Signals Detection Activities including Direct Patient Reporting

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Vigilance and Risk Management of Medicines

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Safeguarding public health

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Agenda

- ADR Reporting in the UK
- Patient ADR Reporting
- Signal detection at the MHRA
- Evaluation of the contribution of patient reporting
- Contribution of patient reports to signals
- Challenges ahead for patient reporting & signalling
- Summary
### ADR reporting: 2009 - 2010

<table>
<thead>
<tr>
<th>Yellow Card Statistic</th>
<th>2009</th>
<th>2010</th>
<th>Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of reports</td>
<td>22,444</td>
<td>23,273</td>
<td>↑</td>
</tr>
<tr>
<td>Serious reports</td>
<td>82%</td>
<td>85%</td>
<td>↑</td>
</tr>
<tr>
<td>Fatal reports</td>
<td>5%</td>
<td>6%</td>
<td>↑</td>
</tr>
<tr>
<td>Industry reports</td>
<td>47%</td>
<td>48%</td>
<td>↑</td>
</tr>
<tr>
<td>Patient reports</td>
<td>(7%)</td>
<td>(7%)</td>
<td>static</td>
</tr>
<tr>
<td>Direct reports</td>
<td>53%</td>
<td>52%</td>
<td>↓</td>
</tr>
<tr>
<td>Direct serious reports</td>
<td>67%</td>
<td>72%</td>
<td>↑</td>
</tr>
<tr>
<td>Direct electronic reports</td>
<td>36%</td>
<td>40%</td>
<td>↑</td>
</tr>
<tr>
<td>Most reported drug</td>
<td>Clozapine (10%)</td>
<td>Clozapine (10%)</td>
<td>-</td>
</tr>
<tr>
<td>Most reported vaccine</td>
<td>Human Papilloma Virus vaccine (65%)</td>
<td>Human Papilloma Virus vaccine (56%)</td>
<td>-</td>
</tr>
<tr>
<td>Most reported drug &amp; reaction pair</td>
<td>Clozapine / neutropenia (1%)</td>
<td>Clozapine / neutropenia (1%)</td>
<td>-</td>
</tr>
<tr>
<td>Reports in &lt;18s</td>
<td>15%</td>
<td>14%</td>
<td>↓</td>
</tr>
<tr>
<td>Gender: M:F:unknown</td>
<td>37%: 57%: 6%</td>
<td>39%: 55%: 6%</td>
<td>↑ male</td>
</tr>
<tr>
<td>Most reported age group</td>
<td>50-64 years</td>
<td>50-64 years</td>
<td>static</td>
</tr>
</tbody>
</table>
Overall ADR Reporting trends (2006 to 2010)
Source of direct HCP reports

Sources of direct health professional reports 2009-2010

% direct health professional reports

- GP
- Nurse
- Hospital Doctor
- Other Health Prof
- Hospital Pharmacist
- Hospital Health Prof
- Hospital Nurse
- Community Pharmacist
- Physician
- Pharmacist
- Dentist
- Optometrist
- Coroner

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Patient Reporting
Patient reporting

· Article 102
· The Member States shall:
(a) take all appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; for these tasks, organisations representing consumers, patients and healthcare professionals may be involved as appropriate;
Patient reporting

Article 107

1. Marketing authorisation holders shall record all suspected adverse reactions in the Union or in third countries which are brought to their attention, whether reported spontaneously by patients or healthcare professionals, or occurring in the context of a post-authorisation study.

2. Marketing authorisation holders shall not refuse to consider reports of suspected adverse reactions received electronically or by any other appropriate means from patients and healthcare professionals.

3. Marketing authorisation holders shall submit electronically all serious suspected adverse reactions that occur in the Union and in third countries within 15 days. Marketing authorisation holders shall submit electronically all non-serious suspected adverse reactions that occur in the Union, within 90 days.
Patient reporting at MHRA

- Yellow Card Scheme (1964, thalidomide tragedy)
  - Voluntary reports submitted of suspicions of ADRs (in confidence) to date >700,000 reports.

