Revealed: the prescription drugs and medications most likely to harm or kill you

Andrew Wasley and Bethany Hubbard | 13th March 2012

Although most people take prescription drugs without suffering side effects, for some patients medications can lead to serious adverse reactions

Official data suggests antidepressants, antipsychotics, stop smoking drugs, vaccines against swine flu and even paracetamol cause adverse drug reactions. So just how safe are they? Andrew Wasley & Bethany Hubbard report

A drug used to treat schizophrenia and thought disturbances in patients with

Parkinson's disease is the medicine most likely to harm or kill you in the UK, figures obtained by the *Ecologist* reveal.

Antidepressants, drugs to help patients give up smoking and vaccines against meningitis, Human Papilloma Virus (HPV) and swine flu are also among medicines most likely to result in adverse reactions, data compiled by the UK's official drug watchdog indicates.

The statistics, recorded by the Medicines and Healthcare Products Regulatory Agency (MHRA), also show that substances used to treat rheumatoid arthritis, eye diseases and blood clotting are among those with the highest number of reported adverse reactions involving a 'fatal outcome'.

The figures record the total number of suspected adverse reaction reports - which can relate to physical or mental side effects - received by the body during a period spanning more than ten years.

A range of medicines were linked to 274,123 suspected adverse reactions reports received by the MHRA between January 2000 to November 2011. 12,020 deaths linked to these adverse reactions were recorded in the same period.

The MHRA compiles the data via its Yellow Card Scheme that enables doctors, drug companies and patients to report reactions they suspect have arisen from specific drugs or medicines.

Patients groups and some medical experts say that officially-recorded figures are only the tip of the iceberg however, with many adverse reactions linked to prescription drugs going unreported. 'Consultants and doctors do not [always] report adverse reactions,' Millie Kieve, from the Adverse Psychatric Reactions Information Link (APRIL), said. 'Patient Yellow Card reporting is not well publicised'.

'Harms are often unrecognised, ignored, denied, hidden, or

attributed to other causes,' Professor Andrew Herxheimer, pharmacologist and Emeritus Fellow of the UK Cochrane Centre, told the *Ecologist* in a written statement.

A 2004 study by the University of Liverpool suggested that as many as 10,000 patients annually were dying in the UK because of adverse reactions. The researchers stressed the overwhelming majority taking medication do not suffer side effects.

A later report by the think tank Compass claimed that more than a million patients were admitted to UK hospitals in 2006 as a result of the drugs they were prescribed, and estimated the problem cost the NHS nearly £2 billion a year.

The MHRA acknowledges that the true number of adverse reactions is higher than official figures show as the Yellow Card Scheme is associated with 'an unknown level of under-reporting.'

In most cases however the number of those suffering from reactions to specific drugs is very small in comparison to the volume of patients taking the medicine with no apparent side effects. Many of the side effects prompting reports to the Yellow Card Scheme are minor reactions causing little or no long term harm.

Doctors point out that all medicines used in the UK have to go through a strict testing and licensing procedure in order to be approved, and claim medicines are constantly reviewed by drug manufacturers. They also caution that proving that a drug caused an adverse reaction is fraught with difficulty.

Serious side effects

According to the figures, Clozapine – used to treat patients suffering from schizophrenia – was the subject of 17,649 suspected adverse reaction reports between January 1st 2000 and 20th November 2011. The drug was linked to the deaths of 1,972 patients in the same period, the MHRA data reveals.

Clozapine, which is also used to treat patients with Parkinson's disease, has been linked to a number of serious side effects including blood disorders. One of the conditions associated with the drug is agranulocytosis, which sees the number of white blood cells decrease and impairs the body's ability to fight off infections.

The drug - usually administered after other antipsychotic

substances have failed to work - has been the subject of a dedicated Patient Monitoring Scheme since 1990 where patients receive regular blood tests for agranulocytosis and blood counts are routinely monitored.

The MHRA figures also show that Neisseria meningitidis vaccine - used to protect against bacterial meningitis - has been the subject of 13,460 suspected adverse reaction reports between 2000 and 2011.

The drug, administered via an injection, is routinely prescribed in the UK to children over two months, to adolescents and to adults. Many adverse reactions linked to the vaccine are relatively minor including headaches and irritability, fainting and dizziness, although cases of lymphadenopathy - swelling of the lymph nodes – and other more serious reactions have been reported.

