



North West London Cardiac Network

## CLOPIDOGREL PRESCRIBING AUDIT May 2007

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## Introduction

The Primary Care Sub-group of the NW London Cardiac Network produced guidance on Clopidogrel prescribing in March 2006. This guidance was distributed to all GPs in NW London via the PCT Prescribing leads. It was also circulated to all acute trusts/tertiary centres in NW London.

During 2007, the Network commissioned Dr Navtej Chahal to carry out an audit to assess subsequent Clopidogrel prescribing practice across NW London.

## Background

In July 2004 NICE<sup>1</sup> recommended the use of Clopidogrel for acute coronary syndrome (non ST elevation myocardial infarction – NSTEMI) patients in combination with aspirin for up to 12 months. Clopidogrel therapy has not just been limited to these patients, however. Percutaneous Coronary Intervention (PCI) has been associated with two major limitations: acute or threatened vessel closure, and restenosis. Early studies utilizing older stent deployment techniques showed that acute (usually less than 24 hours) or sub-acute (five to six days) thrombosis occurred in approximately 18 percent of cases. The 2002 ACA/AHA<sup>2</sup> guidelines update recommended Clopidogrel therapy for at least one month and as long as 9 months in patients undergoing PCI based on data from the CREDO<sup>3</sup> trial which demonstrated that at 1 year, long-term Clopidogrel therapy was associated with a 26.9% relative reduction in the combined risk of death, MI, or stroke.

The cost of Clopidogrel prescribing across primary care is significant. For example, Brent Teaching Primary Care Trust (tPCT) has the 10<sup>th</sup> highest expenditure per prescribing unit on antiplatelet drugs out of all the London PCTs<sup>4</sup>. The annual cost of Clopidogrel prescribing in Brent increased by 25% in 2004/2005; this is mirrored elsewhere in other PCTs.

Whilst guidance on Clopidogrel prescribing had been issued by the North West London Cardiac Network in 2006 (Appendix 1), the Network wished to establish whether local GP's were either aware of this or indeed any additional local PCT guidance and, if so, how closely such guidance was being adhered to. In addition to assessing this, the study also aimed to identify any areas where Clopidogrel was being inappropriately prescribed with regards to either indication and/or duration of treatment. We, therefore, distributed a questionnaire (appendix 2) to all the practices in the NWL Cardiac Network with a pre-paid envelope allowing them to be completed and returned anonymously.

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<sup>1</sup> Clopidogrel in the treatment of non-ST-segment-elevation acute coronary syndrome, National Institute for Health and Clinical Excellence, July 2004, ref: TA80, available at <http://guidance.nice.org.uk/TA80>

<sup>2</sup> Smith et al., ACC/AHA Guidelines for Percutaneous Coronary Intervention, (Revision of the 1993 PTCA Guidelines), JACC VOL. 37, NO. 8, JUNE 2001:2239i-lxvi, available at: <http://www.acc.org/qualityandscience/clinical/guidelines/percutaneous/dirIndex.htm>

<sup>3</sup> Steinhubl SR., Berger PB., Mann JT., Fry ET., Delago A., Wilmer C., Topol EJ: CREDO Investigators, Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial, JAMA 2002; 288:2411

<sup>4</sup> Clopidogrel Prescribing in Brent tPCT GP Practices, 2004-2005, Prescribing and Medicines Management Team

## Results

The questionnaire was distributed to general practitioners in the London Boroughs of Brent, Ealing, Harrow, Hammersmith & Fulham, Hounslow, Hillingdon, Kensington and Chelsea and Westminster, representing 567 GPs. Responses were received from GPs in all boroughs with the exception of Hounslow. A total of 160 fully completed questionnaires were returned during the time period September to December 2006.