- Need for consumer reporting highlighted:
  - Independent Review of access to the Yellow Card Scheme (Metters, 2004)

- Until 2005, only HCPs could report directly

- Patient Reporting Working Group and engagement with patient organisations / charities
Patient reporting – the beginning

• When?
  - January 2005 - Pilot scheme for patient reporting introduced

• How?
  - paper
  - internet reporting
  - telephone

• What?
  - all reports welcomed, especially for serious or unlabelled suspected side effects
Experience from pilot scheme

By 2007 end:
• > 6,000 patient reports received
• Majority received via paper; 31% via the internet
• Evaluation: Detailed review of reports received during first 6 months of pilot scheme (CHM November 2005)

Key findings from pilot scheme
• Similar levels of reports of serious reactions
• Fewer reactions to black triangle drugs
• Less complete reports: but no difference in causality, or proportion of unlabelled reactions
• More information on impact of ADRs on quality of life
• Low levels of consumer awareness of the YC Scheme
Formal Launch of Patient reporting – 18th February 2008

- 6 week campaign, supported by RPSGB
- Community Pharmacies
- Information packs (leaflets, posters)
- Advice & support for patients
- Engaging with patient groups and charities to promote the scheme

PLUS Media Coverage:
- BBC News/Radio
- Article in Pharmaceutical Journal
Updated internet reporting platform

electronic Yellow Card

- UAT by patient groups
- Easy to complete
- Smart fields
- Registering details (optional)
- Saveable

Reporting links on:
- NHS Choices
- EMC
- MIMS
Promotional material

YellowCard® report
Use blue or black ink. Complete all the lines marked with ** and give as much other information as you can

1 About the suspected side effect
* What were the symptoms of the suspected side effect, and how did it happen? If there isn't enough space here, attach an extra sheet of paper.

How bad was the suspected side effect? Tick the box that best describes how bad the symptoms were.

☐ Mild ☐ Unpleasant, but did not affect everyday activities ☐ Bad enough to affect everyday activities ☐ Bad enough to see doctor
☐ Bad enough to be admitted to hospital ☐ Caused very serious illness ☐ Caused death ☐ Other

When did the side effect start?

How is the person feeling now? Tick the box that best describes whether the person still has symptoms of the suspected side effect.

☐ Better (no more symptoms) ☐ Getting better ☐ Still has symptoms ☐ More seriously ill ☐ Died ☐ Other

Can you give any more details? For example, did the person take or receive any other treatment for the symptoms? Did they stop taking the medicine as a result of the side effect?

2 About the person who had the suspected side effect
* Who had the suspected side effect?

☐ You ☐ Your child ☐ Someone else

Information about the person. Supply as much information as you can, even if you prefer not to give a name.

First name or initials ☐ Family name

☐ Male ☐ Female

☐ Age ☐ Weight ☐ Other measurements ☐ Height

☐ Notes ☐ Last name

Any other relevant information? For example, does the person have any medical conditions or allergies?

Make sure you have completed all the lines marked ** Please turn over →

What is the MHRA?
The Medicines and Healthcare products Regulatory Agency (MHRA) is a UK government body. Its principal aim is to protect the public's health. It does this by making sure that medicines and medical devices work properly and are acceptably safe.

When any possible problem is found, the MHRA takes prompt action to protect the public and reduce risk.

For more information about the MHRA, visit www.mhra.gov.uk or telephone 0800 7084 2000

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A side effect of your medicine?
If you have a symptom which you think may be a side effect of your medicine:

1. Check the patient information leaflet supplied with the medicine. This lists the known side effects, and advises you what to do.
2. Ask your doctor or pharmacist for advice.
3. You can report the side effect using Yellow Card, especially if it is not mentioned in the patient information leaflet.

Always talk to your doctor if you have any symptom that worries you.

How to report a suspected side effect
There are three ways to use the Yellow Card Scheme:
• use the online Yellow Card at www.yellowcard.gov.uk
This is the easiest way to make a report, if you have access to the Internet.
• ask your pharmacist for a Yellow Card form which you can complete and post
• call the Yellow Card hotline on 0808 100 3302

You can report suspected side effects of any medicine or herbal remedy, whether it was prescribed by your doctor or bought without a prescription.

What happens to Yellow Card reports?
The MHRA (or oversea's authorities) collects Yellow Card reports from people taking medicines, as well as from healthcare professionals such as doctors, pharmacists and nurses.

These reports are used to identify side effects and other problems which might not have been known about before. If a new side effect is found, the MHRA will review the way that the medicine can be used, and the warnings that are given to people taking or seeing it.

