17 August 2010

Patient Health Protection

STUDY REPORT

Cardiac profile of patients using rosiglitazone-containing anti-diabetes medicines: a study using the THIN database

SUMMARY

A matter relevant to debate concerning the clinical impact of cardiac adverse events associated with rosiglitazone is the extent to which it is currently prescribed in patients who might be particularly susceptible to such events. This analysis based on the UK GP database, THIN, suggests that about 8% of patients take rosiglitazone despite having cardiac contraindications as defined by the current SPC – congestive heart failure or acute coronary syndrome. A further 9% have ischaemic coronary disease of a kind not currently contraindicated.

INTRODUCTION

Three thiazolidinediones (TZDs) have been used in clinical practice (troglitazone, rosiglitazone, and pioglitazone); however, troglitazone was withdrawn from use because it was associated with severe hepatic toxicity. TZDs, also known as glitazones, are selective agonist for nuclear peroxisome proliferator-activated receptor-γ (PPARγ) nuclear receptor. These drugs bind to PPARγ, which activates insulin-response genes that regulate carbohydrate and lipid metabolism. TZDs exert their principal effects by increasing insulin sensitivity in peripheral tissue but also may lower glucose production by the liver. The TZDs also can activate genes that regulate fatty acid metabolism in peripheral tissue[1].

Avandia® (rosiglitazone) was initially authorised in the European Union in July 2000 as second-line diabetes type-2 treatment to be used when other treatments have either failed or are unsuitable for a patient[2]. Avandia has been contra-indicated in patients with heart failure or a history of heart failure since its first authorisation. It was subsequently approved in combination with metformin as Avandamet (2003) and with glimepiride as Avaglim (2006). Since then, the use of these medicines has been further restricted several times by new warnings and contra-indications on their use in patients with heart problems[3,4].

In October 2007, the Committee for Human Medicinal Products of the European Union (CHMP) concluded that the benefits of both marketed TZDs, rosiglitazone and pioglitazone, continue to outweigh their risks. However, the prescribing information was updated to add Acute Coronary Syndrome (ACS) as a contra-indication to all rosiglitazone-containing products and to include a warning that, in patients with ischaemic heart disease, rosiglitazone should only be used after careful evaluation of each patient's individual risk[5]. These changes were effective in the Summary of Product Characteristics (SPC) on March 3, 2008.

Anecdotal evidence has shown that that some patients are either started or continue treatment with rosiglitazone despite having cardiac contraindications listed in the SPC.

On the request of the European Commission, rosiglitazone-containing medicines are currently reviewed by the CHMP to determine whether new data on the risk of cardiovascular problems[6,7] have an impact on their benefit-risk profile.

This study aims to measure the proportion of patients treated with rosiglitazone with concomitant cardiac disorder listed as contraindicated conditions in the SPC. These include cardiac failure or history of cardiac failure and acute coronary syndrome (unstable angina, non-ST segment elevation myocardial infarction –NSTEMI- and ST segment elevation myocardial infarction-STEMI-). This information will help the CHMP decide

whether additional risk minimisation measures are necessary to reduce the risk of cardiovascular disorders in patients treated with rosiglitazone.

The proportion of patients treated with rosiglitazone and with antecedents of other myocardial ischaemic disorders, including stable angina, will also be measured. Were the CHMP decide to broaden the list of contraindications to all ischaemic diseases, this information will help assess how many patients would be affected by this decision, e.g. how many patients would need to switch from rosiglitazone to another antidiabetic agent.

METHODS

- **Study design**

The study is a retrospective analysis of a cohort of patients prescribed rosiglitazone.

- **Source population and data**

We performed the study using The Health Improvement Network (THIN) database, which is representative of the general population in the United Kingdom[7] and includes almost 9 million patients (more than 3.4 million active) collected from over 430 GP practices in the UK. The data provide anonymous demographic, medical, and prescription information on individual patients, and they provide a longitudinal medical record for each patient[9].

