

NICE TA 236: Ticagrelor for acute coronary syndromes

<p>1</p>	<p>Name of Commissioning Team</p> <p>Unscheduled Care Commissioning Team</p>
<p>2</p>	<p>Summary of NICE TA 236 - Ticagrelor for acute coronary syndromes</p> <p>NICE recommends Ticagrelor combined with low-dose aspirin for up to a year as a possible treatment for some people with acute coronary syndromes (see below). Patients should be able to have Ticagrelor if they:</p> <ul style="list-style-type: none"> • have a condition called ST- segment elevation myocardial infarction (major heart attack) - that their cardiologist intends to treat with a procedure to widen the narrowed artery (called primary percutaneous coronary intervention (pPCI)); • a condition called non-ST-segment elevation myocardial infarction (mild heart attack); or • have been admitted to hospital with unstable angina. <p>If patients are treated with Ticagrelor because they have unstable angina, this diagnosis should be confirmed, ideally by a cardiologist, before they are offered treatment with Ticagrelor.</p> <p>There is uncertainty associated with the predictions of uptake of Ticagrelor for ACS in Northern Ireland. The NICE costing template seeks predictions on the future uptake of the drug and allows associated cost implications to be modelled and predicted.</p> <p>Ticagrelor could potentially be offered to all patients who have acute coronary syndromes who meet NICE criteria in preference to the existing drug, Clopidogrel. The NICE TA does not provide any additional criteria to assist in determining the proportion of patients will be offered Clopidogrel or Ticagrelor in the future. Clinical opinion from the local cardiologists has suggested that the uptake of Ticagrelor would be conservative resulting in an increased cost of approx £1.044m, however this is not based on the application of any criteria to identify sub-groups of patients who would be more likely to receive Ticagrelor than Clopidogrel.</p> <p>Based on experience of the uptake of new drugs in Northern Ireland and the estimates made by the drug manufacturer Astra Zeneca, the uptake could potentially be 90% resulting in an annual cost of approx. £3.6m. The conservative estimates are based on clinical opinion at a time when the drug is not routinely available and when experience with the drug locally is limited. However, it is likely that uptake will increase over a number of years as experience grows and in 3-5 years time, Ticagrelor may replace Clopidogrel as the drug of choice in most or all of these indications.</p>

	<p>Dual antiplatelet treatment for ACS is usually for 12 months and it has always been a significant challenge for Trusts and GPs to ensure that treatment is not routinely continued beyond 12 months. Given the substantially higher cost of Ticagrelor compared to Clopidogrel, it will be essential that patients are properly reviewed at 12 months to ensure that treatment is stopped appropriately. This will be included in the agreed clinical pathway.</p> <p>Affordable at 40% of patients (i.e. £1.044m) but rising to 90% of patients (over £3 million) would present significant difficulties in providing the funding necessary in future years.</p>																																																								
3	<p>Number of people in Northern Ireland expected to take up service/ therapy (new cases per year)</p> <p>C 1,500 patients. (based on 40% of current patients meeting the guideline's criteria for treatment)</p>																																																								
4	<p>Outcomes</p> <p>The expected improvements in patient outcomes are discussed below and derived from the following research data from the PLATO trial.</p> <p>Numbers needed to treat for primary and secondary outcomes:</p> <table border="1"> <thead> <tr> <th></th> <th>Ticagrelor</th> <th>Clopidogrel</th> <th>HR (95% CI)</th> <th>p value</th> <th>ARR</th> <th>NNT</th> </tr> </thead> <tbody> <tr> <td colspan="7">Primary endpoints</td> </tr> <tr> <td>CV death + MI + stroke</td> <td>9.8%</td> <td>11.7%</td> <td>0.84 (0.77-0.92)</td> <td><0.001</td> <td>1.9%</td> <td>54</td> </tr> <tr> <td colspan="7">Secondary endpoints</td> </tr> <tr> <td>Total mortality + MI + stroke</td> <td>10.2%</td> <td>12.3%</td> <td>0.84(0.77-0.92)</td> <td><0.001</td> <td>2.1%</td> <td>48</td> </tr> <tr> <td>Myocardial infarction</td> <td>5.8%</td> <td>6.9%</td> <td>0.84(0.75-0.95)</td> <td>0.005</td> <td>1.1%</td> <td>91</td> </tr> <tr> <td>CV death</td> <td>4.0%</td> <td>5.1%</td> <td>0.79(0.69-0.91)</td> <td>0.001</td> <td>1.1%</td> <td>91</td> </tr> <tr> <td>Stroke</td> <td>1.5%</td> <td>1.3%</td> <td>1.17(0.91-1.52)</td> <td>0.22</td> <td>0.2%</td> <td>NA</td> </tr> </tbody> </table>		Ticagrelor	Clopidogrel	HR (95% CI)	p value	ARR	NNT	Primary endpoints							CV death + MI + stroke	9.8%	11.7%	0.84 (0.77-0.92)	<0.001	1.9%	54	Secondary endpoints							Total mortality + MI + stroke	10.2%	12.3%	0.84(0.77-0.92)	<0.001	2.1%	48	Myocardial infarction	5.8%	6.9%	0.84(0.75-0.95)	0.005	1.1%	91	CV death	4.0%	5.1%	0.79(0.69-0.91)	0.001	1.1%	91	Stroke	1.5%	1.3%	1.17(0.91-1.52)	0.22	0.2%	NA
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4.1	<p>Additional life expectancy gain / progress improvement</p> <p>With use as currently proposed by HSCT cardiologists, 26 deaths in patients treated for acute coronary syndrome could be prevented in Northern Ireland annually.</p>																																																								
4.2	<p>Reduction in morbidity</p> <p>With use of Ticagrelor as currently proposed by HSCT cardiologists, 14.5 myocardial infarctions and four stent blockages could be prevented annually in Northern Ireland people with treated Acute Coronary Syndrome.</p>																																																								
4.3	<p>Cost per patient per annum</p> <p>Based on a model of 40% of patients being prescribed with Ticagrelor – 1,514 patients @ £690 each</p>																																																								

