, the primary analysis of the primary endpoint will be repeated and will include an interaction term (treatment group* subgroup) in the ANOVA model. If a treatment group*subgroup interaction is observed at a significance level of 0.10, then the primary analysis may be repeated for each level of the subgroup. In addition, reasons for stopping the ETTr will be summarized by treatment group using the EAS.

10.5.2 Analyses of Secondary Efficacy Endpoints

The secondary endpoints are time to onset of exercise-induced angina and time to onset of ≥ 1 mm ST-segment depression.

For time-to-event endpoints, only the first occurrence will be considered. If no event is observed during ETTr, then this subject will be considered as censored at the end of ETTr.

Kaplan-Meier estimates of the event-free time to ST-segment depression and exercise induced angina will be computed and graphically displayed using the EAS. For each endpoint, a stratified (< 7 or ≥ 7 minute randomization strata) log-rank test statistic will be calculated to compare the two treatment groups at a significance level of 0.10.

As a secondary analysis, the hazard ratio and its 90% CI for AMG 334 vs placebo will be estimated using a stratified (< 7 or ≥ 7 minute randomization strata) Cox proportional hazards regression model. The proportional hazards assumption will be assessed by visual inspection for parallel lines over time in the plot of log-negative-log of the survival function vs. log (time) (Hosmer and Lemeshow, 1999). If there is strong evidence of non-proportional hazards for the treatment group, then a piece-wise Cox model (Collett, 2003) or an accelerated failure time (AFT) model will be considered. Regardless of non-proportionality, the main analysis of the primary endpoint will be in terms of the Cox model.

Summary statistics (mean, median, Q1, Q3, and 90% CI) of time to event will be provided by treatment group. The number and percentage of subjects with an observed event will also be provided.

Sensitivity analyses described below will be performed for the secondary endpoints:

- Repeat the secondary analysis (Cox proportional hazards regression) using baseline TET as a continuous measure
- Repeat the primary and secondary analysis using PPS

10.6 Safety Analyses

10.6.1 Adverse Events

The Medical Dictionary for Regulatory Activities (MedDRA) version 18.0 or later will be used to code all events categorized as AEs and Disease-related Events (DREs) to a system organ class and a preferred term.

Subject incidence of AEs will be summarized for all treatment-emergent AEs, serious AEs, AEs leading to withdrawal of IP and fatal AEs. Subject incidence of all treatment-emergent AEs, serious AEs, AEs leading to withdrawal of IP and fatal AEs, will be tabulated by system organ class and preferred term in descending order of frequency. Subgroups group analyses (if there is a medical rationale) will be presented by system organ class and preferred term in descending order of frequency. All races (if appropriate) with less than 5% of the total enrolled subjects will be pooled together for summary purposes.

Subject-level data may be provided instead of tables if the subject incidence is low.

Subject incidence of DREs will be summarized for all treatment-emergent DREs and fatal DREs.

10.6.2 Columbia-Suicide Severity Rating Scale (C-SSRS)

No statistical testing will be performed on C-SSRS. The number and percentage of subjects reporting any suicidal ideation and any suicidal behavior will be summarized descriptively by treatment group. Shift table of C-SSRS maximum severity of suicidal ideation/behavior compared to baseline will be provided by treatment group.

10.6.3 Laboratory Test Results

Shifts tables of the laboratory toxicity for selected lab analytes (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, creatinine) based on Common Terminology Criteria for Adverse Events (CTCAE) grade (version 4) relative to baseline will be tabulated by treatment group for entire study

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period. In the cases when CTCAE grading scales include numeric ranges in combination with clinical assessment (eg, Potassium [Hypokalemia]), laboratory test results may be summarized based on standard normal ranges or by CTCAE grade utilizing investigator's input.

Summary of change from baseline for absolute neutrophil count (ANC), alanine transaminase (ALT), aspartate aminotransferase (AST) and creatinine will also be provided.

Additional liver test summary table will provide the number and percentage of subjects by treatment group for the following categories:

- AST and ALT (> 3x ULN; > 5x ULN; > 10x ULN; > 20x ULN respectively)
- AST or ALT (> 3x ULN; > 5x ULN; > 10x ULN; > 20x ULN respectively)
- Total Bilirubin (> 1x ULN; >1.5x ULN; >2x ULN respectively)
- ALP (>1.5 ULN)
- ALT or AST > 3x ULN and Total Bili ≥ 2x ULN and ALP < 2x ULN

10.6.4 Vital Signs

Descriptive summaries of blood pressures and HR will be provided at baseline and at each study visit. In addition, blood pressures and HR collected during ETTr will be summarized at specific time points (baseline, peak and last measurement). Descriptive summaries will be provided for the maximum change from baseline in SBP and HR on day 1 post dose during ETTr for Country Specific Supplement countries.

10.6.5 Antibody Formation

The incidence and percentage of subjects who develop anti-AMG334 antibodies (binding and if positive, neutralizing) at any time will be tabulated by treatment group.

10.6.6 Exposure to Concomitant Medication

Number and proportion of subjects receiving therapies of interest will be summarized by category for each treatment group as coded by the World Health Organization Drug (WHODRUG) dictionary. See Appendix D for a list of selected medications and their groupings.

10.7 Pharmacokinetic Analysis

All PK-related tables, figures, listings and other deliverables will be generated by PKDM. Serum AMG 334 concentrations will be summarized using descriptive statistics.