- **Study population**

Patients were eligible for inclusion in the primary study population if they received at least one prescription of rosiglitazone-containing products in a clinical practice during a time window of 20 months from (April 1, 2008 through November 30, 2009). The date of April 1, 2008 has been chosen as this the date at which additional cardiac contraindications were added to the rosiglitazone-containing products.

- **Exposure medication**

Rosiglitazone-containing products (single and combination products) were identified using ATC codes, active substance or brand names. The list of products included in the analyses is in appendix 1.

- **Case identification**

Medical conditions representing cardiac contraindications for rosiglitazone (cardiac failure and ACS) were identified from the SPC. Corresponding terms used in THIN were identified with Read codes (see appendix 2). Non contraindicated cardiac ischemic disorders were also identified (see appendix 3). The index date was the date when the last Read code was recorded. Patients were followed until death, loss to follow-up, or the end of the study period, whichever came first. All analyses were conducted with the use of Statistical Analysis Systems (SAS® Enterprise Guide 4.1, Cary, NC, USA).

- **Analyses**

The total number of patients taking rosiglitazone-containing products was analysed. The primary outcome measure was the proportion of patients who had a medical term representing a contraindication (cardiac failure or ACS) any time before the date of any prescription. Although the cardiac failure and ACS contraindications are different in that 'history of cardiac failure' is explicitly mentioned in the SPC, no upper limit was put on the delay between ACS symptoms and prescription of rosiglitazone.

A second analysis identified only the subgroup of patients who had a cardiac contraindication prior to the first recorded prescription (when this occurred after 1 April 2008) of rosiglitazone containing products. In other words, the group in whom a course of treatment was initiated in spite of existing contraindications.

The analyses above were repeated restricting to only coronary heart failure contraindications. Since this contraindication was instated at the time of authorisation of rosiglitazone the time window for this calculation was extended back to July 2000.

Lastly the analyses were repeated with an extended list of coronary medical terms – including the current contraindications (Appendix 2) and the terms in (Appendix 3). This analysis was again restricted to the more recent time window in order to reflect the current cardiac status of UK patients prescribed rosiglitazone. Since these terms are not all currently contraindicated only the proportion of treated patients with such terms was calculated, not those commencing treatment for the first time.

RESULTS

The tables in this section show counts of patients.

CHF or ACS – From 1 April 2008 to 30 November 2009

	X	N	Proportion (95% CI)
Symptoms prior to first prescription	42	915	0.046 (0.033,0.062)
Symptoms prior to any prescription	802	10043	0.080 (0.075,0.085)

CHF – From July 2000 to 30 November 2009

	X	N	Proportion (95% CI)
Symptoms prior to first prescription	770	24140	0.032 (0.030,0.034)
Symptoms prior to any prescription	1071	24140	0.044 (0.042,0.047)

The following table is an estimate of the proportion of current UK patients who are taking rosiglitazone and have ischaemic cardiac events recorded in their GP notes.

Extended list of coronary ischaemic events - From 1 April 2008 to 30 November 2009

	X	N	Proportion (95% CI)
Symptoms prior to any prescription	1690	10043	0.168 (0.161,0.176)

DISCUSSION

The current study examines the profile of patients who receive rosiglitazone with respect to cardiac ischaemic disease. There is no attempt to examine any possible causal relationship between the products and such disease but just to estimate the extent to which the cardiac contraindications stated in the SPC are obsrved and also the possible impact on exposure to the products of any widening of the contraindications to include other coronary ischaemic events.