The information you provide will be kept safe, secure and confidential. No details that could identify you will be passed on without your permission.

Helping to make medicines safer

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Increased accessibility to Patients

- TV advert for some GP surgeries
- Poster campaign
- Nationwide Leaflet Distribution
- Translation into 10 languages

5 Regional Centres for promotion (MI hospital based)
- Scotland (Edinburgh)
- Wales (Cardiff)
- West Midlands (Birmingham)
- Northern and Yorkshire (Newcastle)
- North West (Liverpool)

Education / awareness - patient groups
Conferences
Patient reporting

- Proportion of total reports: 7.3% (2009) & 7.0% (2010)

- Proportion of serious reports: 86.7% (2009) & 88.3% (2010)

Patient Yellow Cards by reporter type (2010)

- Patient: 83%
- Parent: 11%
- Carer: 6%

Patient Yellow Cards by reporter type (2009)

- Patient: 83%
- Parent: 10%
- Carer: 7%

Patient Reporter Types 2005-2009

- Year 2005: 1637
- Year 2006: 3500
- Year 2007: 2000
- Year 2008: 1637
- Year 2009: 1642
- Year 2010: 2000

> 80% report themselves
Electronic reporting

- 70% eYC patient reports in 2010; 4% ↑ Direct HCP – constant 35%

Direct Electronic Yellow Card Reporting 2009-2010
(excluding pandemic portal reports)

<table>
<thead>
<tr>
<th>Year and reporter qualification type</th>
<th>HCP 2009</th>
<th>Patient 2009</th>
<th>HCP 2010</th>
<th>Patient 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Direct ADRs (Paper)</td>
<td>3573</td>
<td>1079</td>
<td>3687</td>
<td>150</td>
</tr>
<tr>
<td>Proportion of Direct ADRs (Electronic)</td>
<td>685</td>
<td>558</td>
<td>6731</td>
<td>492</td>
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</tbody>
</table>
## Drug-Reaction Combinations 2010

<table>
<thead>
<tr>
<th>Drug substance</th>
<th>ADR term (*Serious PT)</th>
<th>No. reports</th>
<th>% Total HCP reports</th>
<th>Drug substance</th>
<th>ADR term (*Serious PT)</th>
<th>No. reports</th>
<th>% Total patient reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV ▼</td>
<td>Dizziness</td>
<td>354</td>
<td>3.4</td>
<td>Simvastatin</td>
<td>Myalgia *</td>
<td>25</td>
<td>1.5</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Nausea</td>
<td>292</td>
<td>2.8</td>
<td>HPV ▼</td>
<td>Headache</td>
<td>25</td>
<td>1.5</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Headache</td>
<td>277</td>
<td>2.7</td>
<td>Simvastatin ▼</td>
<td>Arthralgia *</td>
<td>19</td>
<td>1.1</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Pain in extremity</td>
<td>229</td>
<td>2.2</td>
<td>Paroxetine</td>
<td>Withdrawal syndrome *</td>
<td>18</td>
<td>1.1</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Fatigue</td>
<td>124</td>
<td>1.2</td>
<td>HPV ▼</td>
<td>Nausea</td>
<td>18</td>
<td>1.1</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Malaise</td>
<td>116</td>
<td>1.1</td>
<td>Paroxetine</td>
<td>Paraesthesia</td>
<td>15</td>
<td>0.9</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Vomiting</td>
<td>112</td>
<td>1.1</td>
<td>HPV ▼</td>
<td>Dizziness</td>
<td>15</td>
<td>0.9</td>
</tr>
<tr>
<td>Varenicline ▼</td>
<td>Nausea</td>
<td>105</td>
<td>1</td>
<td>Simvastatin ▼</td>
<td>Pain in extremity</td>
<td>14</td>
<td>0.8</td>
</tr>
<tr>
<td>Varenicline ▼</td>
<td>Depressed mood *</td>
<td>104</td>
<td>1</td>
<td>HPV ▼</td>
<td>Fatigue</td>
<td>14</td>
<td>0.8</td>
</tr>
<tr>
<td>HPV ▼</td>
<td>Syncope *</td>
<td>103</td>
<td>1</td>
<td>Desogestrel</td>
<td>Depression **</td>
<td>13</td>
<td>0.8</td>
</tr>
</tbody>
</table>