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10.8 Additional Safety Endpoints for Country Specific Supplement Countries

This section is for countries that were originally aligned with EU VHP (European Union Voluntary Harmonization Procedure) requirements. These countries are listed in the Country Specific supplements of the protocol (ie, Czech Republic, Latvia, Romania, Bulgaria and Poland).

After the end of ETT, all subjects will be followed at the site for at least 4 hours. At the end of the 4-hour follow-up period, the following procedures will be performed:

- 12-lead rest ECG in a sitting position
- Blood pressure measurement in a sitting position
- Blood sampling for measurement of cardiac biomarker (troponin I)

Additional visits for anti-AMG334 antibody (Day1 Pre-dose, week 4, and week 12) and C-SSRS (visit 2, visit 3, visit 4, and week 2) will be collected for countries listed in Country Specific Supplement.

These additional data will be included in the analysis.

11. Changes From Protocol-specified Analyses

There are no changes to the protocol-specified analyses.

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12. Literature Citations / References

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13. Data Not Covered by This Plan

There are no plans to specifically analyze or summarize the following data points.

- PK
- Data for biomarker development

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14. Appendices

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Appendix A. Post-baseline Study Visits

Since the actual visit for a subject may not exactly coincide with their targeted visit date, the actual visit date is mapped to the study visit as following. The study day window will be utilized to define study visit for labs, antibody, vital signs and physical measurements collected at office visits.

Study Visit	Target Day	Study Day
Week 4	29	16-43
Week 8	57	44-71
Week 12	85	72 to Min (EOS Date, last IP dose date + 84 days)

Note:

1. If more than one visit (including unscheduled visits, ie, CPEVENT = 'UNSCHED') fall within the same defined window, scheduled visit will be used regardless of the distance from the target day. Unscheduled visit will only be used when there is no scheduled visit in the defined window. The closest visit to the target day among the same type of visit (scheduled vs. unscheduled) will be considered for analysis. If two assessment dates are equidistant from the target date, the latter visit will be considered for analysis.
2. For Country Specific Supplement countries, CSSRS and ECG data are collected at week 2 (target day 14), corresponding to study day 1-28.

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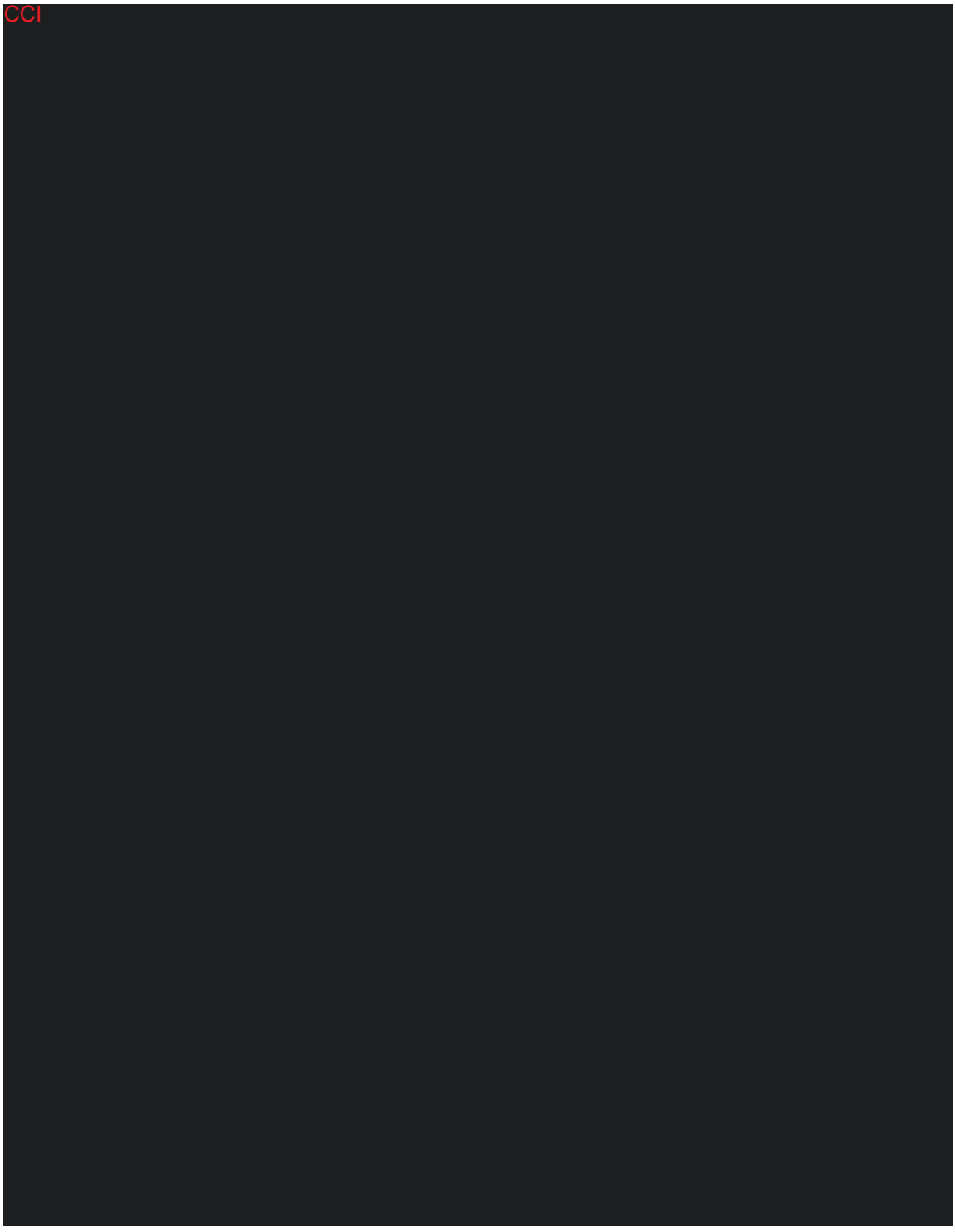
Appendix B. Technical Detail and Supplemental Information Regarding Statistical Procedures and Programs