The limitations of our retrospective cohort study should be noted. The study is based on routine coding of prescriptions and clinical events by GPs. No attempt was made to validate the diagnoses of cardiac events based on medical chart or to ensure that the prescriptions were actually dispensed and the drug taken. In addition, because prescription drug data from THIN have not been used extensively for purposes of comparative safety, issues related to data quality must be considered. To partially counter this, Read codes case definitions that we adhered to in this study have been consistently well validated in previous studies[8]. Furthermore, although we ascertained that patients received prescriptions even after the recording of contraindications we have not undertaken a longitudinal analysis to examine whether such prescriptions eventually ceased. Nor have we looked at the delays between last ACS symptoms and prescriptions. Clearly those patients who experienced ACS during ongoing treatment had current symptoms but it is possible that some patients had ACS symptoms that were controlled at the start of treatment with rosiglitazone. In addition, no fixed time-window was required between the start of patient data and the first prescription of rosiglitazone. It is difficult to nominate a time delay within which existing symptoms would be likely to be discussed with a GP and hence manifest in THIN. Hence some patients may have had prior symptoms not recorded in the database and the proportion with such symptoms may be underestimated. Because the THIN data currently available at EMA was covering a period up to November 2009 a change in prescribing behaviour resulting from public debate concerning rosiglitazone over the last 10 months cannot be precluded. Lastly, only UK patients are covered by this dataset.

The results of this study suggest that contraindications are not rigorously applied in the case of rosiglitazone. Around 8% of patients received the product despite having a cardiac contraindication. Of course, it may be that many others with contraindications were not prescribed it on that account. We cannot investigate this point and nor can we investigate whether those who did receive rosiglitazone represented a less severely diseased group of patients. However, our result does show that around one in twelve patients fall within a group demonstrably predisposed to potential cardiac adverse events of rosiglitazone.

If the presence of any cardiac ischaemic event can be taken to constitute a risk factor for such cardiac adverse reactions then this group may be nearer to one in 6 (16.8%).

REFERENCE LIST

1. Goodman LB, Gibman A. The pharmacological basis of therapeutics. 11th ed. New York: MacGraw-Hill, 2006: 1613-1645.

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http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000268/WC500029108.pdf

3. A press release on the ongoing benefit-risk review of Avandia, Avandamet and Avaglim in July 2010 is available on the Agency's website:
http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/07/WC500094981.pdf

4. A press release on the ongoing review of rosiglitazone-containing products in July 2010 is available on the Agency's website:
http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2010/07/WC500094417.pdf

5. A press release on the assessment of the benefits and risks of rosiglitazone and pioglitazone concluded in October 2007 is available on the Agency's website:
http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500011009.pdf

6. Graham DJ, Ouellet-Hellstrom R, Macurdy TE, Ali F, Sholley C, Worrall C, Kelman JA. Risk of Acute Myocardial Infarction, Stroke, Heart Failure, and Death in Elderly Medicare Patients Treated With Rosiglitazone or Pioglitazone. JAMA. 2010 Jun 28. [Epub ahead of print]

7. Nissen SE, Wolski K. Rosiglitazone Revisited: An Updated Meta-analysis of Risk for Myocardial Infarction and Cardiovascular Mortality. Arch Intern Med. 2010 Jun 28. [Epub ahead of print]

8. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, Brindle P. Performance of the QRISK cardiovascular risk prediction algorithm in an independent UK sample of patients from general practice: a validation study. Heart. 2008;94(1):34-9.

9. The Health Improvement Network. [cited 2010 August]; Available from: http://www.thin-uk.com.

APPENDIX 1.

AVANDAMET tabs 1mg + 500mg
AVANDAMET tabs 2mg + 500mg
AVANDAMET tabs 2mg + 1000mg
AVANDAMET tabs 4mg + 1000mg
AVANDIA tabs 2mg
AVANDIA tabs 4mg
AVANDIA tabs 8mg
METFORMIN + ROSIGLITAZONE tabs 1000mg + 2mg
METFORMIN + ROSIGLITAZONE tabs 1000mg + 4mg
METFORMIN + ROSIGLITAZONE tabs 500mg + 1mg
METFORMIN + ROSIGLITAZONE tabs 500mg + 2mg
ROSIGLITAZONE tabs 2mg
ROSIGLITAZONE tabs 4mg
ROSIGLITAZONE tabs 8mg
ROSIGLITAZONE + GLIMEPIRIDE (IPU) tabs 4mg + 4mg
ROSIGLITAZONE + GLIMEPIRIDE (IPU) tabs 8mg + 4mg
ROSIGLITAZONE + METFORMIN tabs 2mg + 500mg
ROSIGLITAZONE + METFORMIN tabs 1mg + 500mg
ROSIGLITAZONE + METFORMIN tabs 2mg + 1000mg
ROSIGLITAZONE + METFORMIN tabs 4mg + 1000mg

APPENDIX 2.

