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NICE implementation uptake report: Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome

NICE implementation uptake reports provide information on national trends and activity associated with recommendations in NICE guidance.

Overview

Prescribing of clopidogrel in primary care shows considerable variation with increases in use following the publication of guidance followed by a more recent decrease. The pattern of uptake in secondary care is different where the use of clopidogrel continued to increase following the publication of technology appraisal 80 and has been maintained at a certain level. The increases in cost of prescribing clopidogrel following the publication of TA80 were in the direction anticipated. However, this cannot be specifically related to the figures estimated in the NICE costing report due to the other indications for the use of this medicine. Further analysis is required when data becomes available to determine the long term trend of clopidogrel prescribing in both primary and secondary care.

Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome

'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome' NICE technology appraisal 80 (July 2004).

1 Guidance

'Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome' NICE technology appraisal 80 (July 2004) was developed using the multiple technology appraisal process.

NICE have published three further technology appraisals related to the prescribing of clopidogrel:

- Vascular disease – clopidogrel and dipyridamol, NICE technology appraisal 90 (May 2005). A review of this technology appraisal is currently in progress and is expected to be published in September 2010
- Acute coronary syndrome - glycoprotein IIb/IIIa inhibitors, NICE technology appraisal 47 (2002)
- Acute coronary syndrome – prasugrel, NICE technology appraisal 182 (October 2009)

A technology appraisal for clopidogrel in combination with aspirin for the prevention of vascular events in people with atrial fibrillation is also in development, although expected publication date is still to be confirmed.

2 Context

The term acute coronary syndrome (ACS) is used to refer to any group of clinical symptoms associated with acute myocardial ischaemia. It encompasses a spectrum of disorders including acute myocardial infarction

(MI) and unstable angina pectoris. ACS is usually the result of an acute or subacute primary reduction of myocardial oxygen supply provoked by disruption of an atherosclerotic plaque associated with inflammation, thrombosis, vasoconstriction and microembolisation. The presence of persistent ST-segment-elevation on an ECG usually indicates total occlusion of the affected artery, resulting in necrosis of the tissue supplied by that artery (acute MI).

ACS without ST-segment-elevation is classified as either unstable angina or non-ST-segment-elevation myocardial infarction (NSTEMI). Unstable angina and NSTEMI differ primarily in the severity of myocardial ischaemia.

It is difficult to estimate the incidence of non-ST-segment-elevation ACS in England and Wales. It is thought that there may be variations in the coding of this condition, leading to underestimates of the true incidence. Hospital episode statistics for the financial year 2002–03 show 144,450 finished consultant episodes for angina pectoris in England, of which 83,842 were specified as unstable angina. The corresponding figures for Wales are 8812 episodes of angina pectoris, of which 4421 were specified as unstable angina. In the same period, there were 105,476 finished consultant episodes for MI in England and 6749 in Wales. It is uncertain how many of these were NSTEMI because this information is not recorded in hospital episode statistics (NICE technology appraisal 80). More recent data has been reviewed but does not provide a clearer picture of this situation.

3 Recommendations and uptake

3.1 Recommendations

***The following recommendation is taken from NICE technology appraisal 80, and uptake can be assessed using routinely collected NHS data*.**

1.1 Clopidogrel, in combination with low-dose aspirin, is recommended for use in the management of non-ST-segment-elevation acute coronary syndrome (ACS) in people who are at moderate to high risk of myocardial infarction (MI) or death.

3.2 Estimated levels of uptake

NICE technology appraisal 80 suggests that clopidogrel is already prescribed for a high proportion of patients after an episode of non-ST-segment-elevation ACS, but there is anecdotal evidence to suggest that the duration of treatment is variable and may be as short as 1–3 months. The additional cost of treating people for up to 12 months will depend on the proportion of episodes that are characterised as non-ST-segment-elevation ACS. If it is assumed that 100,000 people are treated for an additional 6–9 months, then this would result in an additional cost of £21–32 million.

