THE ROYAL MARSDEN

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DC/WM

25th January 2001

Professor J M Ritter
Chairman of MREC
Dept of Clinical Pharmacology
St Thomas' Hospital
Lambeth Palace Road
London SE1 7EH

Dear Professor Ritter

MREC(1)98/101 CLL4: A LRF sponsored trial from the MRC Adult Leukaemia Working Party [Our Ref M99/284]

The approval of an **oral form of fludarabine** has resulted in the need for a slight modification of the protocol for this study, in which we are now allowed to use either the IV form of fludarabine, as in the original protocol, or the new oral form. This will facilitate the management of patients, particularly those who live far from hospitals, and it could increase further the recruitment to this trial. The absorption of fludarabine (and cyclophosphamide which may be given also by mouth) has been taken into account in the revised protocol. **The information sheet** has also been revised to include a reference to the existence of the new form, which can be given by agreement between the patient and the doctor. These changes do not alter in any other way this trial which is recruiting well; 150 patients have been entered to date. I enclose the new protocol, which includes the new information sheet, together with a newsletter which gives details of the running of this study.

We will require a new DDX regarding the oral form of fludarabine and this is currently in hand. A number of other centres in the UK are now entering patients, which were not included in the original list; I enclose the new list.

Because the oral form will shortly be available, I would appreciate if your committee could revise these proposals and let us know the outcome as soon as possible, so that we can communicate this to the various LRECs. Let me know if you require any further clarification.

Thank you for your help.

Yours sincerely

Professor Daniel Catovsky

Encs

The radiotherapy service
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An NHS Trust

Patron: Her Majesty The Queen
Chairman: Mrs Tessa Green
Chief Executive: Miss Cally Palmer

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Please reply to: Professor J M Ritter, Chairman of the MREC
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Enquiries to: MREC Administrator
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Professor Daniel Catovsky
The Royal Marsden
Fulham Road
London SW3 6JJ

27th February 2001

Dear Professor Catovsky

MREC 98/1/101 **CLL4: A LRF sponsored trial from the MRC Adult Leukaemia working party (M99/284)**
Protocol amendment and revised PIS dated 25 01 01

The amendment and associated documents, as detailed, to the above named study, have been reviewed by a sub-group of the South Thames MREC.

The sub-committee had no ethical objections to the amendment and associated documents and therefore approval is given. You are asked to send a copy of the amendment and associated document, as detailed, and this letter to LRECs that have been involved in the review of this study for information only.

Yours sincerely

Jane Martin

pp **PROFESSOR J M RITTER**
Chairman, South Thames MREC

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Department of Health
MEDICINES CONTROL AGENCY
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Professor D Catovsky
Royal Marsden NHS Trust
Fulham Road
LONDON SW3 6JJ

Our Ref: MF8000/10800

21 February 2001

Dear Professor Catovsky

THE MEDICINES (EXEMPTION FROM LICENCES) (SPECIAL CASES AND MISCELLANEOUS PROVISIONS) ORDER 1972
PRODUCT: Fludarabine

I am writing in connection with your notification under the Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972 which relates to a proposed trial using Fludarabine supplied by Schering Health Care Limited.

This exemption is effective from 21 February 2001; the above-named supplier may lawfully supply the product for the purpose outlined in your notification: the Licensing Authority have decided not to issue a direction under article 4(2)(v) of the Order. There is no need for a marketing authorisation or for a clinical trial certificate for the purpose of the trial.

Please note that all serious unexpected adverse reactions occurring during the trial should be notified to the Licensing Authority.

In coming to its decision the Licensing Authority has not evaluated the safety, quality and efficacy of the product, and this notice should not be taken to imply approval of the product in terms of safety, quality or efficacy.

Remarks:
**** This DDX notification has been approved to permit the oral administration of fludarabine in the MRC CLL4 trial.***
**** It is noted that the proposed study is a multi-centre, -investigator study. Therefore, it is assumed that each additional investigator will be notified to the Licensing Authority (Clinical Trials Unit) and that s/he will not admit patients to this clinical trial until approval has been obtained.***

We shall be pleased to see a copy of any report which is produced as a result of this trial.

Yours sincerely

Mrs O Olayinka
CLINICAL TRIALS UNIT
ddxappro

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