With respect to the guidance (figures 1-6), GPs were asked whether they had specifically received any guidance such as information sheets, audit packs or verbal advice on Clopidogrel prescribing. 76% of GPs answered “yes” with the majority (67%) citing their PCT as the source of this guidance – (it is unclear from the responses whether this is Network generated guidance or local PCT guidance). Although the majority (86%) felt that the guidance provided was clear and that in 94% of cases Clopidogrel was being initiated by or in the hospital, only 49% felt a clear reason had to be provided as to why the drug had been prescribed in the first place. Similarly only 30% of GPs felt that they had been provided with a clear indication as to the length of duration of treatment required.

Figure 1

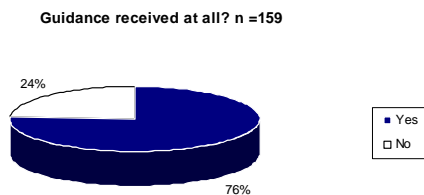


Figure 2

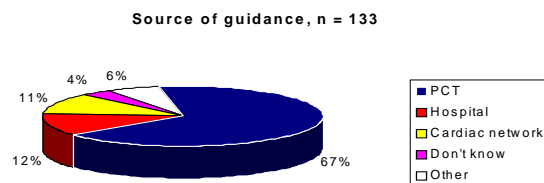


Figure 3

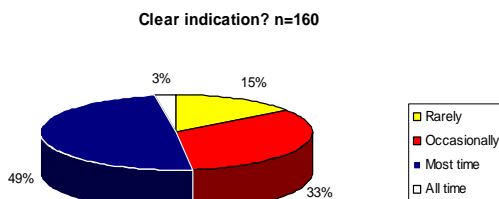


Figure 4

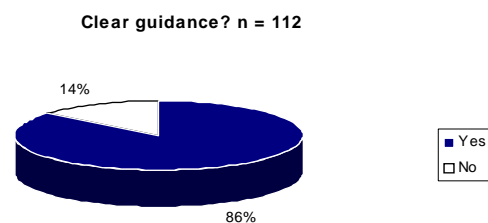


Figure 5

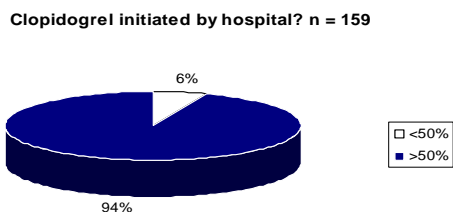
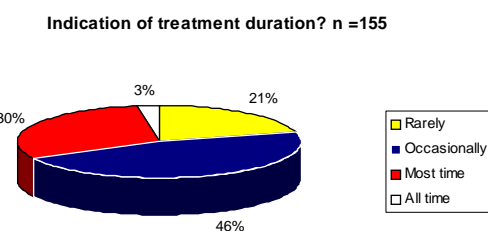


Figure 6



On analysing the data against guidance, there appeared to still be some confusion over the duration of Clopidogrel prescribing (figure 7) with 17% (n=44) of respondents who felt that 1 month was the correct minimum treatment period for a patient having suffered an acute coronary syndrome or NSTEMI and 8 respondents who answered that 1 month of Clopidogrel was sufficient post drug eluting stent deployment. With regards to

deployment of bare metal stents (figure 8), 50% of respondents (n=65) incorrectly stated that 12 months minimum therapy was necessary with Clopidogrel.

Figure 7

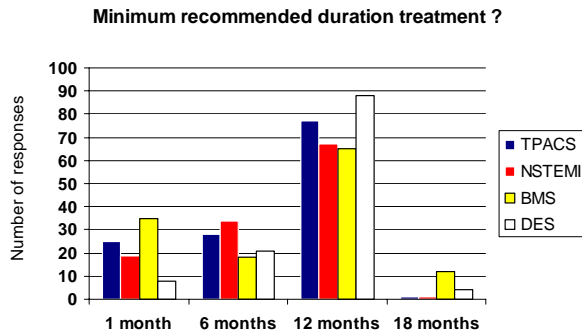
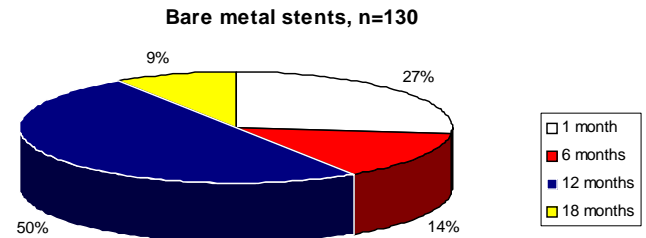


