A Multi-Center, Randomized, Double-Blind, Placebo-Controlled Study Comparing the Safety and Effectiveness of Drug A 20 mg Once Daily Versus Placebo Using 24-Hour Ambulatory BloodPressure Monitoring in Patients with Mild to Moderate Hypertension

CASE REPORT FORM

Protocol Number: ABC01

☐☐ Site No ☐☐☐ Patient No ☐☐☐ Patient Initials

Study Sponsor: Medifacts International
Gaither Road
Suite 400
Rockville, MD 20850

Screening (Visit 1)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

INFORMED CONSENT

Have the nature and risks of this study been explained to the patient and written informed consent obtained? ☐ Yes ☐ No If "**No**", do not proceed.

Date informed consent was signed: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

DEMOGRAPHICS

Date of Birth: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

Race: ☐ Caucasian ☐ Black ☐ Asian ☐ Hispanic/Latin

☐ Other, please specify_____

Gender: ☐ Male ☐ Female

If "**Female**", please complete below:
Pregnancy Potential:

☐ Post-menopausal for at least 2 years

☐ Surgically sterile

☐ Able to bear children

If "**Able to bear children**", pregnancy test must be completed.

Screening (Visit 1)

INCLUSION CRITERIA		
All answers must be "**Yes**" or "**NA**" (only for Q#9) for the patient to be included in the study. **Check Yes or No**	**Yes**	**No**
1.Patients must be males or females >= 18 years of age.	☐	☐
2.Patients must have a history of Stage I to Stage II hypertension (defined as a seated DBP >= 95 mmHg and <= 110 mmHg at Baseline-Week0).	☐	☐
3.Patients must be able to communicate effectively with the study personnel.	☐	☐
4.Patients must be adequately informed of the nature and risks of the study and give written informed consent prior to screening.	☐	☐
5.Patients must be ambulatory and able to maintain a normal daily activity schedule.	☐	☐
6.Patients must have a mean 24-hour ambulatory diastolic blood pressure (DBP) >= 85 and <= 105 mmHg as determined by ABPM at the end of the Baseline period (Visit 6).	☐	☐
7.Patients must have a mean seated diastolic blood pressure >= 95 and <= 110 mmHg at the end of the Baseline period (Visit 6).	☐	☐
8.Patients under treatment for hypertension must be willing and able to discontinue all previous anti-hypertensive medication for the duration of the study (as defined in Protocol Section 5.7).	☐	☐
9.Women of childbearing potential must be using a medically acceptable form of birth control for the duration of the trial, must have a negative serum pregnancy test at screening, and must have a negative urine pregnancy test prior to randomization (Visit 6).	☐	☐ ☐ **NA**

Screening (Visit 1)

EXCLUSION CRITERIA		
All answers must be "**No**" for the patient to be included in the study. **Check Yes or No**	**Yes**	**No**
1.Patients who have a known hypersensitivity or allergy to metoprolol tartrate or vehicle components.	☐	☐
2.Patients who have insulin-dependent or uncontrolled Diabetes Mellitus (glycosolated hemoglobin > 9%) or hypoglycemia.	☐	☐
3.Systolic blood pressure > 179 mmHg either at the screening visit or at the end of the single-blind placebo run-in phase of the study as measured by "office" cuff pressure.	☐	☐
4.Difference > 10 mmHg in office measured mean diastolic blood pressures between any two office visits during the run-in phase of the study.	☐	☐
5.Patients who have hypertension secondary to a disease or condition or who have a history of malignant hypertension including retinal hemorrhage, exudates and papilledema.	☐	☐
6.Patients who have an AV block greater than first degree including sick sinus syndrome.	☐	☐
7.Patients who have chronic atrial fibrillation or recurrent tachyarrhythmia	☐	☐
8.Patients who have significant bradycardia defined as a resting heart rate < 50 beats per minute (bpm).	☐	☐
9.Patients who have clinically significant aortic or mitral valve disease.	☐	☐
10.Patients with target organ damage or clinical cardiovascular disease that would preclude their safe inclusion in a placebo-controlled trial. This would include unstable angina pectoris, previous myocardial infarction or CVA in the last 6 months, congestive heart failure, transient ischemic attack (TIA).	☐	☐
11.Patients who have severe peripheral vascular disease.	☐	☐
12.Patients with significant thyroid, renal or hepatic disease [TSH > 1.5 times upper limit of normal, urine protein > 1+, creatinine > 2.2 mg/dL, AST (SGOT) and/or ALT (SGPT) greater than twice the upper limit of normal].	☐	☐

