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Newsreader - The Health Secretary, Jeremy Hunt, has said it's worrying that some of the key data surrounding the anti-viral drug 'Tamiflu' appeared not to have been made available to the scientific community for a very long time. He was responding to the findings of the Cochrane Collaboration, a network of academics, which has claimed the drug is ineffective because it shortens the length of time a person is ill only by a small amount. The government has spent hundreds of millions of pounds stockpiling the drug to combat a potential flu pandemic. Here's our medical correspondent, Fergus Walsh.

Fergus Walsh - During the swine flu pandemic of 2009, Tamiflu was given to hundreds of thousands of Britons. The Cochrane Researchers say the drugs don't work or at least not very well. They analysed clinical trial data, the Gold Standard of medical research, and concluded the manufacturers, Roche, had cherry picked evidence that showed the drug in the best light. But another team from Nottingham University whose study was funded by Roche looked at adults admitted to hospital during the pandemic involving the sickest patients and found it was highly effective in cutting the risk of death if given early enough. The two teams were looking at different sets of data but it doesn't completely explain why they came to such radically different conclusions. Tamiflu has made billions for Roche. For critics, it's become symbolic of the secretive nature of some pharmaceutical companies. The Cochrane team had to fight for five years to get all the study reports released. The Health Secretary, Jeremy Hunt, said the amount of time it took was worrying.

Jeremy Hunt - We need to know all the information that can help us make a judgement as to whether that vaccine, that injection, those drugs work and I am concerned by suggestions in this case that it took far too long for the Cochrane Collaboration to actually get access to that data.

Fergus Walsh - New European regulations means pharmaceutical companies will be forced to release all data on future clinical trials of drugs. But the rules don't cover existing medications. Roche has promised to be more open but dispute the findings of the Cochrane team. It's principal clinical scientist, Barry Clinch, pointed out the World Health Organisation, US and European health bodies all recommended Tamiflu.

Barry Clinch – There's a clear consensus across all of those people and that is a significant body of expertise that have looked at our data and share the same position that we do that Tamiflu is a very useful medicine for treating what is a serious respiratory infection that can lead to death in some instances.

Fergus Walsh – The government will have to decide whether to renew its stockpile of Tamiflu. But that decision will become easier in 2016 when its patent expires after which cheaper generic versions will be available.

HM Treasury

Treasury Minutes

Government responses on the Thirty Fifth to the Forty Fifth Reports from the Committee of Public Accounts: Session 2013-14.

This publication includes revisions to the Twenty Eighth and Thirty Second reports.

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April 2014

Thirty Fifth Report

Department of Health

Access to clinical trial information and the stockpiling of Tamiflu

All new medicines require a licence. UK-only licences are granted by the MHRA. European Union (EU)-wide licences are granted by the European Commission with the licensing process coordinated by the EMA. In England, some medicines are also appraised by NICE to assess the clinical and cost-effectiveness for use in the NHS. Clinical trials on humans are the key source of information used to understand the safety and efficacy of a medicine. The majority of clinical trials are undertaken, or sponsored, by the medicine manufacturer.

The number one risk on the Government's national risk-assessment for civil emergencies, ahead of both coastal flooding and a major terrorist incident, is the risk of pandemic influenza. Antiviral medicines contain an active substance which interferes with the influenza virus, stopping it from spreading. Between 2006-07 and 2012-13, the department spent £560 million on antiviral medicines for use in an influenza pandemic - £424 million on Tamiflu and £136 million on Relenza. Just under 40 million units of Tamiflu were purchased.

On the basis of a report by the NAO, the Committee took evidence, on 17 June 2013, from the Department of Health, MHRA, NICE and the British Medical Journal on the availability of clinical trial results; how the MHRA and NICE share information; and on the stockpiling of Tamiflu. The Committee published its report on 3 January 2014. This is the Government response to the Committees report.

Background resources

- NAO report: *Access to clinical trial information and the stockpiling of Tamiflu* - Session 2013-14 (HC 125)
- PAC report: *Access to clinical trial information and the stockpiling of Tamiflu* – Session 2013-14 (HC 295)

1: Committee of Public Accounts conclusion:
The Committee was surprised and concerned to discover that information is routinely withheld from doctors and researchers about the methods and results of clinical trials on treatments currently prescribed in the UK.