Code Fragments

Section 10.5.1

CCI



CCI

[redacted]

CCI

Appendix C. Reference Values/Toxicity Grades

Adverse event severity and laboratory parameters are graded based on National Cancer Institute (NCI) Common Toxicity Criteria version 4 or higher, which is available at the following: http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf

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Appendix D. Concomitant Medications

Group	Medications
Beta-blockers	BETA BLOCKING AGENTS
	ADAPROLOL
	ANTIARRHYTHMIC AGENTS
	BETA BLOCKING AGENTS
	BUFETOLOL
	BUFETOLOL HYDROCHLORIDE
	DILEVALOL
	DILEVALOL HYDROCHLORIDE
	ISAMOLTAN
	MABUTEROL
	MABUTEROL HYDROCHLORIDE
	MOPROLOL
	MOPROLOL HYDROCHLORIDE
	NADOXOLOL
	NADOXOLOL HYDROCHLORIDE
	NIFENALOL
	NIFENALOL HYDROCHLORIDE
	OBERADILOL
	ALPRENOLOL
	ALPRENOLOL BENZOATE
	ALPRENOLOL HYDROCHLORIDE
	BETA BLOCKING AGENTS, NON-SELECTIVE
	BETAMED /02298401/
	BLOCOTIN /00716001/
	BOPINDOLOL
	BOPINDOLOL FUMARATE
	BOPINDOLOL MALONATE
	BUCINDOLOL
	BUCINDOLOL HYDROCHLORIDE
	BUFURALOL
	BUFURALOL HYDROCHLORIDE
	BUNITROLOL
	BUNITROLOL HYDROCHLORIDE

AMGEN®

	BUPRANOLOL
	BUPRANOLOL HYDROCHLORIDE
	CARAZOLOL
	CARTEOLOL
	CARTEOLOL HYDROCHLORIDE
	CLORANOLOL
	CLORANOLOL HYDROCHLORIDE
	CLOTAS PLUS
	EXAPROLOL
	EXAPROLOL HYDROCHLORIDE
	INDENOLOL
	INDENOLOL HYDROCHLORIDE
	MEPINDOLOL
	MEPINDOLOL SULFATE
	METIPRANOLOL
	METIPRANOLOL HYDROCHLORIDE
	NADOLOL
	NIPRADOLOL
	OXPRENOLOL
	OXPRENOLOL HYDROCHLORIDE
	PENBUTOLOL
	PENBUTOLOL SULFATE
	PINDOLOL
	PRONETALOL
	PRONETALOL HYDROCHLORIDE
	PROPRANOLOL
	PROPRANOLOL HYDROCHLORIDE
	PROPRANOLOL PHENOBARBITAL
	SOLOPOSE BETA
	SOTACOR/ASA
	SOTALOL
	SOTALOL HYDROCHLORIDE
	TENSYN PLUS
	TERTATOLOL
	TERTATOLOL HYDROCHLORIDE
	TILISOLOL

AMGEN®

	TILISOLOL HYDROCHLORIDE
	TIMOLOL
	TIMOLOL HEMIHYDRATE
	TIMOLOL MALEATE
	TIMOLOL MALEATE, R-ENANTIOMER
	TIMOLOL MALEATE, S-ENANTIOMER
	ZEPRO /02777801/
	ACEBUTOLOL
	ACEBUTOLOL HYDROCHLORIDE
	ATENOLOL
	ATENOLOL HYDROCHLORIDE
	BELOC /01739801/
	BETA BLOCKING AGENTS, SELECTIVE
	BETAXOLOL
	BETAXOLOL HYDROCHLORIDE
	BEVANTOLOL
	BEVANTOLOL HYDROCHLORIDE
	BISOBLOCK PLUS
	BISOPROLOL
	BISOPROLOL FUMARATE
	BUCUMOLOL
	BUCUMOLOL HYDROCHLORIDE
	BUTIDRINE
	CELIPROLOL
	CELIPROLOL HYDROCHLORIDE
	DEXNEBIVOLOL
	DIACETOLOL
	DIACETOLOL HYDROCHLORIDE
	EPANOLOL
	ERAMID
	ESATENOLOL
	ESMOLOL
	ESMOLOL HYDROCHLORIDE
	LANDIOLOL
	LANDIOLOL HYDROCHLORIDE
	LEVONEBIVOLOL

