L: The use of Licenced Drugs beyond their Product Licences.

L.1 All marketed drugs require a Product Licence. Amongst other things, this defines the clinical conditions for which a drug company can promote its product, along with the appropriate doses and routes of administration that the drug company can promote.

L.2 A Product Licence does not limit the clinical or prescribing freedom of doctors as described in The Medicines Act 1968. The responsibility for the consequences of prescribing outside the Product Licence lies with the prescribing doctor. Drugs prescribed for use outside their Product Licence can be dispensed by Pharmacists and administered by nurses and midwives. It is good practice for Pharmacists to ensure that doctors are aware that they are prescribing beyond the Product Licence.

L.3 Up to 25% all prescriptions in palliative care do not comply with the respective Drug Licence, typically for one or more of the following reasons:

- The clinical indication is not listed in the Drug Licence.
- The route of administration is not listed in the Drug Licence.
- The prescribed dose does not fall within the Drug Licence.

L.4 In a survey of Palliative Care Specialists in the United Kingdom, the majority of palliative care physicians considered it impractical to advise patients every time a drug was prescribed beyond the Product Licence. Furthermore, they considered it potentially harmful to the patient to act in such a way, as it would unnecessarily raise patient anxiety in many cases. Therefore, it seems reasonable to conclude that it is *not* standard practice in palliative care to obtain written informed consent each time a drug is prescribed in a way not described on the Product Licence. The Trustees and clinical staff at Katharine House Hospice agree with this general approach but appreciate that there are occasions when it is important to inform the patient more fully about prescribing issues and choices, *just as this can equally be the case for drugs prescribed within their Product Licences.*

L.5 Our procedure for informing patients about prescribing issues and choices is outlined below:

1) We inform all patients and relatives that we are always happy to discuss any aspect of their care and management with them and we always try to tailor our discussion of such matters to the expressed wishes of the patient. This approach is also highlighted in the following passage, taken from the Patient Information Leaflet entitled "A Way of Caring":
   "We try our best to put the patient at the heart of all discussions and decisions regarding their management. In conversation, we try to relate to people in ways that meet their individual needs. For example, whilst some people like as much detail as possible regarding their care, we are sensitive to the fact that others prefer to keep such conversations to a minimum… We hope that we succeed in our efforts

to care and we always welcome feedback and suggestions about how we might further improve."

A similar message is contained in the leaflet entitled "Information for Health Care Professionals".

2) The only times we routinely highlight the prescription of a drug in a manner not described in its Product Licence is when one or more of the following conditions apply:
   - The patient has clearly expressed a wish to know every relevant detail regarding their ongoing care.
   - If other treatment options exist that do not require prescribing beyond the Product Licence.
   - If the potential benefit of the proposed treatment is considered small or is even unsubstantiated.
   - If the potential risks of the proposed treatment are considered large.
   - If the proposed treatment has not been used in this hospice before.
   - If the drug has no Product Licence at all.
3) With as many as 25% all palliative care prescriptions falling outside the relevant Product Licence, it is self evident that certain examples of prescribing beyond the Product Licence can be considered "established practice" in this clinical context. Specialist palliative care clinicians have developed a good understanding of the indications, alternatives and potential risks of such prescribing, as is clearly demonstated in "Palliative Care Formulary 2". A list of off-licence prescribing regularly performed or recommended by Katharine House Hospice is summarised in Appendix Four, all of which is detailed in Palliative Care Formulary 2. We believe that patients need not be routinely and specifically advised each time such established practice is employed.
4) Whenever it is felt that a particular patient might benefit from the prescription of a drug in a manner not described in its Product Licence and the prescription in question is not part of our "established practice" as detailed in Table Two, the hospice Consultant must be generally in favour of the proposed line of management. The consultant must be satisfied that more established management options have already been considered and tried as appropriate. This being the case, it is therefore fitting for the Consultant to take the lead in discussing the proposed treatment option with the patient unless this task has been clearly delegated by the Consultant to another member of the medical team. If a doctor decides to prescribe a drug beyond its Product Licence without advising and receiving the support of the Consultant beforehand, then the Consultant cannot be held responsible if there is subsequently a serious adverse outcome that is attributable to this act before the Consultant becomes aware of it.

