

Specifications Defining Parameters for this Request

SOC is using the CIDA tool [version 12.1.2] to replicate a known positive association between ACE inhibitors and angioedema with beta blockers as a comparator, in Market Scan and CMS data from pandemic years to understand how pandemic-related changes in healthcare utilization impact a known positive association.

This is part 2, in which we introduce subgroup analysis by quarter-year.

Query Period: 1/1/2018-6/30/2022

Coverage Requirement: Medical & Drug Coverage

Pre-index enrollment requirement (ENRDAYS): 183
Post-index enrollment requirement (REQDAYSAFTIND): N/A
Post-episode requirement for T2 analyses (REQDAYSAFTEPI): N/A

Enrollment gap: 45

Restrictions: Demographic: M/F sex only **Age groups:** 18-44, 45-64, and ≥ 65

Stratifications: quarter-year

Censor output categorization: N/A

Envelope macro: Reclassify encounters during inpatient stay

Never-exposed cohort: N/A

Distribution of index-defining codes: N/A

Freeze data: Yes

| | RUN01 | |
|---|---|---------------|
| Pre-index enrollment requirement | 183 | |
| Group | ACEi | ВВ |
| Drug/Exposure | | |
| Index Exposure/Comparator | ACEi | Beta Blockers |
| Cohort Definition | First valid exposure episodes during query period | |
| Stockpiling | See stockpiling tab | |
| Build Episodes on Point Exposure? | No | |
| Treatment Episode Gap | 14 | |
| Exposure episode extension | 14 | |
| Minimum days supplied | 1 | |
| Incidence Criteria Care Setting | N/A | |
| Principal Diagnosis Position | N/A | |
| Forced supply to attach to dispensings | N/A | |
| Create Baseline Table? | Yes | |
| Inclusion/Exclusion Criteria | | |
| Inclusion/Exclusion group | Aliskiren, | Aliskiren, |
| Type of criteria | Exclusion | |
| Evaluation Period Start | -183 | |
| Evaluation Period End | -1 | |
| Care Setting/PDX | N/A | |
| Principal Diagnosis Position | N/A | |
| Exclude evidence of days supply if inclusion/exclusion evaluation period | Evaluation period should search for evidence of | |
| includes dispensings | days supply | |
| Number of instances the criteria should be found in the evaluation period | 1 | |
| Minimum Days Supplied | 1 | |

cder_mpl2p_wp051 Page 1 of 4



Specifications Defining Parameters for this Request

| Specifications Defining Parameters for this Request | | |
|---|--|--|
| Minimum cumulative dose | N/A | |
| Minimum average filled daily dose | N/A | |
| Maximum average filled daily dose | N/A | |
| Minimum current filled daily dose | N/A | |
| Maximum current filled daily dose | N/A | |
| Forced supply to attach to dispensings | N/A N/A | |
| | | |
| Inclusion/Exclusion group | - | |
| Type of criteria | 4 | |
| Evaluation Period Start | -183 | |
| Evaluation Period End | -1 | |
| Care Setting/PDX | Any | |
| Principal Diagnosis Position | Any | |
| Exclude evidence of days supply if inclusion/exclusion evaluation period | N/A | |
| Number of instances the criteria should be found in the evaluation period | 1 | |
| At Risk Time | | |
| Minimum exposure episode duration | 0 | |
| Maximum exposure episode duration (MAXEPISDUR) | 90 | |
| Risk window interval start | | |
| Censor treatment episode at evidence of: | 4 | |
| Censor treatment episode at evidence or. | | |
| | 1 | |
| | ARBs, beta blockers; ARBs, ACEi; occurrence of | |
| | occurrence of angioedema; | |
| | angioedema; disenrollment | |
| | disenrollment | |
| Blackout Period | | |
| Event/Outcome | | |
| Event/Outcome | Angioedema DX | |
| Care Setting | IP, ED, AV | |
| Principal Diagnosis Position | | |
| Exclude evidence of days supply if event washout includes dispensings | • | |
| Event de-duplication | · · | |
| | and code type on the same day | |
| | | |
| Forced supply to attach to dispensings | N/A | |
| Propensity Score Model Parameters | | |
| PS Model Label | ps_base | |
| Covariates | Age; sex; see also Covariates, Utilization, & | |
| | Comorbidity tabs | |
| Firth Logistic Intercept Correct (FLIC) Method | , | |
| High-dimensional Propensity Score | | |
| Output Kaplan Meier Plot | | |
| PS Stratification | 163 | |
| | atrot have | |
| Stratification Comparison Identifier | strat_base | |
| Percentiles | | |
| PS Trimming Indicator | | |
| | | |
| Percentile Distribution Indicator | | |
| Percentile Distribution Indicator PS Matching | | |
| | O (Overall) | |