Screening (Visit 1)

EXCLUSION CRITERIA (CONT.)		
All answers must be "**No**" or "**NA**" (only for Q#17) for the patient to be included in the study. **Check Yes or No**	**Yes**	**No**
13.Patients who perform alternate shift or night work.	☐	☐
14.Patients with arm circumference > 42 cm (ABPM Cuff).	☐	☐
15.Patients with any history of alcohol abuse, illicit drug use, significant mental illness, physical dependence to any opioid in the past year, or any history of drug abuse or addiction in the past year.	☐	☐
16.Patients who have a history or presence of bronchospastic disease (e.g. asthma, chronic obstructive pulmonary disorder [COPD]).	☐	☐
17.Women who are pregnant or breast-feeding, or who are not using or are not willing to use a medically accepted method of birth control.	☐	☐ ☐ **NA**
18.Patients who have received an investigational drug or device within a period of 30 days prior to enrollment (Visit 2) in the study.	☐	☐
19.Patients who require concurrent use of prohibited prescription (Rx) or over-the-counter (OTC) medications (as defined in Protocol Section 5.7).	☐	☐
20.Patients who have previously participated in a study of the Sponsor's metoprolol tartrate ER tablets.	☐	☐
21.Patients who, in the opinion of the Investigator, have any other medical condition which renders the patient unable to complete the study or which would interfere with optimal participation in the study or produce significant risk to the patient.	☐	☐
22.Patients are participating in or planning to enroll in a weight reduction program during the time of the study.	☐	☐

Screening (Visit 1)

MEDICAL HISTORY			
Please list **ALL** significant abnormalities or diseases for the following systems**.**			
Body System	**Yes**	**No**	**If "Yes", please specify (Description and Onset Date mm/yyyy)**
1.HEENT	☐	☐	
2.Dermatologic	☐	☐	
3.Cardiovascular	☐	☐	
4.Hematological	☐	☐	
5.Respiratory	☐	☐	
6.Endocrine*	☐	☐	
7.Gastrointestinal	☐	☐	
8.Musculoskeletal	☐	☐	
9.Genitourinary	☐	☐	
10.Neurologic	☐	☐	
11.Psychiatric	☐	☐	
12.Allergic	☐	☐	
13.Immunologic	☐	☐	
14.Other	☐	☐	

*** Diabetes history will not be included in the system of Endocrine, see CRF page 7.**

Screening (Visit 1)

HYPERTENSION / DIABETES HISTORY

Date hypertension was diagnosed: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Did patient have Diabetes? ☐ Yes ☐ No If "**Yes**", complete below.

Diabetes Type ☐ Type I ☐ Type II

Date Diabetes was diagnosed: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐/min

Height: ☐☐☐ in **Weight:** ☐☐☐.☐ lb

Arm Circumference: ☐☐.☐ in **Oral Temperature:** ☐☐.☐ °F

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings.