AMGEN®

	METOPROLOL
	METOPROLOL FUMARATE
	METOPROLOL SUCCINATE
	METOPROLOL TARTRATE
	METOPROLOL W/MORPHINE
	METPURE ST
	NEBIVOLOL
	NEBIVOLOL HYDROCHLORIDE
	PAFENOLOL
	PRACTOLOL
	SELOKEN ZOC/ASA
	TALINOLOL
	TOLAMOLOL
	TOLAMOLOL HYDROCHLORIDE
	ZOLAT /03453901/
	ALPHA AND BETA BLOCKING AGENTS
	AMINO ACIDS NOS W/CAFFEINE/CARVEDILOL/CHOLINE
	AMOSULALOL
	AMOSULALOL HYDROCHLORIDE
	AROTINOLOL
	AROTINOLOL HYDROCHLORIDE
	CARVEDILOL
	CARVEDILOL HYDROCHLORIDE
	CARVEDILOL PHOSPHATE HEMIHYDRATE
	LABETALOL
	LABETALOL HYDROCHLORIDE
	MEDROXALOL
	MEDROXALOL HYDROCHLORIDE
	PROXODOLOL
	BETA BLOCKING AGENTS AND THIAZIDES
	BETA BLOCKING AGENTS, NON-SELECTIVE, AND THIA
	BETACENTYL
	CORGARETIC
	CORINDOCOMB

AMGEN®

	DOCIDRAZIN HIPERDON /00991401/ INDERETIC INDERIDE PRESTYL SOTAZIDE TIMOLIDE TORRAT TRASIDREX TRI-TORRAT VISKAZIDE ATENOLOL W/HYDROCHLOROTHIAZIDE ATPURE-D BELOC-ZOC COMP BETA BLOCKING AGENTS, SELECTIVE, AND THIAZIDE BISELECT /01166101/ BISOPROLOL W/HYDROCHLOROTHIAZIDE /06833601/ CO-BETALOC NEATENOL DIU NEATENOL DIUVAS NEBICARD-H RANEZIDE SECADREX SECTRAZIDE /00774201/ SELOKEN COMP. TRELOC ALPHA AND BETA BLOCKING AGENTS AND THIAZIDES CO-DILATREND NORMOZIDE /00897401/ BETA BLOCKING AGENTS AND OTHER DIURETICS BETA BLOCKING AGENTS, NON-SELECTIVE/90118901/ BETARELIX HIPERDON /00991401/

AMGEN®

	LASIPRESSIN
	SANDORETIC
	SPIROPROP
	TRASITENSIN
	TREPRESS
	VISKALDIX
	BETA BLOCKING AGENTS, SELECTIVE, AND OTHER DI
	INDAPAMIDE W/NEBIVOLOL HYDROCHLORIDE
	LOPRESORETIC
	NOR-PA
	SALI-PRENT
	SELECTURON
	TEKLO
	TENORETIC
	TRI-NORMIN
	VINICOR D
	ALPHA AND BETA BLOCKING AGENTS AND OTHER DIUR
	CARVEDILOL + CLORTALIDONA
	TRANDIUR
	BETA BLOCKING AGENTS, THIAZIDES AND OTHER DIU
	BETA BLOCKING AGENTS, NON-SELECTIVE, THIAZIDE
	CARDIOTENSIN /01682501/
	DOCITEREN
	DOCITON 80 DYTIDE H
	MODUCREN
	BETA BLOCKING AGENTS, SELECTIVE, THIAZIDES AN
	KALTEN
	KERLIDEX
	BETA BLOCKING AGENTS AND VASODILATORS
	BETA BLOCKING AGENTS, NON-SELECTIVE, AND VASO
	BETA-INTENSAIN
	NITRISKEN
	NITRO-OBSIDAN

AMGEN®

	OXYCARDIN /00391901/
	PRIZIDILOL
	PRIZIDILOL HYDROCHLORIDE
	PRIZIDILOL HYDROCHLORIDE ANHYDROUS
	BETA BLOCKING AGENTS, SELECTIVE, AND VASODILA
	MET XL R
	METOPROLOL W/RAMIPRIL
	NEBICARD V
	STARPRESS R
	BETA BLOCKING AGENTS AND OTHER ANTIHYPERTENSI
	BETA BLOCKING AGENTS, NON-SELECTIVE/90119501/
	BETADIPRESAN
	INDUCOR
	INDUCOR D
	OBSILAZIN
	REDUPRESS /03518901/
	TRASIPRESSOL
	TRIMECRYTON
	AMLODIPINE W/METOPROLOL
	AMLODIPINE W/NEBIVOLOL
	AMLONG-A
	ARBITEL MT
	ATPURE-SA
	BELNIF
	BETA BLOCKING AGENTS, SELECTIVE, AND OTHER AN
	BETAFIT AM
	BETAONE AM
	CARDIF BETA
	CARDIORETIC A
	CARVEDIPINA D
	CILNIDIPINE W/METOPROLOL SUCCINATE
	CILNIPAR M
	CONCOR AM