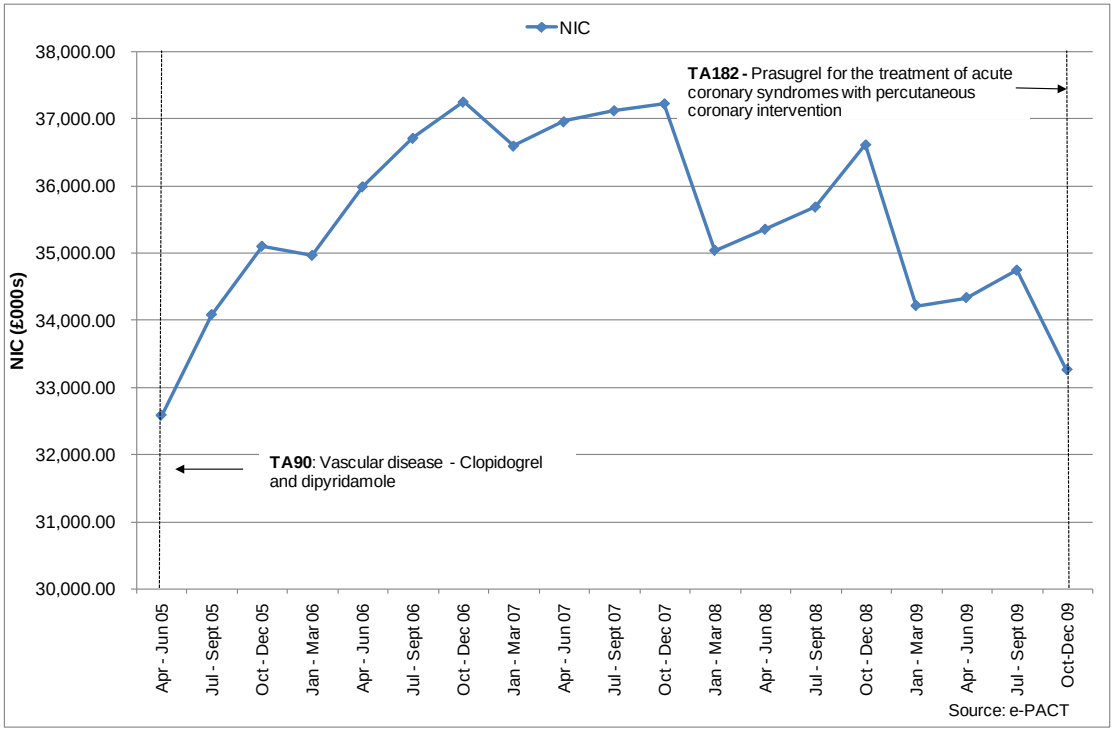
3.3 Actual level of uptake: Primary Care Prescriptions in England (at December 2009)

This section provides information on prescribing cost and volume for clopidogrel in primary care in England. The data are obtained from the electronic Prescribing Analysis Cost Tool (ePACT) system which is maintained by the Prescription Services Division of the NHS Business Services Authority (BSA). All costs stated in this report are based on net

ingredient cost (NIC). The data does not link to patient diagnosis. It should also be noted that clopidogrel is licensed for other indications, including:

- the prevention of atherosclerotic events in peripheral arterial disease (within 35 days of myocardial infarction or 6 months of ischemic stroke) and
- the prevention of atherosclerotic events in acute coronary syndrome with ST-segment elevation (British National Formulary 59 March 2010).

Figure 1 Total Net Ingredient Cost (NIC) for clopidogrel prescribed and dispensed in primary care in England.



Note: TA80, Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome was published in July 2004 but data is only available from April 2005

At nine months following the publication of TA80, the cost of prescribing clopidogrel was increasing and this continued following the publication of TA90. However, since January 2007 there has been considerable variation in primary care prescribing costs. It must be noted that these patterns are not

necessarily attributable to prescribing for non-ST-segment-elevation acute coronary syndrome as clopidogrel is also licensed for a number of other indications. In the 12 months to December 2009, prescription items for clopidogrel increased by 2% in volume, with a decrease in cost of 4% for the same period (table 1).

Table 1 Clopidogrel prescribed and dispensed in primary care in England in the 12 months to December 2009

	Items	% annual change (items)	Cost	% annual change (cost)
Clopidogrel	3,671,423	2%	136,574,664	-4%

3.4 Actual level of uptake: Secondary Care Prescriptions in England (at September 2009)

Information on the use of clopidogrel in hospitals in England is derived from the IMS HEALTH Hospital Pharmacy Audit database. The costs stated in this report are based on list price. Defined Daily Doses (DDDs) are used as a system of measuring volume of drug use, maintained by the World health Organisation. The definition of a DDD is “the assumed average maintenance dose per day for a drug used for its main indication in adults” and can therefore be used to give an indication of the levels of use as well as costs.