Screening (Visit 1)

PHYSICAL EXAMINATION			
Body System	**Not Done**	**Assessment**	**If Abnormal, please specify**
1.Skin	☐	☐ Normal ☐ Abnormal	
2.HEENT	☐	☐ Normal ☐ Abnormal	
3.Neck	☐	☐ Normal ☐ Abnormal	
4.Lymph nodes	☐	☐ Normal ☐ Abnormal	
5.Thorax	☐	☐ Normal ☐ Abnormal	
6.Lung	☐	☐ Normal ☐ Abnormal	
7.Heart	☐	☐ Normal ☐ Abnormal	
8.Abdomen	☐	☐ Normal ☐ Abnormal	
9.Extremities	☐	☐ Normal ☐ Abnormal	
10.Musculoskeletal	☐	☐ Normal ☐ Abnormal	
11.Neurologic	☐	☐ Normal ☐ Abnormal	
12.Other	☐	☐ Normal ☐ Abnormal	

Screening (Visit 1)

12-LEAD ELECTROCARDIOGRAM

Was the 12-Lead ECG performed? ☐ Yes ☐ No

Date and Time ECG was done: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Results: ☐ Normal ☐ Abnormal If "**Abnormal**" , please specify: _____

_____

If ECG not done, provide the reason:_____

LABORATORY TESTS

Was a blood sample drawn and sent to central lab? ☐ Yes ☐ No

Date and Time a blood sample drawn: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If blood sample not drawn, provide the reason:_____

Was a urine sample collected and sent to central lab? ☐ Yes ☐ No

Date and Time a urine sample collected: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If urine sample not collected, provide the reason:_____

SERUM PREGNANCY TEST

Was a serum pregnancy test completed? ☐ Yes ☐ No ☐ NA

Date and Time a blood sample drawn: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Pregnancy test results: ☐ Positive ☐ Negative If "**Positive**", patient should be withdrawn.

Please attach a copy of the patient's ECG and Laboratory Test results to the CRF.

Visit 2 (Week -3, Run-in period)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Have the prohibited medications, if any, been discontinued? ☐ Yes ☐ No

Patients must be off all prohibited medications by the start of the run-in period.

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:
Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 2 (Week -3, Run-in Period)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Dispensing

Was Single-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 3 (Week -2, Run-in Period)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (Time (24-hr clock))

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:

(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 3 (Week -2, Run-in Period)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Study Drug Dispensing

Was Single-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 4 (Week -1, Run-in Period)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:

(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 4 (Week -1, Run-in Period)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Study Drug Dispensing

Was Single-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 4A (Week -1A, Run-in Period)

☐ NA **If Visit 4A not required, please check NA.**

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings.

BLOOD PRESSURE STABILIZATION ASSESSMENT

Did the patient have a mean seated DBP >= 95 mmHg and <= 110 mmHg? ☐ Yes ☐ No

If "**Yes**", please complete all the Visit 5 assessments on CRF Pages 18, 19, 20.
If "**No**", please complete all the Visit 4A assessments on CRF Pages 16 and 17.

Visit 4A (Week -1A, Run-in Period)

☐ NA **If Visit 4A not required, please check NA.**

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Study Drug Dispensing

Was Single-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 5 (Week 0, Baseline)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: ☐☐☐/☐☐☐ (Systolic/Diastolic) mmHg Reading 2: ☐☐☐/☐☐☐ mmHg

Reading3: ☐☐☐/☐☐☐ mmHg **Standing BP:** Reading4: ☐☐☐/☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: ☐☐☐/☐☐☐ mmHg Reading 2: ☐☐☐/☐☐☐ mmHg

Mean BP: ☐☐☐/☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings.

BLOOD PRESSURE STABILIZATION ASSESSMENT

Did the patient have a mean seated DBP >= 95 mmHg and <= 110 mmHg? ☐ Yes ☐ No

If "**Yes**", please complete all the Visit 5 assessments on CRF Pages 18, 19, 20.

If "**No**", patient should be withdrawn from the study.