-  HCP all BT, patients - 40% in 2009 to 60% in 2010
-  Vaccines make up 15.9% patient reports

* - serious PT; **Signal – RMS - Sweden
Age and gender reporting

Summary for gender breakdown:
• (male): simvastatin (2009 4.1%, 2010 3.0%)
• (female): HPV vaccine (2009 5.2%, 2010 4.1%)
• (male): fatigue (2009) and headache (2010)
• (female): dizziness (2009) and nausea (2010)
• serious (male): depression (2009), arthralgia (2010)
• serious (female): depression (2009 & 2010)
Evaluation of patient ADR reporting to Yellow Card Scheme

- Higher median number of ADRs per patient report than HCPs and more detailed description
- Similar proportion of “serious” reports
- More signals when combined HCP and patient reports - 47 new serious Some signals in HCP only set were lost but fewer than those gained
- Different patterns of drugs and reactions reported by patients

Avery et al 2011 HTA; vol 15; no 20
Signal Detection
Signal detection & prioritisation process

Signal management review meeting → RPPS → Impact Analysis

Signal detection meeting(s) ← Signal evaluation

RPPS ← Regulatory action
Methodologies & Processes (1)

Empirica Signal used for analysis and data provision:

- Empirical Bayes Geometric Mean (EBGM) routine statistic of disproportionate reporting (SDR) since 2006. PRR used since 1996, and still computed alongside EBGM.

- Statistic calculated and analysed weekly for all products

- Drugs/ Vaccines analysed separately

- Patient & HCP reports analysed together
Empirica Signal – essential features for signal analysis:

- Different ‘views’ of the data enable different thresholds for groups of products
- Only DECs which meet thresholds in the given week are displayed for review
- Products allocated to named assessors each week; minimal manual intervention
MHRA Thresholds

- **UK reports (Black Triangle Products):**
  - All DECs reviewed

- **UK reports (Established Medicines):**
  - Non-listed DECs with $N \geq 3$, $EBGM \geq 2.5$, $EB05 \geq 1.8$
  - All fatal, paediatric, parent-child reports, all Alert Terms
  - Frequency change ($\geq 8\%$ reports received in last quarter)

- **Non-UK reports (Black Triangle Products):**
  - Serious unlisted reactions (excluding 1st cases with no UK cases)
    - All serious reactions from fatal reports
    - All unlisted alert term reactions

- **Non-UK reports (Established Medicines):**
  - Serious unlisted reactions with non-UK $n \geq 7$, $EBGM \geq 2.5$ & $EB05 \geq 1.8$
    - All serious reactions from fatal reports (excluding 1st cases with no UK cases)
    - All serious unlisted paediatric, parent-child, alert term reactions (excluding 1st cases with no UK cases)
Signal detection at the MHRA

For established drugs (Non-black triangle)
- Approximately 2000 drug – event combinations are assessed for UK & Foreign reports each week.
- 80 signals of which are discussed at the weekly signal generation meeting.

For new drugs (Black triangle)
- Approximately 4000 drug – event combinations are assessed for UK & foreign reports each week.
- 190 signals of which are discussed at the weekly signal generation meeting.
Timelines for signal review

2011/2012 Agency Signal target:
- Ensure all potential UK signals (relating to medicines and vaccines) from whatever source are acted on promptly: 80% initially evaluated within 5 working days