cder_mpl2p_wp051 Page 2 of 4



Specifications Defining Parameters for this Request

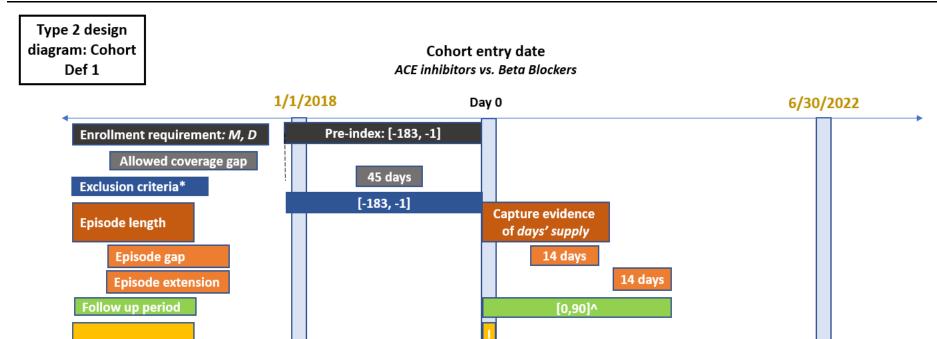
| Ratio Type | Fixed ratio matching | |
|---|--|--|
| Matching Ratio | 1:1 | |
| Matching Caliper Settings | 0.025 | |
| Analysis Type | Conditional and unconditional | |
| Subgroup Analyses | | |
| Stratifying variable | Quarter-year (Phase 2) | |
| Subgroup Categories | Each 3-month period beginning January of a given | |
| | calendar year (n = 18) (2018Q1, 2019Q1, etc.) | |
| Firth Logistic Intercept Correct (FLIC) Method | No | |
| Re-estimate Propensity Score within subgroup level | No | |
| Should subgroup re-matching be restricted to the matched population | Yes | |
| 100 0 014 110000 1 007 1 | 1 | |

ICD-9-CM, HCPCS, and CPT codes are provided by Optum360. NDC codes are checked against First Data Bank's "National Drug Data File (NDDF®) Plus."

cder_mpl2p_wp051 Page 3 of 4



Diagram Detailing the Design of this Request



II: [-183, -1]

Window II: History of: allergic reaction, diabetes, heart failure, ischemic heart disease, NSAID use; Comorbidity Score; Drug Utilization (dispensings, unique generics); Medical Utilization (IP hospital stays, non-acute institutional stays, ED visits, AV visits, OA visits), CCW conditions (acquired hypothyroidism, acute myocardial infarction, Alzheimer's disease & related disorders or senile dementia, anemia, asthma, atrial fibrillation, benign prostatic hyperplasia, cancer (breast, colorectal, endometrial, lung, prostate), cataract, chronic kidney disease, chronic obstructive pulmonary disease & bronchiectasis, depression, glaucoma, hip/pelvic fracture, hyperlipidemia, hypertension, osteoporosis, rheumatoid arthritis/osteoarthritis, stroke/transient ischemic attack)

cder_mpl2p_wp051 Page 4 of 4

^{*}Exclusion Criteria: Aliskiren, ARBs, ACE inhibitors/beta blockers; angioedema

[^] The follow up period begins on the day of the index date and ends at the earliest occurrence of the end of at-risk time; angioedema; comparator drug, aliskiren, or ARBs; disenrollment; Data Partner end date; or death.

^{**}Covariates: Window I: Age, sex, quarter-year