Visit 5 (Week 0 Baseline)

12-LEAD ELECTROCARDIOGRAM

Was the 12-Lead ECG performed? ☐ Yes ☐ No

Date and Time ECG was done: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Results: ☐ Normal ☐ Abnormal If "**Abnormal**" , please specify: _____

_____

If ECG not done, provide the reason:_____

Please attach a copy of ECG results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

LABORATORY TESTS

Was a blood sample drawn and sent to central lab? ☐ Yes ☐ No

Date and Time a blood sample drawn: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If blood sample not drawn, provide the reason:_____

Was a urine sample collected and sent to central lab? ☐ Yes ☐ No

Date and Time a urine sample collected: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If urine sample not collected, provide the reason:_____

Please attach a copy of Laboratory Test results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

URINE PREGNANCY TEST

Was a urine pregnancy test completed? ☐ Yes ☐ No ☐ NA

Date and Time urine sample collected: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Pregnancy test results: ☐ Positive ☐ Negative If "**Positive**", patient should be withdrawn.

Visit 5 (Week 0 Baseline)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Please incorporate the final dose of Single-Blind study drug given at this visit into the calculated Tablet count compliance.

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Final dose of Single-Blind study drug administration

Date and Time of dose administration: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) APPLICATION

Date and Time (beginning of test) : ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

ABPM File ID: ☐☐☐☐–☐☐☐

REMINDER:
Have the patient take the final dose of Single-Blind study drug after ABPM is initiated and instruct the patient to return to the Principal Investigator's office the next day to have the ABPM device removed.

Visit 6 (Week 0, Baseline/Randomization)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) REMOVAL

Date and Time (conclusion of test): ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

Mean 24-hour diastolic BP (M24DBP) ☐☐☐ mmHg

ABPM Quality Control ☐ Pass ☐ Fail ☐ QC override via sponsor pass

If "**Pass**" or "**QC override via sponsor pass**", please complete the assessments for Visit 6 on CRF pages 25 and 26.

If "**Fail**", will the ABPM be repeated? ☐ Yes ☐ No

If "**No**", patient should be withdrawn.
If "**Yes**", please complete **Repeat ABPM and dispense study drug**.

STUDY DRUG RETRIEVAL / DISPENSING

☐ **NA** **If ABPM passed Quality Control, please check NA.**

Study Drug Dispensing

Was Single-Blind Study Drug dispensed this visit? ☐ Yes ☐ No
(dispense from the bottle returned at Visit 5)

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

Visit 6 (Week 0, Baseline/Randomization)

☐ **NA** **If ABPM passed Quality Control, please check NA.**

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:
(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 6 (Week 0, Baseline/Randomization)

☐ **NA** **If ABPM passed Quality Control, please check NA.**

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Please incorporate the final dose of Single-Blind study drug given at this visit into the calculated Tablet count compliance.

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Final dose of Single-Blind study drug administration

Date and Time dose administration: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) APPLICATION

Date and Time (beginning of test): ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

ABPM File ID: ☐☐☐☐–☐☐☐

REMINDER:
Have the patient take the final dose of Single-Blind study drug after ABPM is initiated and instruct the patient to return to the Principal Investigator's office the next day to have the ABPM device removed.

Visit 6 (Week 0, Baseline/Randomization)

☐ **NA** **If ABPM passed Quality Control, please check NA.**

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) REMOVAL

Date and Time (conclusion of test): ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

Mean 24-hour diastolic BP (M24DBP) ☐☐☐ mmHg

ABPM Quality Control ☐ Pass ☐ Fail ☐ QC override via sponsor pass

If "**Pass**" or "**QC override via sponsor pass**", please complete the assessments for Visit 6 on CRF pages 25 and 26.

If "**Fail**", the patient should be withdrawn.

Visit 6 (Week 0, Baseline/Randomization)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐/min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:
(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 6 (Week 0, Baseline/Randomization)

ASSESSMENT FOR ELIGIBILITY FOR RANDOMIZATION

All answers for the following questions must be "**Yes**" for the patient to be randomized.

