



24.2 Appendix 2 Modified Safety Reporting

All SAEs listed below are exempted from routine SAE reporting. However they will be assessed for relatedness to the study drug and if the event is considered related and not expected *i.e.* it is a SUSAR it will be reported in an expedited manner.

All SAEs not listed below will be reported as per standard guidelines and processes. In addition a quarterly line listing of these SAEs will be submitted to the sponsor.

1.Primary and secondary study endpoints

These events will prompt the investigator to complete an endpoint package which will then be adjudicated according to the Clinical Events Classification (CEC) charter:

- Cardiovascular (CV) death e.g. fatal myocardial infarction [MI]/cerebrovascular accident [CVA]/ congestive heart failure [CHF]/arrhythmia, cardiac arrest, death following CV intervention
- Non-fatal MI
- Acute coronary syndrome
- Non-fatal CVA
- CHF requiring hospitalization
- Unstable angina requiring hospitalization
- All cause mortality

2.Other Cardiovascular Events of Interest

- Atrial fibrillation/Atrial flutter
- Ventricular fibrillation/tachycardia requiring intervention
- Deep Vein Thrombosis (DVT)
- Pulmonary embolism
- Percutaneous Coronary Intervention (PCI) – (including non-serious events)
- Coronary Artery Bypass Graft (CABG)
- Coronary catheterization
- Stress test (including non-serious events)
- Abdominal aortic aneurysm/repair
- Carotid endarterectomy/ carotid angioplasty and/or stenting
- Any hospitalization due to cardiovascular events (i.e., whether or not the hospitalisation was for an obvious study endpoint)
- Shock/hypotension
- Accelerated or malignant hypertension/hypertensive urgency
- Transient Ischemic Attack (TIA)
- Syncope
- Renal artery angioplasty and/or stenting
- Other arterial angioplasty and/or stenting

3.Non-cardiovascular events of interest

- Any non-melanoma incident cancer
- Any non-melanoma recurrent cancer
- Death due to cancer (any non-melanoma type)
- Physician diagnosed T2DM

4.Known adverse reactions of metformin

- GI upset / diarrhoea
- Hypoglycaemia