

## **Appendix D:**

This document contains the list of terms related to cardiotoxicity which were used to evaluate evidence returned from the endpoints. If it is found that a term from these lists is associated with a drug, this would provide evidence to support that a drug is cardiotoxic.

### **1) MP terms**

<b>MP TERM</b>	<b>MP Identifier</b>
dilated cardiomyopathy	MP:0002795
decrease left ventricular ejection fraction	MP:0005598
LV dilatation	MP:0002753
dilated heart atrium	MP:0003140
enlarged heart	MP:0000274
pericardial edema	MP:0001787
hemopericardium	MP:0005244
pericardial edema	MP:0001787
hemorrhage	MP:0001914
thick aortic valve	MP:0010594
increased heart rate	MP:0002626
thick aortic valve	MP:0010594
intraventricular hemorrhage	MP:0001917
poor circulation	MP:0001633
bradycardia	MP:0005333
distended pericardium	MP:0000292
cardiac ischemia	MP:0004120
heart inflammation	MP:0001853
LV hypertrophy	MP:0002625
hypertension	MP:0000231

decreased ventricular ejection fraction volume	MP:0005598
increased myocardial infarction size	MP:0003037
congestive heart failure	MP:0006138
atrial thrombosis	MP:0001855
thin ventricular wall	MP:0000280
abnormal heart left ventricle morphology	MP:0003921
increased heart rate	MP:0002626
abnormal ST segment	MP:0003897
abnormal QRS complex	MP:0003898
abnormal QT interval	MP:0003899
abnormal blood flow velocity	MP:0000233
abnormal cardiac stroke volume	MP:0000304
cardiac fibrosis	MP:0003141
increased heart ventricle size	MP:0008772
enlarged heart left ventricle	MP:0010579
enlarged heart left ventricle	MP:0008774
increased left ventricle weight	MP:0003915
abnormal cardiac stroke volume	MP:0000304
abnormal blood flow velocity	MP:0000233
dilated heart ventricle	MP:0004937
prolonged QT interval	MP:0003233
irregular heartbeat	MP:0001636
abnormal cardiac stroke volume	MP:0001628
angina	MP:0006112

decreased cardiac muscle contractility	MP:0005140
decreased cardiac muscle contractility	MP:0002974
cardiac hypertrophy	MP:0001625
decreased cardiac output	MP:0003393
abnormal heartbeat	MP:0004085
cardiomyopathy	MP:0005330
increased heart rate	MP:0002833

## 2) SIDER UMLS terms

<b>Side effect indicating Cardiotoxicity</b>	<b>Identifier (UMLS)</b>
Prolongation of QT interval	C0151878
Congestive heart failure (CHF)	C0018802
Decrease LVEF	C0428772
Left Ventricular Dysfunction	C0242698
Acute coronary syndrome (ACH)	C0948089
Myocardial infarction (MI)	C0027051
Myocardial Ischaemia	C0151744
Pericardial effusion	C0031039
Arrhythmia	C0003811
Pericarditis	C0031046
Cardiomyopathy	C0878544

Cardiac Failure (HF)	C0018801
Cardiomegaly	C0018800
Cardiac Disorder	C0018799
Cardiac fibrillation	C0232197
Left Ventricular Failure	C0023212
Cardiac Hypertrophy	C1383860
Cardiac Failure Acute	C0264714
Diastolic dysfunction	C0520863
Cardiac Murmur	C0018808
Ventricular Dysfunction	C0242973
Cardiac tamponade	C0007177
Supraventricular tachycardia	C0039240
acute myocardial infarction	C0155652
bradycardia	C0428977
cardiac death	C0859934
cardiac enzymes increased	C0741921
cardiac output decreased	C0007166
cardiogenic shock	C0036974
cardiopulmonary failure	C1444565
cardiotoxicity	C0854612
cytotoxic cardiomyopathy	C0852940
ecg signs of myocardial	C1141959