1. **Did the patient meet all inclusion criteria and none of the exclusion criteria?** ☐ Yes ☐ No

2. **Did the patient have a valid M24DBP >= 85 mmHg and <= 105 mmHg?** ☐ Yes ☐ No

3. **Did the patient have a mean seated DBP >= 95 mmHg and <= 110 mmHg?** ☐ Yes ☐ No

4. Was medication compliance during Single-Blind placebo run-in period >= 80% and <= 120% as specified in the protocol? ☐ Yes ☐ No

NOTE: Please complete questions 6, 7 and 9 of the Inclusion Criteria on CRF page 3 at this time.

Patient's assigned randomization number: ☐☐☐☐☐

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Dispensing

Was Double-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", please complete below.

Date and time dispensed: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

Number of tablets dispensed: ☐☐ (including tablet dispensed in office)

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 7 (Week 2, Double-Blind Treatment)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:

(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 7 (Week 2, Double-Blind Treatment)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Study Drug Dispensing

Was Double-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 8 (Week 4, Double-Blind Treatment)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (Time (24-hr clock))

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:

(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 8 (Week 4, Double-Blind Treatment)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Is the patient at least 80% compliant? ☐ Yes ☐ No

If "**No**", patient should be counseled and re-instructed on dosing procedures.

Study Drug Dispensing

Was Double-Blind Study Drug dispensed this visit? ☐ Yes ☐ No

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

REMINDER:
Instruct the patient NOT to take the morning dose of study medication before coming to the next scheduled visit and remind the patient to take the last dose of study medication **24+/-2** hours prior to the next scheduled visit.

Visit 9 (Week 6, End of Study/Early Termination)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Previous Dose Administration

Date and Time of last dose taken prior to this visit:

☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:

(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 9 (Week 6, End of Study/Early Termination)

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Please incorporate the final dose of Double-Blind study drug given at this visit into the calculated Tablet count compliance.

Is the patient at least 80% compliant? ☐ Yes ☐ No

Final dose of Double-Blind study drug administration

Date and Time of dose administration: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (Time (24-hr clock))

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) APPLICATION

Date and Time (beginning of test): ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ (Time (24-hr clock))

ABPM File ID: ☐☐☐☐–☐☐☐

REMINDER:
Have the patient take the final dose of Double-Blind study drug after ABPM is initiated and instruct the patient to return to the Principal Investigator's office the next day to have the ABPM device removed.

Visit 10 (Week 6, End of Study/Early Termination)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) REMOVAL

Date and Time (conclusion of test): ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Mean 24-hour diastolic BP (M24DBP) ☐☐☐ mmHg

ABPM Quality Control ☐ Pass ☐ Fail ☐ QC override via sponsor pass

If "**Pass**" or "**QC override via sponsor pass**", please complete the assessments for Visit 10 on CRF pages 37, 38 and 39.

If "**Fail**", will the ABPM be repeated? ☐ Yes ☐ No

If "**No**", patient should be withdrawn.
If "**Yes**", please complete **Repeat ABPM and dispense study drug**.

STUDY DRUG RETRIEVAL / DISPENSING

☐ **NA** **If ABPM passed Quality Control, please check NA.**

Study Drug Dispensing

Was Double-Blind Study Drug dispensed this visit? ☐ Yes ☐ No
(dispense from the bottle returned at Visit 9)

If "**Yes**", Number of tablets dispensed: ☐☐

If "**No**", please provide the reason:_____

_____

Visit 10 (Week 6, End of Study/Early Termination)

☐ NA **If ABPM passed Quality Control, please check NA.**

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:
(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 10 (Week 6, End of Study/Early Termination)

☐ NA **If ABPM passed Quality Control, please check NA.**

STUDY DRUG RETRIEVAL / DISPENSING

Study Drug Retrieval

Number of tablets returned: ☐☐

Tablet count compliance: ☐☐☐.☐ %

Please incorporate the final dose of Double-Blind study drug given at this visit into the calculated Tablet count compliance.

Is the patient at least 80% compliant? ☐ Yes ☐ No

Final dose of Double-Blind study drug administration

Date and Time dose administration: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) APPLICATION

Date and Time (beginning of test): ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

ABPM File ID: ☐☐☐☐–☐☐☐

REMINDER:
Have the patient take the final dose of Double-Blind study drug after ABPM is initiated and instruct the patient to return to the Principal Investigator's office the next day to have the ABPM device removed.