Figure 2 Use of clopidogrel in Hospitals in England by DDD.

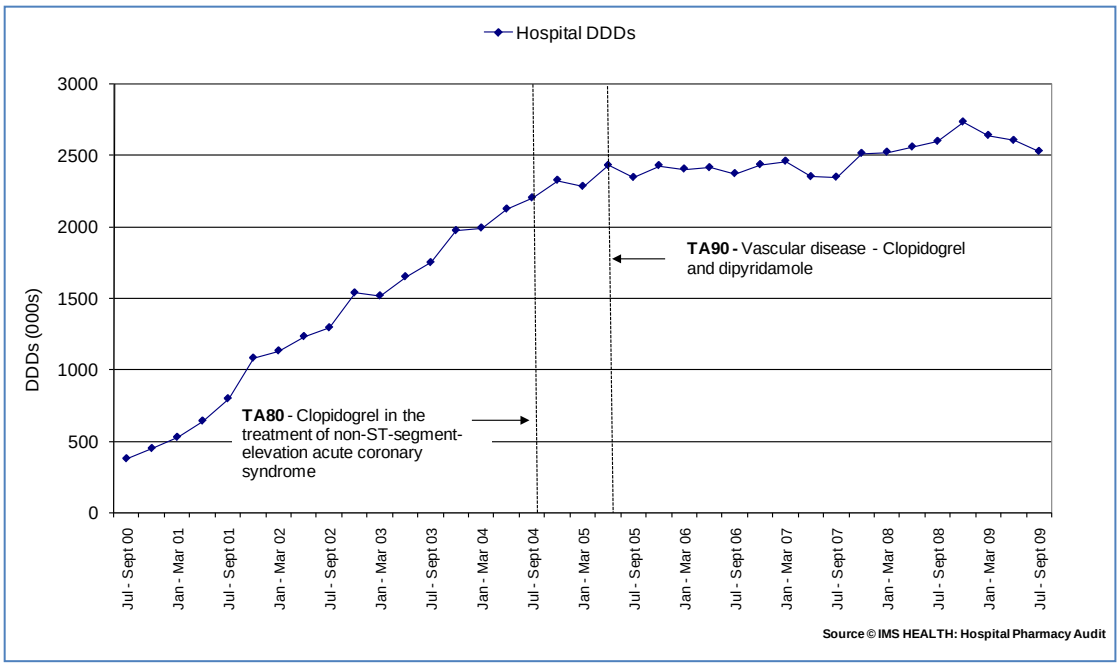
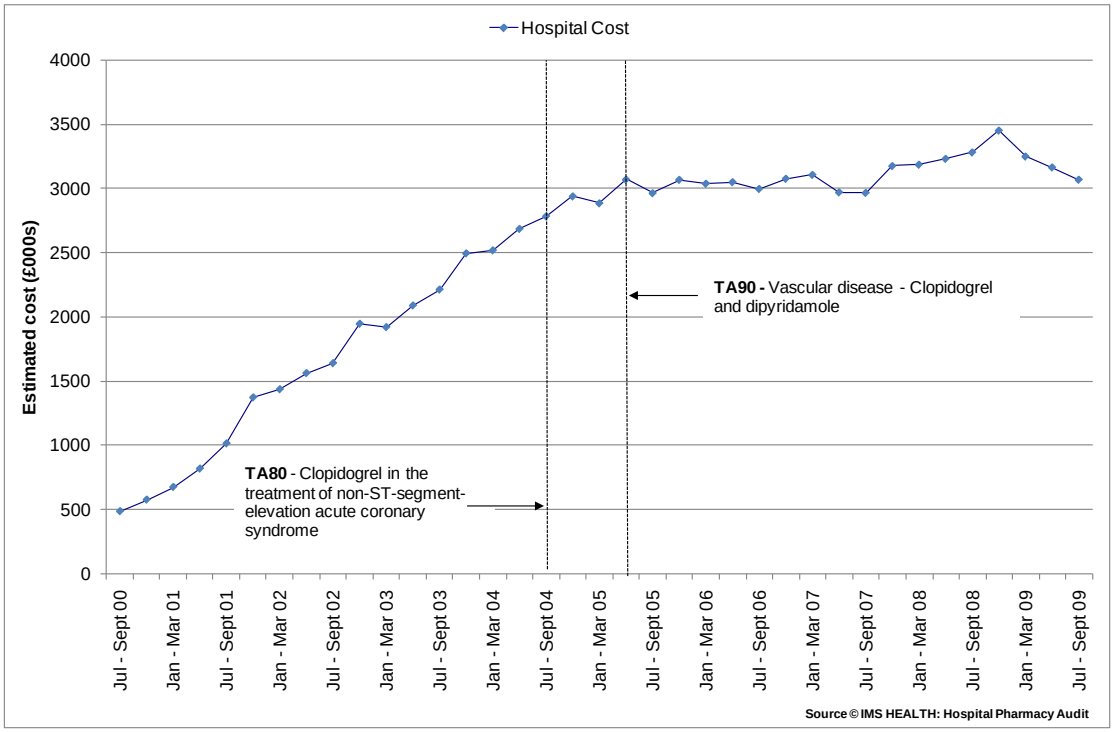