2.1. CARDIAC FAILURE TERMS

H/O: HEART FAILURE
H/O: HEART FAILURE IN LAST YEAR
HEART FAILURE CONFIRMED
CONGESTIVE HEART FAILURE MONITORING
CARDIAC FAILURE THERAPY
ADMIT HEART FAILURE EMERGENCY
HEART FAILURE FOLLOW-UP
HYPERTENSIVE HEART DISEASE NOS WITH CCF
HYPERTENSIVE HEART&RENAL DIS WTH (CONGESTIVE) HEART FAILURE
HEART FAILURE
CARDIAC FAILURE
CONGESTIVE HEART FAILURE
CONGESTIVE CARDIAC FAILURE
RIGHT HEART FAILURE
RIGHT VENTRICULAR FAILURE
BIVENTRICULAR FAILURE
ACUTE CONGESTIVE HEART FAILURE
CHRONIC CONGESTIVE HEART FAILURE
DECOMPENSATED CARDIAC FAILURE
COMPENSATED CARDIAC FAILURE
CONGESTIVE HEART FAILURE DUE TO VALVULAR DISEASE
LEFT VENTRICULAR FAILURE
ACUTE LEFT VENTRICULAR FAILURE
ACUTE HEART FAILURE
HEART FAILURE NOS
CARDIAC FAILURE NOS
CARDIAC FAILURE FOLLOWING ABORTIVE PREGNANCY
HEART FAILURE AS A COMPLICATION OF CARE

2.2. ACUTE CORONARY SYNDROME TERMS

H/O: MYOCARDIAL INFARCT <60
H/O: MYOCARDIAL INFARCT >60
H/O: MYOCARDIAL INFARCTION IN LAST YEAR
ECG: MYOCARDIAL INFARCTION
ECG: OLD MYOCARDIAL INFARCTION
ECG: ANTERO-SEPTAL INFARCT.
ECG:POSTERIOR/INFERIOR INFARCT
ECG: SUBENDOCARDIAL INFARCT
ECG: LATERAL INFARCTION
ECG: MYOCARDIAL INFARCT NOS
DIAB MELLIT INSULIN-GLUCOSE INFUS ACUTE MYOCARDIAL INFARCT
ADMIT ISCHAEMIC HEART DISEASE EMERGENCY
ACUTE MYOCARDIAL INFARCTION