AMGEN®

	CONCORAM
	FELODIPINE W/METOPROLOL
	FIXOCARD
	LOTENSYL AT
	MET XL AM
	METONCE AM
	METOPROLOL W/TELMISARTAN
	MODILOC
	NEBI AM
	NEBICARD-SM
	NIF-TEN
	NITRENOL
	NUSAR-ATN
	OLSAR M
	RASOTAN BETA
	TELISTA MT
	TONORMA
	TREDALAT
	ADAPROLOL
	ALCON BETAXOLOL
	AZARGA
	BAMOSIRAN
	BEFUNOLOL
	BEFUNOLOL HYDROCHLORIDE
	BETA BLOCKING AGENTS
	BETALOL /03186001/
	BETAXOLOL
	BETAXOLOL HCL W/PILOCARPINE HCL
	BETAXOLOL HYDROCHLORIDE
	BETAXOLOL W/PILOCARPINE
	BLOCANOL /01100601/
	BRIMONIDINE TARTRATE W/TIMOLOL
	BRIMONIDINE W/TIMOLOL

AMGEN®

	CARPILO
	CARTEOL /00853401/
	CARTEOLOL
	CARTEOLOL HYDROCHLORIDE
	CARTEOPIL
	COMBIGAN
	COSOPT
	DORZOLAMIDE W/TIMOLOL
	DORZOPT /06421101/
	DUOTRAV
	ELAZOP
	GANFORT
	GLAUTIMOL /06108601/
	KRITANTEK OFTENO
	KRYTANTEK OFTENO
	LEVOBUNOLOL
	LEVOBUNOLOL HYDROCHLORIDE
	METIPRANOLOL
	METIPRANOLOL HYDROCHLORIDE
	MOPROLOL
	MOPROLOL HYDROCHLORIDE
	NIPRADOLOL
	NORMOGLAUCON /01482401/
	PILOBLOQ
	PILOFLAX
	PINDOLOL
	PROXODOLOL
	PROXOPHELIN
	RIPIX
	TAFLUPROST W/TIMOLOL MALEATE
	TIMED
	TIMOLO
	TIMOLOL

AMGEN®

	TIMOLOL HEMIHYDRATE TIMOLOL MALEATE TIMOLOL MALEATE, R-ENANTIOMER TIMOLOL MALEATE, S-ENANTIOMER TIMPILO VISTAGAN /00844001/ XALACAR-T XALACOM
Nitrates	ADOCOR /01266201/ ANGIOCARDYL N ANGOR ASPITRATE G BIDIL CAFINITRINA /00702101/ CAFINITRINA /07893501/ CAFINITRINA RETARD CARDIACAP A CARDIOSEDANTOL CEFAVORA COR /08009401/ CONVALLARIA MAJALIS W/GLYCERYL TRINITRATE/LEV CORANGIL DILCORAN /00119101/ ERITRITYL TETRANITRATE ERYTHROMIN /01950501/ EUCARDIN GLYCERYL TRINITRATE GLYCERYL TRINITRATE, COMBINATIONS GOVIL IMAZIN XL ISO-NITROLINGUAL ISOSORBIDE DINITRATE ISOSORBIDE DINITRATE W/SODIUM CHLORIDE ISOSORBIDE DINITRATE, COMBINATIONS ISOSORBIDE MONONITRATE

AMGEN®

	KORDILAT
	MANNITOL HEXANITRATE
	METHYLPROPYLPROPANEDIOL DINITRATE
	MYANGIN
	MYOCARDON /00091601/
	MYOCARDON /02403401/
	MYOCARDON /03439401/
	MYOCORIL
	NATIROSE /01832701/
	NEO-AKTAL
	NITRANGIN COMPOSITUM
	NITRAPAMIL
	NITRIC OXIDE
	NITRO-CRATAEGUTT
	NITRODURAT
	NITROGLIN
	NITROGLYCERIN COMP.
	NITROPENT COMP.
	NITROTHESAL
	NITROUS ETHER SPIRIT
	NUNZANGIL
	ORGANIC NITRATES
	PENTAERITHRITYL TETRANITRATE
	PENTANEURAL
	PENTOXYLON
	PENTRINITROL
	PENTRIUM
	PROPATYLNITRATE
	SEDA-ILDAMEN
	SORBANGIL COMP.
	SPASMOCOR
	STENODILATE
	STENOPTIN
	TENITRAMINE
	THEOPENTRIT
	THEOPENTRIT PAPAV

AMGEN®

	TRINITRINE CAFFEINE TROLNITRATE TROLNITRATE PHOSPHATE VISANOCOR VISANOCOR N
Calcium channel blockers	VERAPAMIL VERAPAMIL HYDROCHLORIDE ISOPTIN S TALUVIAN /00149301/ LIDOFLAZINE PERHEXILINE PERHEXILINE MALEATE GRADULON FENDILINE FENDILINE HYDROCHLORIDE NIFEDIPINE DILTIAZEM DILTIAZEM HYDROCHLORIDE DILTIAZEM MALATE DIGO-SENSIT STENOPTIN CORDICHIN ELTHON /00603601/ NICARDIPINE NICARDIPINE HYDROCHLORIDE GALLOPAMIL GALLOPAMIL HYDROCHLORIDE FELODIPINE ISRADIPINE TIAPAMIL SALI-ADALAT BEPRIDIL BEPRIDIL HYDROCHLORIDE MONOHYDRATE NITRENDIPINE TREDALAT NISOLDIPINE NIF-TEN BELNIF NIMODIPINE VERATIDE