Figure 8



## Discussion

With the information gained from this audit, 3 areas of concern have been identified:

- 1) Only 49% of GPs feel that they are being provided with a clear indication as to why Clopidogrel has been initiated and only 30% feel they know how long the patient is required to stay on the drug.
- 2) Only 57% correctly answered that 12 months treatment minimum was required for an ACS/NSTEMI with 17% who felt that 1 month would suffice.
- 3) Only 27% answered correctly that only 1 month's treatment was required for patients who had had a bare metal stent inserted

From the perspective of the Cardiologist, concern would arise from the fact that there is a perception that GPs feel they are not being provided with adequate information in an area of prescribing that is becoming increasingly complex. Patients who have been diagnosed with an ACS/NSTEMI (which are both essentially the same entity) may be under-treated whereas patients who have received a bare metal stent may be over treated which is not cost effective and exposes the patient to unnecessary bleeding risks. Although the proportion of patients receiving a bare metal stent has recently declined, this may change in the future as a result of recent concerns raised over the safety profile of drug eluting stents.

The guidance issued by the NW London Cardiac Network suggests 12 months treatment as a minimum for drug eluting stents. Although only 8 respondents felt that 1 month's treatment was all that was required for these patients, if this was translated to real life prescribing then potentially fatal complications could occur from stent thrombosis. There is a feeling that many patients are being left on Clopidogrel beyond 12 months due to uncertainty about maximum length of treatment but only 4% of

respondents felt that 18 months treatment was required for any of the possible indications.

## **Recommendations**

This study highlights some of the concerns felt by general practitioners regarding guidance on Clopidogrel which seems not to have been fulfilled by either previous local PCT or Network issued guidance. The following recommendations are suggested:

1. Provision of more specific, mandatory prescribing information on the discharge letter which could be requested by the software if discharge letters are generated electronically in the acute Trust or by the pharmacist before the prescription is authorised and dispensed.
2. Alternatively each patient could be issued with a Clopidogrel card that states specific information regarding the indication and duration of treatment.
3. Repeat survey 6 months post implementation of the above to assess whether they have had a significant impact on prescribing knowledge in this area.

## Guidance for Prescribing Clopidogrel in Primary Care

*This guidance has been produced to ensure that protocols around the prescribing of Clopidogrel are standardised across the sector. **Where prescribing of Clopidogrel is outside the guidance, the reasons should be fully documented (including communicating to GP) and the prescribing responsibility should remain with the initiating hospital doctor.***

### Licensed Indications

Prevention of atherothrombotic events:

- In established peripheral artery disease
- In myocardial infarction (from a few days until less than 35 days)
- In ischaemic stroke (from 7 days until less than 6 months)
- In non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction) in combination with aspirin.

NB. It is not licensed for occlusive vascular events associated with atrial fibrillation.

**Contra-indications for Clopidogrel:** severe liver disease, active peptic ulcer disease, intracranial haemorrhage, breast feeding. See Summaries of Product Characteristics (SPC) for full details of contra-indications, cautions and adverse effects.

**Both aspirin and Clopidogrel cause a variety of GI adverse effects e.g. abdominal pain, dyspepsia, diarrhoea and nausea.**

### 1. Acute Coronary Syndrome (ACS) <sup>1,2</sup>

ACS refers to a range of acute myocardial ischaemic states that include unstable angina, non-ST segment elevation myocardial infarction (NSTEMI) and non-Q-wave myocardial infarction.