Bupropion, used to treat depression and to assist patients wanting to give up smoking, was linked to 9306 suspected adverse reactions in the 11 year period. The drug is one of several antidepressants used to treat nicotine addiction appearing in the MHRA figures.

Varenicline was the subject of 7298 suspected adverse reactions, 80 of which had a fatal outcome. 39 of these reports were suicide, according to the MHRA.

The vaccine for Human Papilloma Virus (HPV), a common sexually transmitted infection that can leader to cervical cancer in women, was linked to 6095 adverse reactions.

Swine flu vaccine was reported for 3561 suspected adverse reactions.

Ranibizumab, prescribed to treat the eye disease Age-related Macular Degeneration (AMD), which sees patients ability to see straight ahead, read, write or perform other everyday actions, was linked to 549 deaths in the period covered by the data.

Infliximab, used to treat rheumatoid arthritis, Crohn's disease and psoriasis, amongst other auto-immune disorders, was linked to 4428 adverse reaction reports, 520 of which had a fatal outcome.

According to one manufacturer of Infliximab, the drug has been linked to serious infections in some patients, including tuberculosis and histoplasmosis. Some of these infections have proved fatal.

Cancers have been reported in some patients being treated with the drug. Another drug used to treat similar conditions, Adalimumab, was the subject of 295 suspect adverse reaction reports with a fatal outcome.

Warfarin, administered to help prevent blood clots forming, was reported in relation to the deaths of 191 people. Paracetamol – one of few drugs featuring in the data that is available over the counter without a prescription – was the subject of 162 suspected adverse reactions with a fatal outcome.

'Focus on harm, not benefits'

Campaigners say the issue of adverse reactions continues to be little understood by the public and want more research into side effects, better education of doctors, and clearer warnings for consumers.

Millie Kieve told the *Ecologist*: 'Doctors fail to recognise adverse reactions, in particular psychiatric reactions, and often increase the dosage with serious consequences.'

Kieve, who founded APRIL after her daughter died following 'years of adverse reactions', said that the training of medical students does not include enough emphasis on recognising or treating adverse reactions.

She also said literature outlining the side effects of particular medicines was not always made available to patients: 'Patient Information Leaflets are not always included in the package if they are split or taken from bulk supply...' she said.

Andrew Herxheimer believes there needs to be a 'complete rethink' of the current pharmacovigilance system:

'A basic fault is that research aiming primarily to find benefits of drugs, devices and procedures gets vastly more funding than the investigation of potential and actual harms from them.

'The ratio between the two seems not to have been properly estimated. We need the data: ethics and common sense demand parity of funding for research on positive and negative effects of treatments,' the pharmacologist said.

He also said that spontaneous reporting alone – such as the Yellow Card Scheme – 'is not an adequete solution and can only

supplement proactive research on adverse effects.'

'Research on harms cannot be left to the industry – manufacturers cannot be expected or made to do it,' Herxheimer said. 'The priorities and the funding must come from society as a whole, and logically that should apply to all therapeutic research.'

Campaigners have previously highlighted the MHRA's links to industry funding – the agency is partly paid for by fees from pharmaceutical companies – although the body denies there is any conflict of interest and says complex licensing decisions are referred to independent advisory committees.

Last year an *Ecologist* investigation revealed how an increasing number of UK patients claim to have been 'poisoned' by the commonly prescribed antibiotic Ciprofloxacin.

Many claimed to have experienced a 'frightening' number of mental and physical side effects after being prescribed the drug that has been linked to more than 40 deaths and 1200 adverse reaction reports in the UK since 2000.

'No proof of reactions'

Medical experts have warned against drawing firm conclusions over adverse reaction reports, arguing that in most cases it is very difficult to pinpoint whether a specific drug is responsible for a specific reaction.

They also point out that the figures need to be considered in the context of the often-serious illnesses drugs are being used to treat, and say that in many cases people prescribed particular drugs suffer no adverse side effects at all.

Jeffrey Aronson, President Emeritus of the British Pharmacological Society, previously told the *Ecologist*: 'Only in a very few – and rare – cases [of adverse reactions] can you be sure. In 99.9 per cent of cases you don't get obvious proof.'