ATTACK - HEART
CARDIAC RUPTURE FOLLOWING MYOCARDIAL INFARCTION (MI)
HEART ATTACK
MI - ACUTE MYOCARDIAL INFARCTION
SILENT MYOCARDIAL INFARCTION
ACUTE ANTEROLATERAL INFARCTION
OTHER SPECIFIED ANTERIOR MYOCARDIAL INFARCTION
ACUTE ANTEROAPICAL INFARCTION
ACUTE ANTEROSEPTAL INFARCTION
ANTERIOR MYOCARDIAL INFARCTION NOS
ACUTE INFEROLATERAL INFARCTION
ACUTE INFEROPOSTERIOR INFARCTION
POSTERIOR MYOCARDIAL INFARCTION NOS
LATERAL MYOCARDIAL INFARCTION NOS
TRUE POSTERIOR MYOCARDIAL INFARCTION
ACUTE SUBENDOCARDIAL INFARCTION
ACUTE NON-Q WAVE INFARCTION
ACUTE NON-ST SEGMENT ELEVATION MYOCARDIAL INFARCTION
INFERIOR MYOCARDIAL INFARCTION NOS
ACUTE Q-WAVE INFARCT
MURAL THROMBOSIS
ACUTE POSTEROLATERAL MYOCARDIAL INFARCTION
ACUTE TRANSMURAL MYOCARDIAL INFARCTION OF UNSPECIF SITE
ACUTE ST SEGMENT ELEVATION MYOCARDIAL INFARCTION
OTHER ACUTE MYOCARDIAL INFARCTION
ACUTE ATRIAL INFARCTION
ACUTE PAPILLARY MUSCLE INFARCTION
ACUTE SEPTAL INFARCTION
OTHER ACUTE MYOCARDIAL INFARCTION NOS
ACUTE MYOCARDIAL INFARCTION NOS
OTHER ACUTE AND SUBACUTE ISCHAEMIC HEART DISEASE
POSTMYOCARDIAL INFARCTION SYNDROME
CRESCENDO ANGINA
IMPENDING INFARCTION
UNSTABLE ANGINA
ANGINA AT REST
UNSTABLE ANGINA
ANGINA AT REST
WORSENING ANGINA
ACUTE CORONARY SYNDROME
OTHER ACUTE AND SUBACUTE ISCHAEMIC HEART DISEASE
ACUTE CORONARY INSUFFICIENCY
MICROINFARCTION OF HEART
SUBENDOCARDIAL ISCHAEMIA
TRANSIENT MYOCARDIAL ISCHAEMIA
OTHER ACUTE AND SUBACUTE ISCHAEMIC HEART DISEASE NOS
OLD MYOCARDIAL INFARCTION
HEALED MYOCARDIAL INFARCTION
PERSONAL HISTORY OF MYOCARDIAL INFARCTION
ANGINA DECUBITUS

NOCTURNAL ANGINA
ANGINA DECUBITUS NOS
POST INFARCT ANGINA
NEW ONSET ANGINA
SILENT MYOCARDIAL ISCHAEMIA
SUBSEQUENT MYOCARDIAL INFARCTION
SUBSEQUENT MYOCARDIAL INFARCTION OF ANTERIOR WALL
SUBSEQUENT MYOCARDIAL INFARCTION OF INFERIOR WALL
SUBSEQUENT MYOCARDIAL INFARCTION OF OTHER SITES
SUBSEQUENT MYOCARDIAL INFARCTION OF UNSPECIFIED SITE
CERTAIN CURRENT COMPLICATION FOLLOW ACUTE MYOCARDIAL INFARCT
HAEMOPERICARDIUM/CURRENT COMP FOLOW ACUT MYOCARD INFARCT
ATRIAL SEPTAL DEFECT/CURR COMP FOLOW ACUT MYOCARDAL INFARCT
VENTRIC SEPTAL DEFECT/CURR COMP FOL ACUT MYOCARDAL INFARCTN
RUPTUR CHORDAE TENDINAE/CURR COMP FOL ACUTE MYOCARD INFARCT
RUPTURE PAPILLARY MUSCLE/CURR COMP FOL ACUTE MYOCARD INFARCT
POSTOPERATIVE MYOCARDIAL INFARCTION
POSTOPERATIVE TRANSMURAL MYOCARDIAL INFARCTION ANTERIOR WALL
POSTOPERATIVE TRANSMURAL MYOCARDIAL INFARCTION INFERIOR WALL
POSTOPERATIVE TRANSMURAL MYOCARDIAL INFARCTION OTHER SITES
POSTOPERATIVE TRANSMURAL MYOCARDIAL INFARCTION UNSPEC SITE
POSTOPERATIVE SUBENDOCARDIAL MYOCARDIAL INFARCTION
POSTOPERATIVE MYOCARDIAL INFARCTION, UNSPECIFIED
POST INFARCTION PERICARDITIS
[X]OTHER CURRENT COMPLICATNS FOLLOWING ACUTE MYOCARD INFARCT
[X]OTHER FORMS OF ACUTE ISCHAEMIC HEART DISEASE
[X]ACUTE TRANSMURAL MYOCARDIAL INFARCTION OF UNSPECIF SITE
[X]SUBSEQUENT MYOCARDIAL INFARCTION OF OTHER SITES
[X]SUBSEQUENT MYOCARDIAL INFARCTION OF UNSPECIFIED SITE

APPENDIX 3.

