New Oral Anticoagulants

New Implications from a Pharmacists Perspective

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NEW PILL TO STOP STROKES

Patients can get wonder drug NOW

A PILL costing less than £3 a day is being hailed as the biggest breakthrough in stroke prevention in 50 years.

The drug, which slashes the risk of suffering a stroke by over a third, will help more than a million Britons. Pradaxa is now available for use in the UK. In trials it was found to significantly reduce the risk of a stroke in patients with an irregular heartbeat, known as atrial fibrillation. This is one of the main causes of strokes.

The drug, taken twice a day at a cost of £2.52, already prevents thousands of deaths each year from blood clot after hip or knee replacement.

By Jo Willee Health Correspondent

£2.50-a-day stroke pill ‘that will help 1million patients’
Warfarin for non-rheumatic AF

Random effects model; Error bars = 95% CI; *p>0.2 for homogeneity;
†Relative risk reduction (RRR) for all strokes (ischaemic and haemorrhagic)

Advancing cardiac and stroke care across South London

Aspirin
RRR 19% 0.7% ARR
Tokyo, Japan - The Japanese Ministry of Health, Labor, and Welfare has issued a safety advisory in that country warning of the potential for adverse events with dabigatran (Pradaxa in Japan) following the deaths of five patients. The advisory notes that there have been 81 cases of serious side effects, including gastrointestinal bleeding, since the launch of dabigatran; the drug has been used in around 64,000 people since its launch in Japan in January 2011.
Increased incidence of reported adverse events

Since more people have started to use Pradaxa the TGA has received an increase in the number of bleeding-related adverse events reports.

Adverse events reported to the TGA for Pradaxa since 2009

<table>
<thead>
<tr>
<th>Type of adverse event</th>
<th>Number since 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adverse events</td>
<td>203</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>124</td>
</tr>
<tr>
<td>Serious bleeding adverse events</td>
<td>47</td>
</tr>
<tr>
<td>Serious gastrointestinal bleeding</td>
<td>30</td>
</tr>
<tr>
<td>Serious intracranial bleeding</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events in patients aged 75 years or older</th>
<th>Number since 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adverse events</td>
<td>121</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>76</td>
</tr>
</tbody>
</table>

Point to note:

Serves a very important reminder ... its an anticoagulant!

Warfarin data has not been compared and no denominator

Includes data from hip/knee surgery

More bleeding in reduced dose - ?suitability of starting, need for strong guidance

The TGA analysis of these reports shows that:

- Some of the bleeding adverse events occurred during the transition from warfarin to dabigatran.
- Many of the adverse events are occurring in patients on the reduced dosage regimen.
- The most common site of serious bleeding for Pradaxa is the gastrointestinal tract, whereas for warfarin it is intracranial.

In clinical trials the risk of bleeding per year of treatment with Pradaxa was 16.6% (1 in 6 patients) when taking 150 mg twice daily, and 14.7% (1 in 6.8 patients) taking 110 mg twice daily) compared to 18.4% (1 in 5.4 patients) for warfarin.
Issues to consider.....

• Who should prescribe?  GPs versus specialists
• Which agent?  Relative strengths and weaknesses
• Assessing bleeding risk?  Use of HASBLED
• Follow up:
  • Monitoring (renal function)
  • Dose adjustment (with aging)
  • Adherence
• Education:  Surgical pre-assessment clinics, dental treatment, acute bleeding protocols
• Managing patient and clinician demand
NICE

- Dabigatran recommended as an option in patients with AF and additional risk factors (Mar 2012)
- Rivaroxaban – guidance due May 2012

Potential cost pressure for South London: up to £17 million!
**Clinical Implications**

Per 1000 patients with AF approximately 50 strokes are expected per annum if untreated. Warfarin will prevent 35 of these strokes; of the remaining 15 strokes per annum; the NOACS will deliver the following:

<table>
<thead>
<tr>
<th>End-Point</th>
<th>Dabigatran 150mg bd over 1 year</th>
<th>Rivaroxaban over 1 year</th>
<th>Apixaban over 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke / SE</td>
<td>5.8</td>
<td>4.5</td>
<td>3.3</td>
</tr>
<tr>
<td>• ischaemic</td>
<td>2.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>• Haemorrhagic</td>
<td>2.8</td>
<td>1.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Deaths</td>
<td>-</td>
<td>-</td>
<td>4.2</td>
</tr>
<tr>
<td>Major Bleeds</td>
<td>2.5</td>
<td>-</td>
<td>9.6</td>
</tr>
<tr>
<td>Cost</td>
<td>£800,000</td>
<td>£760,000</td>
<td>Not known</td>
</tr>
</tbody>
</table>

**Indicative warfarin costs for 1000 patients = £241,000**

(NICE 2012)
Service Redesign: Its Complex issue!