5) In the community or hospital setting, a Clinical Nurse Specialist might advise a doctor to prescribe a medicine in a manner not described on the Product Licence. As prescribing doctors are responsible for the potential consequences of prescribing outside the Product Licence, it is likely that the doctors concerned might express reservations or even refuse outright to follow such advice from time to time. Obviously, the hospice Consultant will support and endorse any prescribing suggestion made by the Clinical Nurse Specialist that clearly follows established practice at the hospice. However, suggestions that clearly fall outside established practice at the hospice should be discussed with the Consultant first if it is felt that Consultant backing might later be appreciated.
6) In discussing the use of drugs beyond their Product Licence with a patient, the level of information exchange must obviously be carefully tailored to the wishes, needs and cognitive abilities of the patient. The whole conversation must be carefully documented in the clinical notes, and written consent must be obtained from the patient if the doctor considers this to be remotely appropriate.
7) Whenever written consent is sought, this must be on a typed form, individualised to the patient, that includes a description of:
   - The drug, dose and route of administration.
   - The clinical indication for this treatment.
   - A brief description of the nature of the evidence that supports this treatment.
   - An estimate of the likelihood of success, when this is known.
   - Possible side effects and the likelihood of these occurring.

   These same areas must also be covered appropriately in any discussion with a patient regarding the use of a drug beyond its Product Licence, even if written informed consent is *not* obtained. If, in tailoring the advice to the patient, it is felt that this level of information is inappropriate, then this must be documented in the notes.
8) The signed and dated consent form must be stored on the back spine of the medical records and a photocopy must be given to the patient.

APPENDIX FOUR

Drug	Common example of use beyond the Product Licence at Katharine House Hospice*
Amitriptyline	Neuropathic pain, urgency of micturition, urge incontinence, bladder spasms.
Antacid	Hiccup.
Ascorbic acid	Decubitis ulcer, furred tongue.
Baclofen	Hiccup.
Celecoxib	Alternative NSAID in patients with gastric intolerance.
Corticosteroids	Long list (Please refer to the Palliative Care Formulary 2).
Cyclizine	Antiemetic for mechanical bowel obstruction or cerebral irritation.
Dalteparin	Thrombophlebitis migrans and DIC.
Depot corticosteroid	Pain in superficial bones, pain caused by spinal metastases.
Diamorphine	Dyspnoea…
Diclofenac	Cancer pain, neoplastic fever.
Docusate	To soften the stool in partial bowel obstruction.
Epoietin	Anaemia of chronic disease.
Etamsylate	Surface bleeding from ulcerating tumours.
Glyceryl trinitrate	Pain from oesophageal spasm, tenesmus or anal fissure.
Haloperidol	Antiemetic, hiccup.
Hyoscine butylbromide	Inoperable bowel obstruction, drooling, respiratory rattle.
Hyoscine hydrobromide patch	Colic, inoperable bowel obstruction, drooling, respiratory rattle.
Ibuprofen	Cancer pain, neoplastic fever.
Inhaled corticosteroid	Stridor, lymphangitis carcinomatosa, radiation pneumonitis, cough after insertion of a tracheal stent.
Ispaghula	To partially firm up the liquid output from an ileostomy.
Lansoprazole	To prevent the denaturing of pancreatic supplements.
Loperamide	To partially firm up the liquid output from an ileostomy.
Lorazepam	Acute agitation, terminal agitation, alcohol withdrawal, serotonin syndrome.
Methadone	Morphine poorly-responsive pain, pain relief in renal failure.
Methylphenidate	Depression in very advanced cancer.
Midazolam	Intractable hiccup.
Morphine	Dyspnoea.
Naproxen	Cancer pain, neoplastic fever.
Nifedipine	To relieve the pain of oesophageal spasm, tenesmus and to treat hiccup.
Octreotide	Pancreatic fistula, enterocutaneous fistula, intractable diarrhea associated with ileostomies, inoperable bowel obstruction.
Pancreatin	Enzyme supplement in certain cases of cancer of the pancreas/cholangiocarcinoma.
Progestogens	Postcastration hot flushes.
Ranitidine	Reduction of gastric secretions, to prevent denaturing of pancreatic supplements.

Drug	Common example of use beyond the Product Licence at Katharine House Hospice*
Risperidone	Delirium, behavioural symptoms in dementia.
Stanozolol	Itch secondary to obstructed bile duct.
Tranexamic acid	Surface bleeding from ulcerating tumours.
Venlafaxine	Hot flushes.
Vitamin K	Bleeding tendency in patients with hepatic impairment.

* All of these indications are described in the Palliative Care Formulary.