Visit 10 (Week 6, End of Study/Early Termination)

☐ **NA** **If ABPM passed Quality Control, please check NA.**

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

AMBULATORY BLOOD PRESSURE MONITORING (ABPM) REMOVAL

Date and Time (conclusion of test): ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

Mean 24-hour diastolic BP (M24DBP) ☐☐☐ mmHg

ABPM Quality Control ☐ Pass ☐ Fail ☐ QC override via sponsor pass

If "**Pass**" or "**QC override via sponsor pass**", please complete the assessments for Visit 10 on CRF pages 37, 38 and 39.

If "**Fail**", the patient should be withdrawn.

Visit 10 (Week 6, End of Study/Early Termination)

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐/min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings**.**

REMINDER:
(1) Office blood pressure measurements should be performed **24+/-2** hours after the previous morning dose of study medication. (2) Patient should NOT smoke or consume any caffeine containing beverage within 2 hours prior to the clinic visit.

Visit 10 (Week 6, End of Study/Early Termination)

PHYSICAL EXAMINATION			
Body System	**Not Done**	**Assessment**	**If Abnormal, please specify**
1.Skin	☐	☐ Normal ☐ Abnormal	
2.HEENT	☐	☐ Normal ☐ Abnormal	
3.Neck	☐	☐ Normal ☐ Abnormal	
4.Lymph nodes	☐	☐ Normal ☐ Abnormal	
5.Thorax	☐	☐ Normal ☐ Abnormal	
6.Lung	☐	☐ Normal ☐ Abnormal	
7.Heart	☐	☐ Normal ☐ Abnormal	
8.Abdomen	☐	☐ Normal ☐ Abnormal	
9.Extremities	☐	☐ Normal ☐ Abnormal	
10.Musculoskeletal	☐	☐ Normal ☐ Abnormal	
11.Neurologic	☐	☐ Normal ☐ Abnormal	
12.Other	☐	☐ Normal ☐ Abnormal	

Visit 10 (Week 6, End of Study/Early Termination)

12-LEAD ELECTROCARDIOGRAM

Was the 12-Lead ECG performed? ☐ Yes ☐ No

Date and Time ECG was done: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Results: ☐ Normal ☐ Abnormal If "**Abnormal**" , please specify: _____

_____

If ECG not done, provide the reason:_____

Please attach a copy of ECG results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

LABORATORY TESTS

Was a blood sample drawn and sent to central lab? ☐ Yes ☐ No

Date and Time a blood sample drawn: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If blood sample not drawn, provide the reason:_____

Was a urine sample collected and sent to central lab? ☐ Yes ☐ No

Date and Time a urine sample collected: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

If urine sample not collected, provide the reason:_____

Please attach a copy of Laboratory Test results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

Study Summary

Did the patient complete the study? ☐ Yes ☐ No

If "**Yes**", please provide date of completion ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

If "**No**", please provide date of last contact with patient ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

If patient did not complete the study, please indicate the primary reason for discontinuation:

1. ☐ Treatment failure (office BP rises to > 179 mmHg systolic and /or > 110 mmHg diastolic in either the seated or standing position)
2. ☐ Lost to follow-up
3. ☐ Withdrawn for discovery of pre-existing violation of entry criteria which present a safety risk to the patient, specify: _____
4. ☐ Significant protocol deviation, specify: _____
5. ☐ Patient request to withdraw
6. ☐ Investigator's decision for patient's best interest.
7. ☐ Withdrawn due to Adverse Event (Specify on AE page)
8. ☐ Death, Date of Death: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)
9. ☐ Other, specify: _____

Was blind code broken: ☐ Yes ☐ No

If "**Yes**", date and time of unblinding: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy) ☐☐:☐☐ Time (24-hr clock)

Reason for unblinding: _____

_____

_____

Concomitant Medications

Did the patient take any concomitant medications from 30 days prior to the Screening Visit throughout the course of the study (including nutriceuticals and dietary supplements)? ☐ Yes ☐ No If "**Yes**" please list ALL medications blow.