4.4	<p>In year cost per patient per annum (for new and prevalent cases)</p> <p>As 4.3 (assuming 12 months prescription per patient as per NICE guidance)</p>
4.5	<p>Any cost savings and how these will be secured</p> <p>NICE recommends that the intervention is cost effective. Based on preventing 14.5 myocardial infarcts and 4 stent blockages annually with an average patient stay in a hospital coronary care bed of 5 days, a total of 92.5 bed days are saved at a cost of £27,750 (i.e. £300 per day).</p>
4.6	<p>Recurrent overall cost</p> <p>£1,044,000</p>
4.7	<p>Cost per QALY</p> <p>The Scottish Medicines Consortium (SMC), The European Society of Cardiology (ESC) and The National Institute of Clinical Excellence (NICE) in its draft advice have endorsed the use of Ticagrelor for the management of acute coronary syndromes. SMC have found that, Ticagrelor in combination with aspirin is proven to be cost effective versus generic Clopidogrel and aspirin for the treatment of Acute Coronary Syndrome (ACS) leading to a published cost per Quality Adjusted Life Year (QALY) of £3,966.</p> <p>In its draft advice, NICE agreed that the most plausible incremental cost effectiveness ratios (ICERs) are:</p> <ul style="list-style-type: none"> • £7897 per QALY for all Acute Coronary Syndromes (ACS) • £8872 per QALY for STEMI (major heart attack) • £7215 per QALY for NSTEMI (other heart attack) and • £9131 per QALY for unstable angina. <p>The accepted cost effectiveness threshold is generally accepted to be any ICER below £20,000 per QALY.</p> <p>Using the previous stated NNT, the following additional drug acquisition costs would be required:</p> <ul style="list-style-type: none"> • to prevent one cardiovascular event - £36,727 (NNT=54), • to prevent one death from any cause - £48,971(NNT=72) and • to prevent one death from cardiovascular causes - £61,892 (NNT=91).
4.8	<p>Other treatments available for this condition</p> <p>There are currently two drugs in use for antiplatelet treatment of patients with acute coronary syndrome, namely Clopidogrel and Prasugrel.</p>

	<p>Following the CURE trial, Clopidogrel is widely accepted as the standard thienopyridine of choice for the treatment of ACS (both medical management and for those undergoing PCI). Clopidogrel when added to aspirin in patients with ACS reduced the composite end point of non fatal MI, stroke and CV death from 11.4% to 9.3%; HR 0.80 (0.72-0.90, p<0.001). This reduction in ischaemic events came at a cost of increased major bleeding rate of 3.7% vs. 2.7%; HR 1.38 (1.13-1.67); p=0.001.</p> <p>Prasugrel, a third generation thienopyridine has been recommended by NICE as an option in the following restricted situations: (i) immediate primary percutaneous coronary intervention for ST-segment-elevation myocardial infarction (STEMI); (ii) when stent thrombosis has occurred during Clopidogrel treatment or (iii) the patient has diabetes mellitus. Being more potent than Clopidogrel, Prasugrel has shown a reduction in the composite outcome of non fatal MI, stroke and CV death (2.1% vs. 9.9%; HR 0.81 (0.73-0.90); p<0.001) although at an increased rate of major bleeding when compared to clopidogrel 2.4% vs. 1.8%; HR 1.32 (1.03-1.68); p=0.03 for major bleeding. Importantly overall mortality was lower with ticagrelor compared with clopidogrel: 4.5% vs 5.4%.</p> <p>There are a number of limitations with Clopidogrel therapy. Clopidogrel has a relatively slow onset of action that is reliant on liver enzymes for metabolism to the active metabolite. This leads to large inter-patient variation of response to Clopidogrel, making drug interactions more likely. Patients with a poor response to Clopidogrel have an increased risk of coronary thrombosis and coronary stent thrombosis.</p> <p>Compared to Clopidogrel, Ticagrelor acts faster. After 30 minutes of a 180mg loading dose of ticagrelor, it has the same platelet inhibition as would be found 2 hours following a 600mg Clopidogrel dose.</p>
<p>4.9</p>	<p>Readiness to implement</p> <p>Clinicians, in supporting the development of this commissioning plan, have indicated that they would start using Ticagrelor as soon as it is commissioned. However it will be necessary for the Board and Agency to put in place an agreed clinical pathway, including criteria/indications for treatment which prioritises patients appropriately. This will be in place during the first quarter of 2012/13 and will adhere to NICE recommendations. Ticagrelor will be available for use after the pathway is agreed.</p>
<p>5</p>	<p>DHSSPS Legislative / Policy Caveats</p> <p>This advice does not override or replace the individual responsibility of health professionals to make appropriate decisions in the circumstances of their individual patients, in consultation with the patient and/or guardian or carer. This would, for example, include situations where individual patients have other conditions or complications that need to be taken into account in determining whether the NICE guidance is fully appropriate in their case.</p>