Recommendation
The department should take action to ensure that the full methods and results are available to doctors and researchers for all trials on all uses of all treatments currently being prescribed, and should also ensure that there is clear and frequent audit of how much information is available and how much has been withheld.

1.1 The Government disagrees with the Committee's recommendation.

1.2 It would not be feasible for the full methods and results to be made available for all trials and uses on currently prescribed treatments, and ensure frequent audit of such information. The department believes it is important for patients, researchers and the NHS that clinical trials are transparent, ensuring trial registration and outcome publication.

1.3 The department supports the European Commission's proposal for greater transparency under the new Clinical Trials Regulation, which will provide a clear legal basis for public access to an EU database for trial documentation and results of clinical trials conducted in the EU. If the trial is used to support a Marketing Authorisation application, then the Clinical Study Report must be submitted by the applicant within 30 days of the application's authorisation, rejection or withdrawal. In December 2013, informal agreement was reached on the proposed Regulation endorsed by Member States. The agreed text has to be formally agreed by the Council of Ministers and European Parliament.

2: Committee of Public Accounts conclusion:
The results of clinical trials on humans are the key evidence used by regulators, researchers and clinicians to assess whether a medicine works and how safe it is. Medicine manufacturers submit evidence on products they wish to market in the UK to the Medicines and Healthcare Products Regulatory Agency (MHRA) or the European Medicines Agency.

The scope for independent scrutiny of a medicine's effectiveness is undermined by the fact that the full methods and results of many clinical trials are not made available to doctors and researchers. The problem of non-publication of clinical trial results has been known since the mid-1980s.

Recommendation
The department and the MHRA should ensure, both prospectively and retrospectively, that clinical trials are registered on an appropriate registry and that the full methods and results of all trials should be available for wider independent scrutiny, beyond the work undertaken by regulators during the licensing process.

2.1 The Government disagrees with the Committee's recommendation.

2.2 The Government supports prospective trial registration. However, it is not feasible to ensure retrospective registration for all trials. The European Medicines Agency (EMA) database (EudraCT) registers all EU-approved clinical trials of investigational medicinal products. Since March 2011, this information has been publicly accessible through the EU Clinical Trials Register (excepting adult Phase 1 trials) - including all EU-conducted trials since May 2004 when the Clinical Trials Directive was implemented.

2.3 Under the proposed Clinical Trials Register, due mid-2016, documentation including the protocol, and a summary of results, will be publically available for all trials in the new EU database (excepting personal or commercially confidential data). Also, for trials supporting Marketing Authorisation, applicants must submit clinical study reports within 30 days of authorisation (rejection or withdrawal). MHRA and EMA have published public assessment reports following approval of new medicines since October 2005. The department supports the EMA's proposed policy on publication and access to clinical trial data.

2.4 From 30 September 2013, the Health Research Authority has required, as a condition of a favourable Ethics Committee approval, that all trials be registered on a publically accessible register.

3: Committee of Public Accounts conclusion:
NICE and the MHRA do not routinely share information provided by manufacturers during the process for licensing medicines.

Recommendation
NICE should ensure that it obtains full methods and results on all trials for all treatments which it reviews, including clinical study reports where necessary; make all this information available to the medical and academic community for independent scrutiny; and routinely audit the completeness of this information. NICE and the MHRA should put in place a formal information sharing agreement to ensure when NICE appraises medicines it has access to all of the information provided to regulators by the manufacturer during the licensing process.

3.1 The Government agrees with the Committee's recommendation.

Target implementation date: December 2014.

3.2 When applying for marketing authorisation of a new medicine, a company is legally required to provide the relevant regulator with the results of all clinical trials relevant to the evaluation of the product concerned (whether the results are favourable or unfavourable). NICE is currently consulting on changes to its technology appraisal process guidance that requires the medical director of the manufacturer or sponsor of the technology under appraisal to confirm that all the data necessary to the appraisal, within the Company's possession, custody, or control in the UK or elsewhere, has been disclosed to NICE or its authorised agents. The proposed changes also include a requirement on companies to consent to NICE being provided directly by the relevant regulatory authorities all data necessary to the appraisal, where the company is not able or willing to submit this directly to NICE. Revised guidance will be published September 2014.