- For potential signals identified by Empirica target measured by addition of comments to DECs
- All Black Triangle product must have a deputy assessor
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>Haematopoietic leucopenia (SMQ) (narrow)</td>
<td>21054032</td>
<td>OC</td>
<td>1</td>
<td>624</td>
<td>170</td>
<td>7.02</td>
<td>9.00</td>
<td>10.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>Haematopoietic leucopenia (SMQ) (broad)</td>
<td>21054032</td>
<td>OC</td>
<td>1</td>
<td>627</td>
<td>171</td>
<td>7.88</td>
<td>8.93</td>
<td>10.1</td>
<td></td>
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</tr>
<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>Haematopoietic cytopenias (SMQ) (narrow)</td>
<td>21054032</td>
<td>OC</td>
<td>1</td>
<td>893</td>
<td>218</td>
<td>5.91</td>
<td>6.62</td>
<td>7.59</td>
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<tr>
<td>CYCLOPHOSPHAMIDE</td>
<td>Haematopoietic cytopenias (SMQ) (broad)</td>
<td>21054032</td>
<td>OC</td>
<td>1</td>
<td>929</td>
<td>221</td>
<td>6.92</td>
<td>6.17</td>
<td>6.80</td>
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<tr>
<td>CYTARABINE</td>
<td>Thrombocytopenia</td>
<td>Blood</td>
<td>Listed</td>
<td>21240853</td>
<td>A</td>
<td>1</td>
<td>33</td>
<td>0.877</td>
<td>1.58</td>
<td>3.80</td>
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<tr>
<td>CYTARABINE</td>
<td>Haematopoietic leucopenia (SMQ) (broad)</td>
<td>21240853</td>
<td>O</td>
<td>1</td>
<td>143</td>
<td>33</td>
<td>3.77</td>
<td>5.06</td>
<td>6.60</td>
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<tr>
<td>CYTARABINE</td>
<td>Haematopoietic leucopenia (SMQ) (narrow)</td>
<td>21240853</td>
<td>O</td>
<td>1</td>
<td>149</td>
<td>33</td>
<td>0.70</td>
<td>4.00</td>
<td>6.60</td>
<td></td>
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<tr>
<td>CYTARABINE</td>
<td>Haematopoietic cytophenias (SMQ) (narrow)</td>
<td>21240853</td>
<td>O</td>
<td>1</td>
<td>183</td>
<td>33</td>
<td>3.03</td>
<td>3.57</td>
<td>3.13</td>
<td></td>
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<td></td>
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<tr>
<td>CYTARABINE</td>
<td>Haematopoietic cytophenias (SMQ) (broad)</td>
<td>21240853</td>
<td>O</td>
<td>1</td>
<td>189</td>
<td>40</td>
<td>2.87</td>
<td>3.75</td>
<td>4.84</td>
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<td></td>
<td></td>
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<tr>
<td>DEXAMETHASONE</td>
<td>Thrombocytopenia</td>
<td>Blood</td>
<td>Listed co-suspect</td>
<td>21240853</td>
<td>A</td>
<td>1</td>
<td>12</td>
<td>0.25</td>
<td>0.73</td>
<td>1.74</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETHANOL</td>
<td>Drug interaction</td>
<td>Grrl</td>
<td>Cannot assess usual</td>
<td>21054031</td>
<td>OA</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>2.63</td>
<td>5.20</td>
<td>9.15</td>
<td></td>
</tr>
<tr>
<td>ETHANOL</td>
<td>Loss of consciousness</td>
<td>Nerv</td>
<td>Listed co-suspect</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>3.33</td>
<td>6.19</td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>ETHANOL</td>
<td>Fatal</td>
<td>(Special PT Group)</td>
<td>PTGrip</td>
<td>No immediate action</td>
<td>21054031</td>
<td>OA</td>
<td>1</td>
<td>18</td>
<td>2.66</td>
<td>4.34</td>
<td>6.99</td>
<td></td>
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<tr>
<td>ETHANOL</td>
<td>Torsade de pointes/QT prolongation (SMQ) (broad)</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>44</td>
<td>19</td>
<td>2.58</td>
<td>2.04</td>
<td>3.76</td>
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<td>ETHANOL</td>
<td>Noninfectious meningitis (SMQ) (broad)</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>38</td>
<td>25</td>
<td>1.95</td>
<td>2.74</td>
<td>3.80</td>
<td></td>
<td></td>
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<tr>
<td>ETHANOL</td>
<td>Noninfectious encephalitis (SMQ) (broad)</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>51</td>
<td>25</td>
<td>2.27</td>
<td>2.84</td>
<td>3.82</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETHANOL</td>
<td>Noninfectious encephalopathy/deirnium (SMQ) (broad)</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>56</td>
<td>20</td>
<td>2.07</td>
<td>2.60</td>
<td>3.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETHANOL</td>
<td>Cardiac arrhythmias (SMQ) (broad)</td>
<td>21054031</td>
<td>O</td>
<td>1</td>
<td>51</td>
<td>24</td>
<td>1.82</td>
<td>2.52</td>
<td>3.40</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>FLUORARABINE</td>
<td>Agranulocytosis</td>
<td>Blood</td>
<td>Listed co-suspect</td>
<td>21054032</td>
<td>AC</td>
<td>1</td>
<td>49</td>
<td>1.43</td>
<td>3.19</td>
<td>6.35</td>
<td></td>
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</tr>
<tr>
<td>FLUORARABINE</td>
<td>Agranulocytosis (SMQ) (narrow)</td>
<td>21054032</td>
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RPPS & Impact Analysis

Evidence based tools for further evaluation of signals:

**Impact Analysis**
- This is a tool to prioritise possible signals and decide the next step that should be taken. This takes into consideration the strength of evidence as well as the public health implications of the signal.