H/O: ANGINA PECTORIS
H/O: ANGINA IN LAST YEAR
H/O: TREATMENT FOR ISCHAEMIC HEART DISEASE
SUSPECTED ISCHAEMIC HEART DISEASE
ECG: MYOCARDIAL ISCHAEMIA
ECG:SHOWS MYOCARDIAL ISCHAEMIA
ECG: MYOCARDIAL ISCHAEMIA NOS
ANGINA CONTROL
ANGINA CONTROL - GOOD
ANGINA CONTROL - POOR
ANGINA CONTROL - IMPROVING
ANGINA CONTROL - WORSENING
ANGINA CONTROL NOS
CORONARY HEART DISEASE ANNUAL REVIEW
CORONARY HEART DISEASE REVIEW
CORONARY ARTERY OPERATIONS
CORONARY ARTERY BYPASS GRAFT OPERATIONS
SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY
SAPHENOUS VEIN GRAFT BYPASS OF CORONARY ARTERY
SAPHENOUS VEIN GRAFT REPLACEMENT OF ONE CORONARY ARTERY
SAPHENOUS VEIN GRAFT REPLACEMENT OF TWO CORONARY ARTERIES
SAPHENOUS VEIN GRAFT REPLACEMENT OF THREE CORONARY ARTERIES
SAPHENOUS VEIN GRAFT REPLACEMENT OF FOUR+ CORONARY ARTERIES
SAPHENOUS VEIN GRAFT REPLACEMENT OF CORONARY ARTERY OS
SAPHENOUS VEIN GRAFT REPLACEMENT CORONARY ARTERY NOS
OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY
OTHER AUTOGRAFT BYPASS OF CORONARY ARTERY
AUTOGRAFT REPLACEMENT OF ONE CORONARY ARTERY NEC
AUTOGRAFT REPLACEMENT OF TWO CORONARY ARTERIES NEC
AUTOGRAFT REPLACEMENT OF THREE CORONARY ARTERIES NEC
AUTOGRAFT REPLACEMENT OF FOUR OF MORE CORONARY ARTERIES NEC
OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY OS
OTHER AUTOGRAFT REPLACEMENT OF CORONARY ARTERY NOS
ALLOGRAFT REPLACEMENT OF CORONARY ARTERY
ALLOGRAFT BYPASS OF CORONARY ARTERY
ALLOGRAFT REPLACEMENT OF ONE CORONARY ARTERY
ALLOGRAFT REPLACEMENT OF TWO CORONARY ARTERIES
ALLOGRAFT REPLACEMENT OF THREE CORONARY ARTERIES
ALLOGRAFT REPLACEMENT OF FOUR OR MORE CORONARY ARTERIES
OTHER SPECIFIED ALLOGRAFT REPLACEMENT OF CORONARY ARTERY
ALLOGRAFT REPLACEMENT OF CORONARY ARTERY NOS
PROSTHETIC REPLACEMENT OF CORONARY ARTERY
PROSTHETIC BYPASS OF CORONARY ARTERY
PROSTHETIC REPLACEMENT OF ONE CORONARY ARTERY
PROSTHETIC REPLACEMENT OF TWO CORONARY ARTERIES
PROSTHETIC REPLACEMENT OF THREE CORONARY ARTERIES
PROSTHETIC REPLACEMENT OF FOUR OR MORE CORONARY ARTERIES
OTHER SPECIFIED PROSTHETIC REPLACEMENT OF CORONARY ARTERY
PROSTHETIC REPLACEMENT OF CORONARY ARTERY NOS