Medication Name (Use Generic Name)	**Dose**	**Frequency**	**Units**	**Route**	**Indication**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)	**On-going**
1.						___/____/_____	___/____/_____	☐
2.						___/____/_____	___/____/_____	☐
3.						___/____/_____	___/____/_____	☐
4.						___/____/_____	___/____/_____	☐
5.						___/____/_____	___/____/_____	☐
6.						___/____/_____	___/____/_____	☐
7.						___/____/_____	___/____/_____	☐
8.						___/____/_____	___/____/_____	☐
9.						___/____/_____	___/____/_____	☐
10.						___/____/_____	___/____/_____	☐

All previous prohibited medications/treatments, if any, must be discontinued for the duration of the study.

Concomitant Procedures

Did the patient have any concomitant procedures throughout the course of the study (including surgery and biopsy)? ☐ Yes ☐ No

If "**Yes**", please list **ALL** concomitant procedures below.

Procedure	**Indication**	**Start Date** (DD/MMM/YYYY)	**Stop Date** (DD/MMM/YYYY)
1.		___/____/_____	___/____/_____
2.		___/____/_____	___/____/_____
3.		___/____/_____	___/____/_____
4.		___/____/_____	___/____/_____
5.		___/____/_____	___/____/_____
6.		___/____/_____	___/____/_____
7.		___/____/_____	___/____/_____
8.		___/____/_____	___/____/_____
9.		___/____/_____	___/____/_____
10.		___/____/_____	___/____/_____

Adverse Events

Did the subject experience any adverse events (AEs) during the study? ☐ Yes ☐ No

If "**Yes**", provide details of all AEs experienced from the time informed consent is signed through the conclusion of the study.

AE diagnosis (if known) or Signs or Symptoms	Date of Onset	Max Intensity	Serious AE?	Outcome		Relation to Study Drug	Action Taken		REF#
				Status	Date		Study Drug	Treatments	
List one per line **Do not abbreviate**		1=Mild 2=Moderate 3=Severe	Y=Yes* N=No	1=Continuing 2=Resolved w/ o sequelae 3=Resolved, w/sequelae 4=Death 9=Unknown	Date of Resolution or Death	1=Probably 2=Possibly 3=Unlikely	0=None 1=Study Drug Interrupted 2=Study Drug Discontinued 3=Study Drug Dose Changed	Check all that apply **N**one **M**edication **S**urgical **O**ther	If the AE is serious, record the REF#**
	dd/mmm/yyyy				dd/mmm/yyyy			**N M S O**	
1								☐☐☐☐	
2								☐☐☐☐	
3								☐☐☐☐	
4								☐☐☐☐	
5								☐☐☐☐	
6								☐☐☐☐	

Principal Investigator Signature **Date** (DD/MMM/YYYY)

*please complete SAE Report Form for all SAEs and fax to Medifacts International FAX: 301-123-4567

** The REF#, is supplied by Medifacts upon receipt of the SAE

Single-Blind Study Drug Labels

Please attach all labels of Single-Blind study drug dispensed below.

☐ NA *(Attach Drug Label for visit 2 Here)*

☐ NA *(Attach Drug Label for visit 3 Here)*

☐ NA *(Attach Drug Label for visit 4 Here)*

☐ NA *(Attach Drug Label for visit 4A Here)*

Double-Blind Study Drug Labels

Please attach all labels of Double-Blind study drug dispensed below.

☐ NA *(Attach Drug Label for visit 5 Here)*

☐ NA *(Attach Drug Label for visit 6 Here)*

☐ NA *(Attach Drug Label for visit 7 Here)*

☐ NA *(Attach Drug Label for visit 8 Here)*

Comment Log

Are there any relevant comments? ☐ Yes ☐ No

If "**Yes**", please write down the comments below.