AMGEN®

	OXODIPINE AMLODIPINE AMLODIPINE BESILATE AMLODIPINE MALEATE AMLODIPINE MESILATE AMLODIPINE CAMSILATE AMLODIPINE OROTATE S AMLODIPINE NICOTINATE AMLODIPINE ADIPATE NILVADIPINE MANIDIPINE MANIDIPINE HYDROCHLORIDE LACIDIPINE BENIDIPINE BENIDIPINE HYDROCHLORIDE MODILOC EFONIDIPINE EFONIDIPINE HYDROCHLORIDE SALOPTASIN BARNIDIPINE BARNIDIPINE HYDROCHLORIDE UDRAMIL MIBEFRADIL MIBEFRADIL HYDROCHLORIDE LEXXEL TECZEM /01366001/ LERCANIDIPINE LERCANIDIPINE HYDROCHLORIDE CILNIDIPINE VERACAPT UNIMAX ADIZEM-XL PLUS ANIPAMIL TILDIAZIDE OCADRIK /01507301/ AZELNIDIPINE ENEAS NIMOREAGIN /01616501/ AMLODIPINE W/BENAZEPRIL AMLODIPINE BESYLATE W/BENAZEPRIL AMLODIPINE W/VALSARTAN

AMGEN®

	AMLODIPINE W/HYDROCHLOROTHIAZIDE
	AMLONG-A
	CADUET
	ARANIDIPINE
	SINERGEN
	HYDROCHLOROTHIAZIDE W/VERAPAMIL
	LOTAR /02225901/
	AMLOPRES L
	RIODIPINE
	DIOVAN AMLO
	MET XL AM
	TONORMA
	FIXOCARD
	LOTRIX /03460001/
	NIMOSOMAZINA
	REDUPRESS /03518901/
	NAPRIX A
	ASOMEX-D
	CARDIF BETA
	LOTENSYL AT
	ATPURE-SA
	NEBICARD-SM
	ACEDIP
	CLEVIDIPINE
	ANTROLIN
	CARDIORETIC A
	NITRENOL
	ETIPRESS-D
	MAXIDIPIN DIU
	NIFEDIP D
	CARVEDIPINA D
	INDUCOR
	INDUCOR D
	BETAONE AM
	AZOR /06230801/
	AMLOZAAR-H
	TWYNSTA
	TELSAR-A
	DIOVAN TRIPLE
	OROSPREVENT
	COVERAM

AMGEN®

	NEMOCEBRAL PLUS
	LEVAMLODIPINE
	LEVAMLODIPINE BESILATE
	LEVAMLODIPINE MALATE
	LEVAMLODIPINE MALEATE
	FELODIPINE W/METOPROLOL
	NIFEDIPINE W/TELMISARTAN
	PONTUC
	DIRONORM
	COZAAR XQ
	BENITEC A /06541301/
	OLMESAFE AM
	CONCOR AM
	CANDESAR A
	AMLODIPINE W/ATORVASTATIN
	TRIBENZOR
	ATACAND DUO
	AMLODIPINE MALEATE W/BENAZEPRIL HYDROCHLORIDE
	RASILEZ AMLO
	AMTAS PRP
	FLORDIPINE
	NIGULDIPINE
	NORVERAPAMIL
	AZIDOPINE
	IGANIDIPINE
	AMLODIPINE W/BENAZEPRIL HYDROCHLORIDE
	VIVACE /06864501/
	FENSARTAN UNIMAX
	AMTURNIDE
	AVOTIN
	AZELNIDIPINE W/OLMESARTAN MEDOXOMIL
	AMLODIPINE BESILATE W/ATORVASTATIN CALCIUM TR
	MOXOVAS A
	OLMAT AMH
	TEKAMLO /07156301/
	AMLODIPINE W/HYDROCHLOROTHIAZIDE/VALSARTAN
	NATRILAM
	BETAFIT AM
	CILACAR T

AMGEN®

	MODLIP AM
	NEBI AM
	DILVAS AM
	R PRIL AM
	AMLODAC D
	TELMICHEK AH
	RASITRIO
	DUPLECOR
	PERINDOPRIL ARG/AMLODIPINE FISHER
	CONCORAM
	AMLATOR
	TAH
	ENALAPRIL W/NITRENDIPINE
	APROVASC
	COROVAL B
	ZANERIL
	ENALAPRIL W/LERCANIDIPINE
	AMLODIPINE W/OLMESARTAN
	ANOBLISS
	ASOMEX TM
	RAMI ASOMEX
	CILNIPAR M
	ASOMEX LTH
	METONCE AM
	ROSUCOR PLUS
	AMLODIPINE W/NEBIVOLOL
	AMLODIPINE W/INDAPAMIDE/PERINDOPRIL
	LERCANIDIPINE HYDROCHLORIDE W/VALSARTAN
	LEVAMLODIPINE BESILATE W/VALSARTAN
	AMLODIPINE W/CHLORTALIDONE/LOSARTAN POTASSIUM
	CILNIDIPINE W/OLMESARTAN MEDOXOMIL
	AMLODIPINE OROTATE W/VALSARTAN
	HYDROCHLOROTHIAZIDE W/LEVAMLODIPINE BESILATE
	AMLODIPINE MESILATE W/HYDROCHLOROTHIAZIDE/VAL
	AMLODIPINE W/CHLORTALIDONE/OLMESARTAN MEDOXOM
	AMLODIPINE W/CHLORTALIDONE/TELMISARTAN
	AMLODIPINE BESILATE W/INDAPAMIDE/PE/08715301/
	AMLODIPINE BESILATE W/PERINDOPRIL TOSILATE
	AMLODIPINE BESILATE W/INDAPAMIDE/PE/08717501/

