CONFIDENTIAL

NEW VARIANT CJD AND BLOOD SAFETY

Issue

1. There is very little firm evidence about nvCJD - the disease is too new. We cannot yet predict the number of people likely to get nvCJD, the human infectious dose, or the incubation period. However, we do know that there is a theoretical but as yet unquantifiable risk of transmission from blood/blood products and that this appears to be associated with the lymphatic system and white blood cells.

2. The European Committee on Proprietary Medicinal Products (CPMP) is about to issue a statement (on 27 February) advising a move away from UK sourced products and extending recall action. Importing companies in four EU countries have already cancelled existing contracts with the NHS Bio Products Laboratory (BPL), part of the National Blood Service and the UK main supplier; other countries are likely to follow. These developments will have major implications for confidence in UK blood and the safety of medical products made from it. The UK Government needs a clear public position on these issues before the CPMP announcement at the end of the month.

Current position

3. To date there have been 23 confirmed cases of nvCJD. The pattern of the BSE epidemic would suggest that we could be looking at anything between a further 200 and 100,000 cases over a 25 year period. Of these, 5% (i.e. between 20 and 5,000 people) are likely to be blood donors. In the light of evidence last November identifying the nvCJD agent as identical to that which causes BSE in cattle, the Government, acting on the advice of scientific committees (SEAC and the Advisory Committee on the Microbiological Safety of Blood and Tissue) announced:

* an urgent assessment of the risks of nvCJD transmission through blood and blood products, and

* that the National Blood Authority should prepare a strategy for the possible removal of white blood cells (leucodepletion), should the risk assessment indicate this to be necessary.

These are both due at the end of February. However, it now appears probable that the risk assessment will be inconclusive as so little is known about nvCJD.

4. A wide-ranging programme of research is also in train covering risk factors, screening tests and transmissibility, but it will be at least 18 months to two years before any results are available. In the meantime the CPMP announcement, action by other countries and public concern could force our hand.

Blood

5. There are some 800,000 blood transfusions every year, necessary to preserve life or avoid severe ill health. The available evidence suggests the nvCJD agent could be in the white blood cells so human to human transmission is theoretically possible with their use. There is also no alternative source of supply. (We could not import the 2.5 million units required to satisfy NHS needs each year.) The Government's position so far has been that it would take all necessary steps recommended by the experts to safeguard patients. Given that any single unit of blood is likely to be used for a maximum of three patients it could be argued that the level of risk is likely to be low. **One option therefore would be to take no further action unless the science were to show this was required.** However, SEAC have said "it is logical to seek to minimise any risk from blood or blood products by reducing the number of lymphocytes (white blood cells) present" and recommended "that the Government should consider a precautionary policy of extending the use of leucodepleted blood and blood products as far as is practicable." To date the Government has always followed SEAC's advice.

6. Blood safety is an emotive subject which depends on the unique gift relationship between donor and patient and safeguarding the blood supply is essential to the functioning of the NHS. **The only option we have at present of making blood for transfusion safer is through leucodepletion**. The technology is proven and there is good evidence that it would reduce white cells by at least 90% and any risk by a factor of up to a thousand. Also, leucodepletion has additional clinical benefits as it reduces post-operative infection.

7. Adopting such an approach would reassure the public, the professions and EU member states that the UK Government was taking all practicable steps to safeguard UK blood.The costs, however, would be high, some £63-82 million pa. This would appear a very high investment in terms of possible health benefit, particularly given that the risk is theoretical and non-quantifiable. (Leucodepletion would add an extra £20 to a unit of blood, compared with £4 for hepatitis C and £1 for HIV testing.)

8. We are however in a similar position to the start of the BSE epidemic. The UK thought then that risks were low and that preventive action was not necessary. This led to significant costs both in terms of human health and social and economic consequences which we now know could have been reduced. It is not impossible that we could see a similar picture developing in the case of nvCJD, as person to person transmission by blood transfusion could prolong the potential epidemic. The high

costs need therefore to be balanced against the potential, but nevertheless still hypothetical, future risk.

9. Further, any action on blood has to take account of decisions to improve the safety of blood products from the nvCJD risk. If it were decided to take steps to safeguard blood products, but leucodepletion was not introduced, there would inevitably be criticism that nothing had been done for patients who have no option but to accept blood transfusion in life-threatening situations.

10. SEAC and MSBT will be considering these matters in early March and may offer further advice to Government.

Blood Products

11. Blood products are different from transfusion blood in that they are created from pools of plasma from up to 66,000 donors and consequently exposure to the implicated agent could be significantly higher. There are some 43 licensed products of which 15 have widespread use - surgical patients (100,000), pregnant women at risk of rhesus babies (90,000), hepatitis travel immunisations (90,000), tetanus immunisations (80,000), diagnostic products (50,000) haemophiliacs (1,300), a total of some 350,000 patients pa. This figure would at least double to 700,000 if we were to include the products which use blood components as stabilisers in other medicines.

12. There are alternative supplies of these products from non UK sourced blood, however BPL is the main supplier to the NHS. It would not, therefore, be possible to move from UK plasma derived products immediately without compromising supply and damaging patients.