Figure 3 Trend in the cost of prescribing clopidogrel in hospitals in England



Note: TA182: Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention was published in October 2009.

Clopidogrel was first recorded on the IMS Health Hospital Pharmacy Audit Index database for hospitals in England in July 2000. Data show that both cost and DDDs were increasing in secondary care prior to the publication of TA80 and that this continued for a further 12 months. Since April 2005 use appears to have been more stable.

Table 2 Cost and Daily Defined Dose (DDD) of prescribing clopidogrel in hospitals in England in the 12 months to September 2009

	DDD	% annual change (DDD)	Cost	% annual change (cost)
Clopidogrel	10,527,265	3.06%	12,941,639	0.47%

The estimated cost for the latest available quarter (July – September 2009) was £3,070,203.

While there was an increase in cost of prescribing clopidogrel following the publication of TA80 as anticipated, this cannot be specifically related to the figures estimated in the costing report due to the other indications for the use of this medicine.

4 Conclusions

Prescribing of clopidogrel in primary care shows considerable variation with increases followed by an apparent decrease. The pattern of uptake in secondary care is different where the use of clopidogrel continued to increase following the publication of technology appraisal 80 and has been maintained at a certain level. Further analysis is required when data becomes available to determine the long term trend of clopidogrel prescribing in both primary and secondary care. It should be noted that there are variations in the coding of non-ST-segment-elevation acute coronary syndrome, leading to

underestimates of the true incidence. Investigation using IMS disease analyser supports this statement. Therefore any further analysis looking at clopidogrel in combination with low-dose aspirin and the duration of treatment in primary care was not feasible.

5 Recommendations

Trusts should consider auditing this area of care to ensure that any variations to the treatment recommended in the NICE guidance are appropriate.

6 Further information and references

6.1 Related NICE guidance

For information about NICE guidance that has been issued, see the website (www.nice.org.uk).

- Guidance on the use of glycoprotein IIb/IIIa inhibitors in the treatment of acute coronary syndromes. NICE technology appraisal 47 (2002). Available from: www.nice.org.uk/TA47
- Vascular disease - clopidogrel and dipyridamole. NICE technology appraisal 90 (2005). Available from: www.nice.org.uk/TA90
- Prasugrel for the treatment of acute coronary syndromes with percutaneous coronary intervention. NICE technology appraisal 182 (2009). Available from: www.nice.org.uk/TA182

Appendix 1

Definitions used in this report

Prescribing analysis and cost tool system

This information comes from the electronic prescribing analysis and cost tool (ePACT) system, which covers prescriptions by GPs and non-medical prescribers in England and dispensed in the community in the UK. The Prescription Pricing Division of the NHS Business Services Authority maintains the system. PACT data are used widely in the NHS to monitor prescribing at a local and national level. Prescriptions written in hospitals but dispensed in the community (FP10 [HP]) are not included in PACT data. Prescriptions dispensed in hospitals or mental health units, and private prescriptions, are not included in PACT data.

Measures of prescribing

Volume: The basic measure of volume in PCA and PACT data is the number of prescription items which refer to a single item on a prescription form.

Cost: The net ingredient cost (NIC) is the basic price of a drug listed in the drug tariff, or if not in the drug tariff, the manufacturer's list price.

Data limitations (national prescriptions)

PCA or PACT data do not link to demographic data or information on patient diagnosis. Therefore the data cannot be used to provide prescribing information by age and sex or prescribing for specific conditions where the same drug is licensed for more than one indication.

IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

Measures of prescribing

Defined Daily Dose: The definition of a DDD is “the assumed average maintenance dose per day for a drug used for its main indication in adults”.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

Data limitations

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.