AMGEN®

	CILNIDIPINE W/VALSARTAN AMLODIPINE BESILATE W/AZILSARTAN ATORVASTATIN CALCIUM W/LEVAMLODIPINE BESILATE CILNIDIPINE W/METOPROLOL SUCCINATE AMLODIPINE W/METOPROLOL AMLODIPINE BESILATE W/CANDESARTAN CILEXETIL/H AMLODIPINE W/LISINOPRIL/ROSUVASTATIN AMLODIPINE W/ROSUVASTATIN AMLODIPINE ADIPATE W/VALSARTAN AMLODIPINE W/CLOPIDOGREL BISULFATE CHLORTALIDONE W/CILNIDIPINE/TELMISARTAN AMLODIPINE OROTATE W/OLMESARTAN MEDOXOMIL CALCIUM CHANNEL BLOCKERS SELECTIVE CALCIUM CHANNEL BLOCKERS WITH MAINL DIHYDROPYRIDINE DERIVATIVES SELECTIVE CALCIUM CHANNEL BLOCKERS WITH DIREC PHENYLALKYLAMINE DERIVATIVES BENZOTHIAZEPINE DERIVATIVES NON-SELECTIVE CALCIUM CHANNEL BLOCKERS
Ranolazine	Ranolazine
ACE inhibitors	CAPTOPRIL ENALAPRIL ENALAPRIL MALEATE CAPOZIDE PERINDOPRIL PERINDOPRIL ERBUMINE PERINDOPRIL ARGININE PERINDOPRIL TOSILATE QUINAPRIL QUINAPRIL HYDROCHLORIDE CILAZAPRIL CILAZAPRIL MONOHYDRATE RAMIPRIL LISINOPRIL LISINOPRIL DIHYDRATE VASERETIC SPIRAPRIL SPIRAPRIL HYDROCHLORIDE

AMGEN®

	BENAZEPRIL
	BENAZEPRIL HYDROCHLORIDE
	FOSINOPRIL
	FOSINOPRIL SODIUM
	ENALAPRILAT
	ZOFENOPRIL
	ZOFENOPRIL CALCIUM
	ALACEPRIL
	DELAPRIL
	DELAPRIL HYDROCHLORIDE
	GEZOR
	TRANDOLAPRIL
	CIBADREX
	SALUTEC
	ARELIX ACE
	DYNORM PLUS
	QUINAPRILAT
	QUINAPRILAT HYDRATE
	TEMOCAPRIL
	TEMOCAPRIL HYDROCHLORIDE
	IMIDAPRIL
	IMIDAPRIL HYDROCHLORIDE
	MOEXIPRIL
	MOEXIPRIL HYDROCHLORIDE
	UDRAMIL
	ELIDIUR
	LEXXEL
	TECZEM /01366001/
	VERACAPT
	LASITACE
	DELAPRIDE
	PRIMOX PLUS
	UNIMAX
	BI PREDONIUM
	BENAZEPRILAT
	PENTOPRIL
	IDRAPRIL
	MOVELTIPRIL
	CERONAPRIL
	TRANDOLAPRILAT
	UTIBAPRIL
	ZABICIPRIL

AMGEN®

	LIBENZAPRIL DINAPRES OCADRIK /01507301/ ENEAS CARACE PLUS /01613901/ AMLODIPINE W/BENAZEPRIL AMLODIPINE BESYLATE W/BENAZEPRIL ALENDRONATE SODIUM W/QUINAPRIL HYDROCHLORIDE SINERGEN AMLOPRES L LORAM-H ENZIX LOTRIX /03460001/ ARBITACE ORAS /03528201/ TERAM NAPRIX A ACEDIP M 100240 VASCORIDE CARDIO-PRES D CARSIPRIL D RAMICAR D CVPILL NORMATEN /06267401/ ATOCOR-R MODLIP-CAD OLMY-R ADPACE BIFRIL PLUS PERINDO COMBI COVERAM PRETERAX ARGININE ZESTORETIC INDAPAMIDE W/PERINDOPRIL HYDROCHLOROTHIAZIDE W/QUINAPRIL FOSINOPRIL W/HYDROCHLOROTHIAZIDE ENAP-HL /06436201/ CAPTOPRIL W/ENALAPRIL DIRONORM POLYCAP ZOPRANOL PLUS

AMGEN®

	AMLODIPINE MALEATE W/BENAZEPRIL HYDROCHLORIDE AMTAS PRP CILAZAPRIL MONOHYDRATE W/HYDROCHLOROTHIAZIDE GEMOPATRILAT HYDROCHLOROTHIAZIDE W/MOEXIPRIL FASIDOTRIL UTIBAPRILAT MOEXIPRILAT MOEXIPRILAT HYDROCHLORIDE OMAPATRILAT AMLODIPINE W/BENAZEPRIL HYDROCHLORIDE BENAZEPRIL W/HYDROCHLOROTHIAZIDE VIVACE /06864501/ CAPTRAL ASA RAMEY D STARPRESS R DILVAS AM R PRIL AM VALZAAR R TERAM H METPURE AR PERINDOPRIL ARG/AMLODIPINE FISHER LOTRIAL VAS ENALAPRIL W/NITRENDIPINE SINCRONIUM /07912401/ COROVAL B ZANERIL ENALAPRIL W/LERCANIDIPINE RAMITORVA METOZ R MET XL R RAMI ASOMEX PERINDOPRIL TOSILATE/ INDAPAMIDE METOPROLOL W/RAMIPRIL SAMPATRILAT AMLODIPINE W/INDAPAMIDE/PERINDOPRIL GLIMEPIRIDE W/METFORMIN HYDROCHLORIDE/RAMIPRI ATORVASTATIN CALCIUM W/GLIMEPIRIDE//08698201/ AMLODIPINE BESILATE W/INDAPAMIDE/PE/08715301/ AMLODIPINE BESILATE W/PERINDOPRIL TOSILATE