REVISION OF BYPASS FOR CORONARY ARTERY
REVISION OF BYPASS FOR ONE CORONARY ARTERY
REVISION OF BYPASS FOR TWO CORONARY ARTERIES
REVISION OF BYPASS FOR THREE CORONARY ARTERIES
REVISION OF BYPASS FOR FOUR OR MORE CORONARY ARTERIES
REVISION OF CONNECTION OF THORACIC ARTERY TO CORONARY ARTERY
OTHER SPECIFIED REVISION OF BYPASS FOR CORONARY ARTERY
REVISION OF BYPASS FOR CORONARY ARTERY NOS
CONNECTION OF MAMMARY ARTERY TO CORONARY ARTERY
CREATION OF BYPASS FROM MAMMARY ARTERY TO CORONARY ARTERY
DOUBLE ANASTOMOSIS OF MAMMARY ARTERIES TO CORONARY ARTERIES
DOUBLE IMPLANT OF MAMMARY ARTERIES INTO CORONARY ARTERIES
SINGLE ANAST MAMMARY ART TO LEFT ANT DESCEND CORONARY ART
SINGLE ANASTOMOSIS OF MAMMARY ARTERY TO CORONARY ARTERY NEC
SINGLE IMPLANTATION OF MAMMARY ARTERY INTO CORONARY ARTERY
CONNECTION OF MAMMARY ARTERY TO CORONARY ARTERY OS
CONNECTION OF MAMMARY ARTERY TO CORONARY ARTERY NOS
CONNECTION OF OTHER THORACIC ARTERY TO CORONARY ARTERY
DOUBLE ANASTOM THORACIC ARTERIES TO CORONARY ARTERIES NEC
DOUBLE IMPLANT THORACIC ARTERIES INTO CORONARY ARTERIES NEC
SINGLE ANASTOMOSIS OF THORACIC ARTERY TO CORONARY ARTERY NEC
SINGLE IMPLANTATION THORACIC ARTERY INTO CORONARY ARTERY NEC
CONNECTION OF OTHER THORACIC ARTERY TO CORONARY ARTERY OS
CONNECTION OF OTHER THORACIC ARTERY TO CORONARY ARTERY NOS
OTHER OPEN OPERATIONS ON CORONARY ARTERY
OPEN ANGIOPLASTY OF CORONARY ARTERY
OTHER SPECIFIED OTHER OPEN OPERATION ON CORONARY ARTERY
OTHER OPEN OPERATION ON CORONARY ARTERY NOS
TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY
PERCUTANEOUS BALLOON CORONARY ANGIOPLASTY
PERCUT TRANSLUMINAL BALLOON ANGIOPLASTY ONE CORONARY ARTERY
PERCUT TRANSLUM BALLOON ANGIOPLASTY MULT CORONARY ARTERIES
PERCUT TRANSLUM BALLOON ANGIOPLASTY BYPASS GRAFT CORONARY A
PERCUT TRANSLUM CUTTING BALLOON ANGIOPLASTY CORONARY ARTERY
TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY OS
TRANSLUMINAL BALLOON ANGIOPLASTY OF CORONARY ARTERY NOS
OTHER THERAPEUTIC TRANSLUMINAL OPERATIONS ON CORONARY ARTERY
PERCUTANEOUS TRANSLUMINAL LASER CORONARY ANGIOPLASTY
PERCUT TRANSLUMINAL CORONARY THROMBOLYSIS WITH STREPTOKINASE
PERCUT TRANSLUM CORONARY THROMBOLYTIC THERAPY- STREPTOKINASE
PERCUT TRANSLUM INJECT THERAP SUBST TO CORONARY ARTERY NEC
ROTARY BLADE CORONARY ANGIOPLASTY
INSERTION OF CORONARY ARTERY STENT
INSERTION OF DRUG-ELUTING CORONARY ARTERY STENT
PERCUTANEOUS TRANSLUMINAL ATHERECTOMY OF CORONARY ARTERY
OTHER THERAPEUTIC TRANSLUMINAL OP ON CORONARY ARTERY OS
OTHER THERAPEUTIC TRANSLUMINAL OP ON CORONARY ARTERY NOS
DIAGNOSTIC TRANSLUMINAL OPERATIONS ON CORONARY ARTERY
INTRAVASCULAR ULTRASOUND OF CORONARY ARTERY
DIAGNOSTIC TRANSLUMINAL OPERATION ON CORONARY ARTERY OS
DIAGNOSTIC TRANSLUMINAL OPERATION ON CORONARY ARTERY NOS
ENDARTERECTOMY OF CORONARY ARTERY NEC
OTHER BYPASS OF CORONARY ARTERY
OTHER SPECIFIED OTHER BYPASS OF CORONARY ARTERY