<b>Dose</b>	Clopidogrel 75mg daily in combination with aspirin 75mg daily
<b>Duration</b>	<b>12 months after the event.</b> Aspirin should then be continued.
<b>Initiating treatment</b>	<b>Hospital</b> (discharged with 28 days supply) <i>Duration of treatment must be clearly specified on discharge</i>
<b>Continuing treatment</b>	<b>GP</b>
<b>Termination of treatment</b>	<b>GP according to initial treatment plan from hospital</b>

*If a patient with ACS is considered to be at high risk of death or MI (TIMI score 5-7)\* and the cardiologist in charge of the patient indicates this on discharge summary, treatment with Clopidogrel combined with aspirin may be continued beyond twelve months (**this is outside NICE Guidance**).*

\*TIMI= Thrombolysis in Myocardial Infarction. The score for unstable angina/non-ST elevation myocardial infarction is graded out of seven and assigns one point for the presence of each predictor variable.

### 2. Post-Stent Insertion and Percutaneous Coronary Intervention (PCI) with ACS <sup>3,4,5</sup>

The use of Clopidogrel for this indication is **unlicensed** and the recommendations are based on published evidence and current practice. The duration of combination treatment with aspirin is dependent on the type of stent inserted. The duration may also vary depending on the complexity of the disease, number of stents inserted and other factors. Where the treatment course exceeds those in this guidance the prescribing responsibility should remain with the hospital and communicated to the GP.

#### Bare metal stents

<b>Dose</b>	Clopidogrel 75mg daily in combination with aspirin 75mg daily
<b>Duration</b>	<b>1 month after stent insertion.</b> Aspirin should then be continued. <i>Duration of treatment must be clearly specified on discharge</i>
<b>Initiating treatment</b>	<b>Hospital</b>
<b>Continuing treatment</b>	<b>Not applicable</b>
<b>Termination of treatment</b>	<b>Full course to be supplied by hospital</b>

### **Drug eluting stents and PCI with ACS**

<b>Dose</b>	Clopidogrel 75mg daily in combination with aspirin 75mg daily <b>Patients having PCI with ACS will already be on this</b>
<b>Duration</b>	<b>12 months after stent insertion.</b> Aspirin should then be continued. <b><i>Duration of treatment must be clearly specified on discharge</i></b>
<b>Initiating treatment</b>	<b>Hospital</b> (discharged with 28 days supply)
<b>Continuing treatment</b>	<b>GP</b>
<b>Termination of treatment</b>	<b>GP according to initial treatment plan from hospital</b>

### **3. Secondary Prophylaxis of Occlusive Vascular Events and Symptomatic Peripheral Arterial Disease<sup>6,7,8,9</sup>**

People who are at increased risk of bleeding or who have a history of gastro-intestinal bleeding and the benefits of continued aspirin therapy outweigh the risks ***should receive appropriate gastro-protective therapy with a proton pump inhibitor (PPI).***

Patients already taking a PPI should be maintained on aspirin 75mg and **not switched to Clopidogrel.**

As per NICE Guidance Clopidogrel alone (within its licensed indications) is recommended for people who have experienced an occlusive vascular event (e.g. transient ischaemic attacks, ischaemic stroke, myocardial infarction) or have symptomatic peripheral arterial disease **and who have**

- *Either* **proven hypersensitivity** to aspirin-containing medicines
- *Or* history of **severe dyspepsia** induced by low-dose aspirin (NB. Clopidogrel is also associated with gastrointestinal adverse effects)

<b>Dose</b>	Clopidogrel 75mg daily
<b>Duration</b>	<b>Indefinite</b>
<b>Initiating treatment</b>	<b>Hospital</b> (discharged with 28 days supply) <b>or GP</b>
<b>Continuing treatment</b>	<b>GP with regular review</b>

Clopidogrel is **NOT** recommended as a first line antiplatelet agent as it is only marginally more effective than aspirin (the number needed to treat (NNT) is 200 over 1 year), has a similar toxicity profile and is far more expensive.