AMGEN®

	AMLODIPINE BESILATE W/INDAPAMIDE/PE/08717501/ AMLODIPINE W/LISINOPRIL/ROSUVASTATIN TEMOCAPRILAT INDAPAMIDE HEMIHYDRATE W/PERINDOPRIL ARGININE ACE INHIBITORS, PLAIN ACE INHIBITORS, COMBINATIONS ACE INHIBITORS AND CALCIUM CHANNEL BLOCKERS ACE INHIBITORS
Angiotensin receptor blockers	LOSARTAN LOSARTAN POTASSIUM HYZAAR TASOSARTAN SAPRISARTAN SAPRISARTAN POTASSIUM VALSARTAN IRBESARTAN IRBESARTAN HYDROCHLORIDE CO-DIOVAN EPROSARTAN EPROSARTAN MESILATE CANDESARTAN CANDESARTAN CILEXETIL KARVEA HCT BLOPRESS PLUS TELMISARTAN HYDROCHLOROTHIAZIDE W/LOSARTAN AMLODIPINE W/VALSARTAN OLMESARTAN OLMESARTAN MEDOXOMIL BENICAR HCT CANDESARTAN W/HYDROCHLOROTHIAZIDE LOTAR /02225901/ DIOVAN AMLO LORAM-H NUSAR-ATN ARBITACE ORAS /03528201/ TERAM DIOCOMB SI AZOR /06230801/ AMLOZAAR-H TWYNSTA TELSAR-A DIOVAN TRIPLE OLMY-R LOSAR BETA-H ADPACE

AMGEN®

	VALTURNA EMBUSARTAN PRITORPLUS EMESTAR PLUS NIFEDIPINE W/TELMISARTAN HYDROCHLOROTHIAZIDE W/OLMESARTAN COZAAR XQ PLEOTOR T BENITEC A /06541301/ OLMESAFE AM CANDESAR A TRIBENZOR ATACAND DUO ABITESARTAN RIPISARTAN AZILSARTAN AZILSARTAN MEDOXOMIL AZILSARTAN KAMEDOXOMIL POMISARTAN PRATOSARTAN FENSARTAN UNIMAX OLSAR M AZELNIDIPINE W/OLMESARTAN MEDOXOMIL OLMAT AMH AMLODIPINE W/HYDROCHLOROTHIAZIDE/VALSARTAN CO IRABEL CILACAR T INDITEL D ZIVAST L VALZAAR R NEBICARD V TERAM H RASOTAN BETA TELISTA MT TELMICHEK AH EDARBYCLOR FIMASARTAN FIMASARTAN POTASSIUM TRIHYDRATE TELROSE CTD L ARBITEL MT TAH APROVASC AMLODIPINE W/OLMESARTAN ERITEL CH OLMESAT ID ALISKIREN W/VALSARTAN METOZ L METOPROLOL W/TELMISARTAN

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	ASOMEX TM OLMESAR AV ASOMEX LTH IRBESARTAN W/TRICHLORMETHIAZIDE FIMASARTAN POTASSIUM TRIHYDRATE W/HYDROCHLORO LERCANIDIPINE HYDROCHLORIDE W/VALSARTAN LEVAMLODIPINE BESILATE W/VALSARTAN AMLODIPINE W/CHLORTALIDONE/LOSARTAN POTASSIUM CHLORTALIDONE W/OLMESARTAN MEDOXOMIL CILNIDIPINE W/OLMESARTAN MEDOXOMIL AMLODIPINE OROTATE W/VALSARTAN AMLODIPINE MESILATE W/HYDROCHLOROTHIAZIDE/VAL ATORVASTATIN CALCIUM W/IRBESARTAN AMLODIPINE W/CHLORTALIDONE/OLMESARTAN MEDOXOM AMLODIPINE W/CHLORTALIDONE/TELMISARTAN OLMESARTAN MEDOXOMIL W/ROSUVASTATIN CALCIUM CILNIDIPINE W/VALSARTAN ROSUVASTATIN CALCIUM W/VALSARTAN AMLODIPINE BESILATE W/AZILSARTAN AMLODIPINE BESILATE W/CANDESARTAN CILEXETIL/H AMLODIPINE ADIPATE W/VALSARTAN CHLORTALIDONE W/CILNIDIPINE/TELMISARTAN AMLODIPINE OROTATE W/OLMESARTAN MEDOXOMIL SACUBITRIL W/VALSARTAN ANGIOTENSIN II ANTAGONISTS, PLAIN ANGIOTENSIN II ANTAGONISTS, COMBINATIONS ANGIOTENSIN II ANTAGONISTS AND CALCIUM CHANNE

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