3.3 NICE and MHRA are currently considering their practical working arrangements on a range of issues including information sharing between both organisations. These arrangements will be made public once agreed and finalised.

4: Committee of Public Accounts conclusion:
The number one risk on the Government's national risk-assessment for civil emergencies, ahead of both coastal flooding and a major terrorist incident, is the risk of pandemic influenza.

There remains a lack of consensus over how well Tamiflu works and there is disagreement about whether regulators and NICE received all the information on Tamiflu during the licensing process.

Recommendation
Once the Cochrane Collaboration has completed its review of Tamiflu using all clinical study report information, the department, MHRA and NICE should consider whether it is necessary to revisit previous judgements about the efficacy of Tamiflu.

4.1 The Government agrees with the Committee's recommendation.

Target implementation date: 2015.

4.2 Tamiflu is a centrally authorised medicinal product (the marketing authorisation was granted by the European Medicines Agency). EMA has regularly reviewed the safety and quality of Tamiflu through the Committee for Medicinal Products for Human Use. MHRA has not seen any new evidence that calls into question the regulatory decisions taken on Tamiflu. Roche is under a legal obligation to share any such information with regulators - if any new information comes to light, it will be carefully considered. Any regulatory action would need to be co-ordinated by the EMA.

4.3 NICE will reconsider the case for reviewing its current guidance on the use of Tamiflu, in the light of an update to the Cochrane Collaboration review, when it is published, together with any new evidence. The decision will be informed by an assessment of the degree to which any new evidence might cast doubt on the current recommendations. NICE guidance does not cover the use of Tamiflu in a pandemic, impending pandemic, or a widespread epidemic of a new strain of influenza to which there is little or no community resistance.

5: Committee of Public Accounts conclusion:
The case for stockpiling antiviral medicines at the current levels is based on judgement rather than evidence of their effectiveness during an influenza pandemic.

Recommendation
Before spending the £49 million to maintain a stockpile at 50% population coverage, scheduled for 2013-14, the department should review the appropriate level of population coverage; the level of stockpiling in other countries; and take into consideration the fact that the patent for Tamiflu expires in 2016.

5.1 The Government disagrees with the Committee's recommendation.

5.2 The 2013-14 exchange programme was already in place. The process is time-critical - outbound stock must be shipped when it has a one month plus shelf life left. If the department had not exchanged the stock, this would have been written off. The decision to exchange the current stocks of Tamiflu for new stocks with a 7-year shelf life supports the department's commitment to be ready for a more severe influenza pandemic and to pay the prices agreed in the current contract. Future stockpile decisions will take account of the latest scientific evidence and international comparisons, which will help to inform the department's policy for the desired population coverage levels and commercial factors, including the patent situation from 2016, which will inform the options available to meet the needs at that time.

6: Committee of Public Accounts conclusion:
The department wrote off £74 million of Tamiflu as a result of poor record-keeping by the NHS on how the medicine had been stored during the 2009 influenza pandemic.

Recommendation
The department should seek assurances that bodies involved in the distribution of antiviral medicines during a pandemic follow the department's revised guidance and have robust storage and quality-control systems in place.

6.1 The Government agrees with the Committee's recommendation.

Recommendation implemented.

6.2 NHS England and Public Health England (PHE) are involved in the arrangements for the distribution of antiviral medicines for an influenza pandemic. The Department of Health seeks assurances from NHS England and PHE through the Pandemic Influenza Preparedness Programme Board chaired by the Chief Medical Officer for the UK Government.

6.3 PHE maintains the Antiviral Distribution guidance and has met with NHS England officials to ensure that these requirements continue to be included as part of pandemic flu preparedness planning. This is built into the department's mobilisation plans for a pandemic response. NHS England continues its work through the Chief Pharmacist and his team to ensure that the distribution of antivirals during a pandemic is in line with the Department's guidance. This includes ensuring that providers of antiviral distribution have storage and quality control systems in place in line with regulatory and industry requirements.