13. For blood products there would appear to be three main options:

The first, as for blood for transfusion, would be to await the risk assessment or further scientific evidence.
This is not really feasible since four EU countries have effectively banned UK sourced products already, and the position will be compounded by the CPMP statement at the end of the month and the possibility of growing concern at home. BPL sales are likely to decline rapidly leading to the plant's collapse within a year. This would cost in the region of £22 - 31 million in 1998/99 rising to £28-39 million in 1999/2000,

The second would be to free up BPL to import non-UK sourced plasma (possibly from paid donors) and to make the full range of products from non-UK sources. This could usefully be combined with a partial move to funding recombinant Factor VIII (the main treatment for haemophilia) for children and previously untreated patients. This would have the double advantage of going part way towards meeting the concerns of the haemophilia community, whilst enabling BPL to compete in the market safeguarding its short-term future. This option would cost £26.7million pa.

The third would be to move fully towards recombinant products for haemophiliacs and non-UK sourced products in all other cases.
While this would have maximum impact in terms of meeting the concerns of the haemophilia community, it would signal the demise of BPL as a national source of blood products and would be difficult presentationally because it would be against the grain of wider NHS policy on clinical effectiveness. This option would cost £49.5 million in 1998/99 rising to £56 million in 1999/00.

BPL

14. The first and third options in para 13 would mark the end of BPL. This would expose the NHS to a narrower choice of blood products, weaker supply and increasing susceptibility to market forces overseas. This would be undesirable, at least in the short term, because of the risk to supply, and in the longer term, if research currently in hand were to prove that nvCJD were not transmissible through blood products, or that the manufacturing process removed the nvCJD agent, thereby making the UK product safety profile comparable with that of non UK sourced products.

Timescales

15. In order to maintain public confidence and safeguard the UK blood supply the Government will need a clear way forward on these issues in advance of the CPMP announcement on 27 February. As CPMP conclusions are already filtering out an even earlier announcement would be helpful. However CPMP, the European Commission and our EU partners would need to be informed of our position in advance. FCO would also need to notify other Governments worldwide.

16. A decision to provide recombinant Factor VIII for children and new patients could be implemented without delay. However the replacement of UK sourced plasma for fractionation by BPL with alternative sources from abroad (Option 2 in paragraph 13) would require several months for full implementation. Similarly leucodepletion even if the decision was taken now could not be fully implemented for all UK blood stocks until next spring.

17. An annex summarising the options, costs and benefits is attached.

Department of Health
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ANNEX

(1) BLOOD FOR TRANSFUSION

Population potentially affected: 800,000 blood transfusions pa
Risk level: Potentially 20 - 5,000 donors with nvCJD over the next 25 years(4 donors with confirmed nvCJD so far). Each unit of blood goes to a maximum of three patients. No available alternative.

OPTION 1

Await the risk assessment or further scientific evidence.

Cost: As yet unquantified, but potential significant public health risk.

Benefits: In line with general NHS approach of basing action/treatment on strong science

Disbenefits: Potential growing public and clinical concern

Europe: Likely to urge precautionary policy of maximum safety - BSE experience made some partners suspicious that UK does not act as promptly as it might to reduce risks.

BPL: Could reinforce doubts about safety of blood products.

OPTION 2

Leucodepletion

Cost: Between £63-85 million pa

Benefits:

- Evidence that it would reduce white cells by at least 90% and any risk by a factor of three.
- Additional clinical benefits (reduction in post-operative infection).
- In line with SEAC advice
- Reassure public/clinicians that Government doing all can

Disbenefits:

- Risk only theoretical (evidence may later demonstrate that leucodepletion unnecessary/ineffective)

Europe: EU members reassured UK taking all possible steps.

BPL: could reassure patients/clinicians using blood products

(2)BLOOD PRODUCTS

Population potentially affected: up to 700,000 people
Risk level: Products made from plasma pools of up to 66,000 donations, potential exposure to implicated agent therefore significantly increased.

Option 1

Await the risk assessment or further scientific evidence.

Cost: £22-31 million (1998/99); £28-£39 million (1999/00 and beyond)

Benefits:

- in line with wider NHS approach of basing action/treatment on strong science

Disbenefits

- potential growing public and clinical concern

Europe: Possible further moves to ban UK products and increasing suspicion that UK not acting promptly

BPL : rapid decline in sales leading to BPL collapse and risk to future supplies

Option 2

Free up BPL to import non-UK sourced plasma (possibly from paid donors) and to make the full range of products from non-UK sources, plus partial use of recombinant products for specific groups of haemophiliacs.

Costs: £27 million pa

Benefits:

- meets concerns of haemophilia community and other patients

- meets clinicians concerns

Disbenefits:

- will lead to pressure to provide recombinant products for all haemophiliacs

- seen as special treatment for haemophiliacs if not combined with leucodepletion

Europe: EU members reassured UK taking all possible steps

BPL: enable BPL to compete in market, safeguarding its short term future

Option 3

Move fully towards recombinant products for haemophiliacs and non-UK sourced products in all other cases.

Costs: £49.5 million(1998/99);£56 million(1999/00 and beyond)

Benefits:

- would meet concerns of haemophilia community

Disbenefits

- contrary to wider NHS policy on clinical effectiveness

- reduces clinician/patient choice

Europe: in line with many Member States' thinking

BPL: demise of BPL as national source of blood products