Aronson said that there is an assumption that people 'take a tablet, get an effect', and therefore that the two are linked. But the reality, according to Aronson, is that 'things happen coincidentally, there is a tension here as [drugs] can cause adverse reactions but whether it was directly to blame for specific symptoms, that's different,' he said.

The MHRA stated that: 'All medicines have side effects – no effective medicine is without risks. Our priority is to ensure that the benefits outweigh the risks. It is important to note that a report of an adverse drug reaction does not prove that it was caused by the drug. Other factors such as the underlying disease or other medicines may contribute to suspected adverse reactions.'

In relation to the drug substances with the highest number of suspected adverse reaction reports, the body said: ‘These are medicines for which reporting is recognised to be high as they include newly introduced medicines (such as swine flu vaccines, Adalimumab and Ranibizumab which are / were on the intensive monitoring scheme), medicines which are widely used (such as Simvastatin, Morphine and Warfarin), those that are the subject of considerable public interest (Varenicline) or those that have a dedicated Patient Monitoring Scheme (Clozapine).

‘The number of reports of adverse reactions that are received in association with a drug depends on many factors including the extent of use of the drug and the publicity surrounding the drug. In addition, reporting tends to be high for newly introduced medicines,’ the MHRA continued.

The body said that when intepreting the data it was important to note that causality has not been established.

‘The fact that an adverse reaction has been reported does not necessarily mean that the medicine has been proven to cause the reaction. Many factors have to be taken into account in assessing the relationship between a drug and suspected reaction including how long after taking the suspected drug the reaction occurred, the possible contribution of other drugs being taken, and the underlying disease,’ the body stated.

In relation to one of the more well known drugs featuring in the statistics, Varenicline – linked to 39 suicides – the MHRA stated: ‘Smoking cessation, with or without drug treatment, is associated with various psychiatric symptoms including depressed mood.

‘Smoking cessation is also recognised to be associated with the deterioration of pre-existing mental health illnesses. A significant proportion of cases of suicide-related events reported for [Varenicline] occurred in people with a history of mental health problems.’

APRIL is lobbying the Government to incorporate greater vigilance

of those believed to be suffering adverse reactions – including pyschiatric problems linked to withdrawal from certain drugs – into the National Suicide Prevention Strategy.

In a letter to the Department of Health last October, signed by several leading pharmacologists, the group stated: 'Every week we receive emails from the public giving details of suicides, agitation and self-harming linked to adverse drug reactions. We have been informed about young people who died by suicide having been discharged, when agitated and suicidal, from A & E without their families being contacted.

'Akathisia (extreme agitation) is an adverse side effect that if not recognised can lead to tragic harm to the patient or others,' the letter continued.

In December, lawyers warned that doctors face being sued for 'creating prescription drug addicts' amid claims that some failed to follow safety guidelines when prescribing tranquilisers known as benzodiazepines.

Some patients have reportedly developed a tolerance after regular doses of the drugs, resulting in them needing a higher dose to have the same affects. Although not all patients have suffered adverse reactions whilst taking benzodiazepines, for some, withdrawal from the drugs has led to serious psychological and physical side effects.

Useful links:

Adverse Psychatric Reactions Information Link (APRIL)

Medicines and Healthcare Products Regulatory Agency (MHRA)

MHRA statistics:

1, Top ten drug substances for which UK spontaneous 'suspected' adverse reactions have been reported between 1st January 2000 and 20th November 2011

Drug Name | Number of adverse reaction reports

Clozapine 17649
Neisseria meningitidis vaccine (meningococcal vaccine) 13460
Bupropion 9306

Varenicline 7298
Human Papilloma virus vaccine 6095
Infliximab 4428
Rofecoxib 3618
Swine origin influenza virus vaccine 3561
Simvastatin 3434
Paroxetine 3084

2, Top ten drug substances for which UK spontaneous 'suspected' adverse reactions with a fatal outcome have been reported between 1st January 2000 and 20th November 2011

Drug Name | Number of fatal reports

Clozapine 1972
Ranibizumab 549
Infliximab 520
Adalimumab 295
Warfarin 191
Olanzapine 189
Methotrexate 177
Risperidone 167
Etanercept 162
Paracetamol 162

Source: MHRA, December 2011

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