CRF Page Reference Number.	Comments

This form is to be used for explaining any relevant events occurring during the course of the study that are NOT noted elsewhere. Comments should be concise. Avoid non-standard abbreviations.

Principal Investigator's Certification

PRINCIPAL INVESTIGATOR CERTIFICATION

I hereby confirm that I have reviewed all of the Case Report Form pages and that they are complete and correct to the best of my knowledge.

_____ _____

Principal Investigator's Signature **Date** (DD/MMM/YYYY)

Note: Do not sign this page until instructed by the Sponsor's appointed Monitor.

Unscheduled Visit(1 of 2)

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd / mmm / yyyy)

Primary reason for this unscheduled visit:

1. ☐ Uncontrolled Hypertension
2. ☐ Adverse Event (Specify on AE page)
3. ☐ Abnormal study assessment (Lab Test, ECG, etc)
4. ☐ Other, specify _____

VITAL SIGNS

Heart Rate (Seated): ☐☐☐ bpm **Respiration:** ☐☐ /min

Weight: ☐☐☐.☐ lb

OFFICE CUFF BLOOD PRESSURE MEASUREMENTS

Please take office BP measurements after resting for 5 minutes and take 4 readings 2 minutes apart

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Reading3: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg **Standing BP:** Reading4: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Do the 3 consecutive seated DBP readings agree within 5 mmHg of each other? ☐ Yes ☐ No

If "**No**", please obtain 2 additional BP readings and incorporate them into the calculated mean pressure.

Seated BP: Reading1: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg Reading 2: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Mean BP: Systolic ☐☐☐ / Diastolic ☐☐☐ mmHg

Note: Mean BP should only be calculated from the three (or five if needed) **Seated** readings.

Unscheduled Visit(2 of 2)

12-LEAD ELECTROCARDIOGRAM

Was the 12-Lead ECG performed? ☐ Yes ☐ NA

Date and Time ECG was done: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Results: ☐ Normal ☐ Abnormal If "**Abnormal**" , please specify: _____

_____

Please attach a copy of ECG results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

LABORATORY TESTS

Was a blood sample drawn and sent to central lab? ☐ Yes ☐ NA

Date and Time a blood sample drawn ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

Was a urine sample collected and sent to central lab? ☐ Yes ☐ NA

Date and Time a urine sample collected ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy) ☐☐:☐☐ Time (24-hr clock)

Accession Number: _____

Please attach a copy of Laboratory Test results to the CRF. If the results constitute a new or worsening adverse event, please record the information on Adverse Event Page (Page 43).

Medifacts INTERNATIONAL

Protocol No: ABC01

Site No | Patient No | Patient Initials

Screen Failure

Date of Visit: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

INFORMED CONSENT

Have the nature and risks of this study been explained to the patient and written informed consent obtained? ☐ Yes ☐ No If "**No**", do not proceed

Date informed consent was signed: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

DEMOGRAPHICS

Date of Birth: ☐☐/☐☐☐/☐☐☐☐ (dd/mmm/yyyy)

Race: ☐ Caucasian ☐ Black ☐ Asian ☐ Hispanic/Latin ☐ Other, please specify_____

Gender: ☐ Male ☐ Female

REASON FOR SCREEN FAILURE

Specify the primary reason for Screen Failure:

1. ☐ Failed to meet Inclusion Criteria [Criteria Number(s)] _____
2. ☐ Failed to meet Exclusion Criteria [Criteria Number(s)] _____
3. ☐ Withdrew Informed Consent
4. ☐ Adverse Event (Specify on AE page)
5. ☐ Other, please specify _____

PRINCIPAL INVESTIGATOR CERTIFICATION

I hereby confirm that I have reviewed all of the Case Report Form pages and that they are complete and correct to the best of my knowledge.

_____ **Principal Investigator's Signature**

_____ **Date** (DD/MMM/YYYY)