### **4. Occlusive Vascular Events while on aspirin for Secondary Prophylaxis of Occlusive Vascular Events and Symptomatic Peripheral Arterial Disease<sup>10,11</sup>**

Current limited evidence and product licence does not support the use of aspirin and Clopidogrel combination treatment for patients who experience occlusive vascular events while on aspirin.

**Clopidogrel for this indication is unlicensed and not recommended.**

**NB.** *The combination of aspirin and Clopidogrel in patients with recent ischaemic stroke or TIA does not significantly lower the incidence of recurrent vascular events but does increase the risk of major and life threatening bleeding (from 1.3% to 2.6%)<sup>10</sup>.*

### **5. Primary Prevention of Occlusive Vascular events<sup>12,13</sup>**

**Clopidogrel for this indication is unlicensed and not recommended.**

Clopidogrel should not be used routinely in patients with type 2 diabetes who require antiplatelet treatment unless truly intolerant. There are no trials specifically studying Clopidogrel in patients with diabetes, atrial fibrillation, clotting disorders and other indications for the primary prevention of CVD.

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**North West London Cardiac Network**

**Clopidogrel Prescribing Questionnaire**

This questionnaire has been developed to enable the NW London Cardiac Network assess the availability and use of any existing guidance, understand effectiveness of communication between primary and secondary care and assess any educational opportunities requiring further development for primary care/hospital clinicians. Your time in completing this short questionnaire would therefore be appreciated. All returns will be anonymous.

**Please indicate by circling one answer only**

1. Have you been issued with any guidance, information sheets, audit packs or verbal advice on Clopidogrel prescribing?
- a) Yes
  - b) No

If yes, can you detail the source?

- a) Local PCT
- b) Local Hospital
- c) Cardiac Network
- d) Don't Know
- e) Other – please specify

.....  
.....

If yes, do you feel that the information provided was clear to follow and met your needs?

- a) Yes
  - b) No
- Please describe

.....  
.....

2. In your opinion, what proportion of Clopidogrel prescribing, for a cardiac indication, is initiated in hospital?
- a) Less than 50% is initiated by hospital
  - b) More than 50% is initiated by hospital
3. When Clopidogrel has been initiated by the hospital, are you generally provided with a clear reason as to why the drug has been commenced for a particular patient?
- a) Rarely
  - b) Occasionally
  - c) Most of the time
  - d) All of the time
4. When Clopidogrel has been initiated by the hospital, are you generally provided with a clear indication as to how long the duration of treatment should be for a particular patient?
- a) Rarely
  - b) Occasionally
  - c) Most of the time
  - d) All of the time

**From your own knowledge and understanding, please indicate:-**

- 6.** Which of the following cardiac conditions is Clopidogrel recommended for?  
**(More than 1 option may be true for this question only)**
- a) Atrial Fibrillation
  - b) Troponin positive acute coronary syndromes (TPACS)
  - c) Non ST elevation myocardial Infarction (NSTEMI)
  - d) ST elevation myocardial infarction (STEMI)
- 7.** What is the minimum recommended duration of treatment of Clopidogrel for a Troponin positive ACS?
- a) 1 month
  - b) 6 months
  - c) 12 months
  - d) 18 months
- 8.** What is the minimum recommended duration of treatment of Clopidogrel for a Non-ST elevation myocardial infarction (NSTEMI)?
- a) 1 month
  - b) 6 months
  - c) 12 months
  - d) 18 months
- 9.** What is the minimum recommended duration of treatment of Clopidogrel for a patient having received a bare metal stent?
- a) 1 month
  - b) 6 months
  - c) 12 months
  - d) 18 months
- 10.** What is the minimum recommended duration of treatment of Clopidogrel for a patient having received a drug eluting stent?
- a) 1 month
  - b) 6 months
  - c) 12 months
  - d) 18 months
- 11.** Please indicate which PCT your practice is situated within
- a) Harrow
  - b) Hillingdon
  - c) Brent
  - d) Hammersmith & Fulham
  - e) Westminster
  - f) Kensington & Chelsea
  - g) Ealing
  - h) Hounslow

**Thank you for taking the time to complete this questionnaire**