ischaemia	
pleuropericarditis	C1167732
silent myocardial infarction	C0340324
heart injury	C0160318
sudden cardiac death	C0085298
arteriosclerotic heart disease	C0010054
dilatation ventricular	C0264733
ecg signs of ventricular hypertrophy	C0919857
ventricular fibrillation	C0042510
cardiac index decreased	C0520870
electrocardiogram poor r-wave progression	C0877038
electrocardiogram pr prolongation	C0600125
electrocardiogram r on t phenomenon	C0877658
electrocardiogram st segment depression	C0520887
electrocardiogram st-t segment depression	C0877452
electrocardiogram t wave inversion	C0520888
Atrioventricular block complete	C0151517
chronic left ventricular failure	C1328381

atrial tachycardia	C0039239
atrial thrombosis	C0340517
dilatation atrial	C1536093
left atrial dilatation	C0344720
left atrial hypertrophy	C0238705
tachycardia	C0039231

### 3) MeSH Terms (in CTD)

mesh term	mesh ID
Myocardial Infarction [mesh:D009203]	mesh:D009203
Myocardial Reperfusion Injury [mesh:D015428]	mesh:D015428
Myocardial Ischemia [mesh:D017202]	mesh:D017202
Tachycardia, Ventricular [mesh:D017180]	mesh:D017180
Cardiomegaly [mesh:D006332]	mesh:D006332
Cardiomyopathy, Hypertrophic [mesh:D002312]	mesh:D002312
Arrhythmias, Cardiac [mesh:D001145]	mesh:D001145
Cardiomyopathies [mesh:D009202]	mesh:D009202
Pericardial Effusion [mesh:D010490]	mesh:D010490
Bradycardia [mesh:D001919]	mesh:D001919
Tachycardia [mesh:D013610]	mesh:D013610
Cardiomyopathy, Dilated [mesh:D002311]	mesh:D002311
Myocarditis [mesh:D009205]	mesh:D009205

Pericarditis [mesh:D010493]	mesh:D010493
Death, Sudden, Cardiac [mesh:D016757]	mesh:D016757
Edema, Cardiac [mesh:D004489]	mesh:D004489
Tachycardia, Supraventricular [mesh:D013617]	mesh:D013617
Cardiac Output, Low [mesh:D002303]	mesh:D002303
Heart Failure [mesh:D006333]	mesh:D006333
Heart Failure, Systolic [mesh:D054143]	mesh:D054143
Heart Failure, Diastolic [mesh:D054144]	mesh:D054144
Hypertension	mesh:D006973
Coronary thrombosis	mesh:D003328

#### 4) Pathways in CTD

Pathway	KEGG ID	Reactome ID
PI3K-Akt signaling pathway	kegg:04150	reactome:75829
MAPK signaling pathway	kegg:04010	reactome:115755
ErbB signaling pathway	kegg:04012	reactome:634
Protein processing in endoplasmic reticulum	kegg:0414	
VEGF signaling pathway	kegg:04370	reactome:12529
Jak-STAT signaling pathway	keggL04630	

#### 5) Pathways in PharmGKB

Pathway	Pathway ID
---------	------------

PI3K/AKT signalling - pharmgkb:PA164714140  
(Reactome via Pathway  
Interaction Database)

erk1/erk2 mapk signaling pharmgkb:PA164713452  
pathway

role of erbb2 in signal pharmgkb:PA164713667  
transduction and oncology

VEGF Signaling Pathway pharmgkb:PA2032

stat3 signaling pathway pharmgkb:PA164713529

## 6) Genes

Gene Name	Gene id
Spp1	6696
Fhl1	2273
Timp1	7076
Ccl7	6354
Reg3b	18489
PRKCD	5580
Serpine1	26135
Bcat1	586
Lmcd1	29995
Rnd1	27289
Tgfb2	7042
GATA4	2626



## 7) Targets

Target	Drugbank Target ID
RAF1	drugbank:40
PDGFR alpha	drugbank:950
PDGFR beta	drugbank:228
VEGFR1	drugbank:32
VEGFR2	drugbank:407
VEGFR3	drugbank:26
AMPK(alpha subunit)	drugbank:748
AMPK(beta subunit1)	drugbank:281
AMPK(Beta subunit2)	drugbank:851

## 8) Other