OTHER BYPASS OF CORONARY ARTERY NOS
OTHER SPECIFIED OPERATIONS ON CORONARY ARTERY
CORONARY ARTERY OPERATIONS NOS
PERC TRANSLUMIN BALLOON ANGIOPLASTY STENTING CORONARY ARTERY
OS PERC TRANSLUMINA BALLOON ANGIOPLAST STENTING CORONARY ART
PERC TRANSLUM BALLOON ANGIOPLASTY STENTING CORONARY ART NOS
ANTIANGINAL THERAPY
CORONARY HEART DISEASE MEDICATION REVIEW
HEART FAILURE CARE PLAN DISCUSSED WITH PATIENT
CORONARY HEART DISEASE RISK CLINICAL MANAGEMENT PLAN
VINCENT'S ANGINA
VINCENT'S ANGINA NOS
ISCHAEMIC HEART DISEASE
IHD - ISCHAEMIC HEART DISEASE
CORONARY THROMBOSIS
THROMBOSIS - CORONARY
REFRACTORY ANGINA
PREINFARCTION SYNDROME NOS
CORONARY THROMBOSIS NOT RESULTING IN MYOCARDIAL INFARCTION
ANGINA PECTORIS
PRINZMETAL'S ANGINA
VARIANT ANGINA PECTORIS
CORONARY ARTERY SPASM
ANGINA PECTORIS NOS
STATUS ANGINOSUS
SYNCOPE ANGINOSA
ANGINA ON EFFORT
ISCHAEMIC CHEST PAIN
STABLE ANGINA
ANGINA PECTORIS NOS
OTHER CHRONIC ISCHAEMIC HEART DISEASE
CORONARY ATHEROSCLEROSIS
CORONARY ARTERY DISEASE
SINGLE CORONARY VESSEL DISEASE
DOUBLE CORONARY VESSEL DISEASE
OTHER SPECIFIED CHRONIC ISCHAEMIC HEART DISEASE
CHRONIC CORONARY INSUFFICIENCY
CHRONIC MYOCARDIAL ISCHAEMIA
OTHER SPECIFIED CHRONIC ISCHAEMIC HEART DISEASE NOS
OTHER CHRONIC ISCHAEMIC HEART DISEASE NOS
ASYMPTOMATIC CORONARY HEART DISEASE
OTHER SPECIFIED ISCHAEMIC HEART DISEASE
ISCHAEMIC HEART DISEASE NOS
IMPAIRED LEFT VENTRICULAR FUNCTION
[X]OTHER FORMS OF ANGINA PECTORIS
[X]OTHER FORMS OF CHRONIC ISCHAEMIC HEART DISEASE
[V]PRESENCE OF AORTOCORONARY BYPASS GRAFT
[V]PRESENCE OF CORONARY ANGIOPLASTY IMPLANT AND GRAFT
[V]PRESENCE OF CORONARY ARTERY BYPASS GRAFT
[V]PRESENCE OF CORONARY ARTERY BYPASS GRAFT - CABG
[V]STATUS FOLLOWING CORONARY ANGIOPLASTY NOS