**RPPS**
- The Regulatory Pharmacovigilance Prioritisation System. This is further signal prioritisation also taking into account public perception of the ADR and Agency obligations.
Impact Analysis

- Interim step between signal detection & detailed signal evaluation
- Summarises impact of a signal through two scores:
  - Evidence (strength of evidence for causality)
    - Mean of EBGM/EB05
    - Strength of evidence from spontaneous reports
    - Biological plausibility
  - Public health (public health implications)
    - Number of cases reported per year
    - Health consequences of the ADR
    - Reporting rate over last year
RPPS

- System of issue prioritisation which follows on from Impact Analysis and uses some of the same principles:
  - Strength of evidence for a causal effect
  - Potential public health implications
  - Public perceptions
  - Agency obligations

- Aid to the management of multiple dynamic issues in the allocation of resources

- Ensures that appropriate timescales are defined to meet MHRA’s public health and other obligations

- Aid to pharmacovigilance audit

- Overall priority linked to timescales
Signal Management

- All signals that warrant further action are discussed at our Signal Management Review Meeting.

- Brings together expertise across the Agency including Assessors, Medics and Epidemiologists.

- Signals are fully evaluated including assessment of biological plausibility and potential class effects.

- Action are discussed and endorsed (including further expert advice required) the priority of the signal is agreed and team allocation is decided.
Signals investigated in 2009 & 2010

- 277 signals - detailed review (53 contributing signals)
- 15 index cases
- 16 signals from Yellow Card data contributed to DSU articles

Outcomes of signals investigated in 2010

- Variation implemented 23%
- Communication delivered 24%
- Other measures implemented 10%
- Await further evidence 43%

- 19% of signals in 2009 & 2010 had contributing reports from members of the public
Patient signals in 2009 & 2010

154 signals investigated 2009 - 24 contributing
123 signals investigated 2010 - 29 contributing

- orlistat and device interaction - MAH review
- amlodipine and food interaction grapefruit juice - update to SPC/PIL.
- hyoscine and visual hallucinations
- spironolactone and drug hypersensitivity - further evidence for strength
- cyproterone and hepatic failure – update to SPC/PIL
- nitrofurantoin and alveolitis fibrosing – update to SPC/PIL
- desogestrel and suicidal ideation - PSUR
- levonorgestrel and suicidal depression – PSUR
- simvastatin and epistaxis – PSUR

Others include:
- pandemic – condition aggravated e.g. convulsions
- internet– investigated by enforcement team e.g. slimming pills.
- herbals– St John’s Wort
Regulatory Action & Communication

- Updating product information (SPC/PIL)
- Restrict indications / introduce new contra-indications / reduce the recommended dose
- Warnings in Drug Safety Update
- Inform rapporteur/RMS
- Raise in PSURs

Most importantly: Who should receive any communications?
- Proactive communication?
Next steps…

Article 102:
‘The Member States shall: (1) take all appropriate measures…..To encourage patients, doctors, pharmacists and other health-care professionals to report suspected adverse reactions to the national competent authority’

Article 107h:
‘…..national competent authorities in collaboration with the Agency, shall take the following measures…(c) monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk-benefit balance.’
Summary

• Every Yellow Card submitted is important to us
• Numbers of patient reports very encouraging– 75% increase since 05
• Promotion +ve impact on reporting; commitment & contribution
• Excellent move towards electronic reporting (70%)
• High quality – descriptive reporting, impact on patient QoL
• Positive contribution to signal detection and drug safety signals increased from 15.6% in 2009 to 23.6% in 2010 from patients.
• Capable of supporting real time pharmacovigilance
• Future system needs to continue to support signal detection from all ADR reports
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