- Need a multidisciplinary team:
  - Clinicians: GPs, cardiology, haematology, stroke physicians
  - Pharmacists: PA’s, anticoagulant, cardiac
  - Public Health
  - Service managers
  - Commissioners: acute and community / primary care
  - Patients!
The Starting Point
July 2010….

• **Clinicians**
  - “Everyone's going to be prescribed the NOACs!”

• **Commissioners**
  - “We’re not going to commission any NOACs!”
New Oral Anticoagulants
The Commissioning Challenge

- Current service provision
- Show me the money!
  - Commissioned services / contracts
  - Prescribing Budget
- Certainties and uncertainties.....?

- Flexible service redesign
- *Reallocation of resources to prescribing budgets*
QIPP Opportunities?

- **Redesigning anticoagulant services**
  - **Quality** Patient centred
  - **Innovation** POCT, Self-monitoring, community based, introduction of new drugs
  - **Productivity** Care closer to home, reduced transport costs, reduced overheads, but possible increased drug costs
  - **Prevention** Improved access, improved patient engagement, improved outcomes, reduced risk
Current Service Provision

• What have you got?
  ▫ Hospital or community services
  ▫ Block contracts or activity based
  ▫ Activity, TTR, cost of current service, non-NHS costs

• Impact of new anticoagulants in the volume of activity and cost of anticoagulation services?
  ▫ Not just AF!
  ▫ Block contracts – lack of flexibility in year, difficult to unbundle / potential to destabilise services / increased unit price for remaining patients
  ▫ But, could relieve pressure on over-booked clinics....
Commissioning Planning Purchasing

- Agreed on an annual cycles or for longer periods
- Intention to substantially change the details of a contract must be flagged in Sept for implementation the following year
- Details to be agreed Oct – Feb
- New contract implemented from April onwards

How do we manage NICE guidance produced in year?
Decommissioning.....?

If we are going to fund NOACS........
What do we stop doing?
South London
Patient Perspective

- Patients want a safe and effective anticoagulant which does not require frequent visits to the clinics
- Patients prioritise
  - Safety
  - Effectiveness
  - Convenience
- Clear information for patients on pros and cons of new agents essential
- Preferred option: warfarin with home based monitoring!
Priority Patient Groups

- Patients who aren’t suitable for warfarin yet high risk e.g. CHADS≥2
  - Allergic to warfarin
  - Contraindications to warfarin
  - Previous severe adverse reaction to warfarin
  - Prior haemorrhagic stroke or major bleeds
  - Dementia, palliative care, alcoholism; falls......
  - Serious mental illness, intellectual/learning disability

- Patients out of range on warfarin

- Other patient groups
  - Declined warfarin – ‘a lifestyle drug’
  - Housebound patients – traditionally poorly managed
UKCPA Initial Positioning of NOACs…..

- Warfarin remains the agent of choice for AF stroke prevention
- NOACS should be considered for patients with stroke risk CHADS ≥ 2:
  - Unable to take warfarin due to allergy or contraindications
  - Unable to comply with warfarin monitoring requirements
  - Unable to achieve an adequate TTR after a suitable trial of warfarin management
The consensus statement states that:

- on balance of risks and benefits, warfarin remains the anticoagulant of clinical choice for moderate or high risk atrial fibrillation patients (CHA$_2$DS$_2$-VASc ≥ 2) with good INR control, and
- clinicians should consider prescribing dabigatran in patients with:
  - poor INR control despite evidence that they are complying, or
  - allergy to or intolerable side effects from coumarin anticoagulants.
South London DRAFT
Position Statement

1. Warfarin to remain first-line treatment
2. NOACs an option for patients:
   ▪ With warfarin allergy or severe intolerance
   ▪ Unable to achieve a satisfactory TTR on warfarin
3. Initiation by specialist in AF stroke prevention – first 3 months hospital only
4. Transfer of care to primary care only in line with agreed SLCSN guidelines for use
Summary:
Implementation of NOACs

- Requires a integrated approach involving all stakeholders
- Will require movement of money from services to pay for increased drug costs
- Costs need to be balanced against the delivery of outcomes:
  - Prioritise patient groups
- Likely to see a phased approach to manage costs in current financial climate
- Will need to consider how to manage patient expectations and demand
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Gaddum's Curve

Gee whiz! - it's wonderful

Academics
Investigational
Restricted

It has its place!

Long experience
Eclipsed by new therapy

I wouldn't give it to a dog!

Practitioners
General release
New Oral Anticoagulants
Addressing Challenges in Implementation

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