<p>6</p>	<p>What will Commissioning Team do to secure funding for the implementation of this TA including any proposals for disinvestment?</p> <p>Ticagrelor treatment will be started by cardiologists in hospitals and usually continue for a year. Therefore over 90% of the prescribing costs for Ticagrelor will occur in primary care.</p> <p>However the primary care prescribing budget is required to deliver an efficiency programme of £30 million annually over the next 3 years. Introduction of Ticagrelor is only affordable if additional efficiencies are created within the prescribing budget or if additional funding is allocated from other sources to boost the primary care prescribing budget and support the introduction of Ticagrelor to reduce the risk of stent blockage, myocardial infarction and death in patients with ACS.</p> <p>The Commissioning Team, working with Directorate of Integrated Care and Local Commissioning Groups, will seek to confirm funding in the first quarter of 2012/13. This will not impede introduction.</p>
<p>7</p>	<p>Commissioning arrangements</p> <p>Once agreed within HSCB and with DHSSPS, HSCB will send a commissioning statement to HSCTs and primary care, seeking implementation plans within three months. This will require Trusts to work together with the Board and Agency to put in place an agreed clinical pathway prior to use of the drug.</p>
<p>8</p>	<p>Monitoring arrangements</p> <p>The drug will be initiated in secondary care and continued in primary care. The primary care expenditure will be monitored through the prescribing data on a monthly basis. This can be monitored at GP practice, LCG and NI level.</p> <p>Ticagrelor is started by cardiologists in Trusts and monitoring and performance management undertaken by the HSCB Pharmacy and Medicines Management Team, Trust Drug and Therapeutics Committees and, if necessary, through Board performance management processes.</p> <p>HSCB and HSCT mid year accountability reviews, GAIN audits and high level RQIA evaluation are other governance and review mechanisms to monitor implementation</p>

NICE TA 236 TRICAGRELOR FOR ACUTE CORONARY SYNDROMES

Addendum

Following Departmental approval of this Commissioning Plan, the commissioner has further discussed introduction of Ticagrelor with HSC Trust clinical leads for cardiology as the basis of putting in place an agreed pathway.

A number of protocols have been agreed to which Trusts will be required to comply:

- From the date of issue of the commissioning plan to HSC Trusts, Ticagrelor may be initiated in the treatment of acute coronary syndromes.
- The drug will be initiated in secondary care only and continued in primary care.
- HSC Board asks that Ticagrelor is only initiated by a cardiologist and that each Trust put in place protocols to prevent other clinicians from initiating treatment without cardiology assessment.
- In due course, it is anticipated that the Cardiac Network will issue an agreed pathway encompassing Ticagrelor initiation to which the Trust will be asked to follow.
- It is anticipated that patients with STEMI and NSTEMI conditions who have been treated with PCI will be the main recipients of Ticagrelor. In discussion with the lead cardiologist in each HSC Trust, the Board does not anticipate that Ticagrelor will be used to treat unstable angina.
- Given that most of the expenditure for Ticagrelor will be borne by Primary Care prescribing budgets, the Board requires that HSC Trusts provide monthly data on the numbers of patients initiated with Ticagrelor and their respective indications to assist with financial planning.
- Moreover and following discussions with lead cardiologists, the Board will keep under close review prescribing practices against projections of anticipated use.

Annex 1

- It is also expected that Trust Drug and Therapeutic Committees will scrutinise the introduction of the drug accordingly.
- Trust will receive an allocation based on NICE costing templates and capitation share. In due course, it will be necessary for an Investment Proposal Template to be agreed in this respect.