

Risk Management comes to Thalidomide

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Thalidomide is still considered a useful drug in dermatology for conditions including erythema nodosum leprosum, nodular prurigo, actinic prurigo, discoid lupus erythematosus, aphthous stomatitis, Behçet's disease and graft versus host disease. However, because of its toxicity it should only be considered when other treatments have failed and where there is unacceptable interference with life, where the potential benefits outweigh the potential risks.

Pharmion have taken over the supply of thalidomide. They have applied for product licensing in the EU and UK and have already been granted a license in Australia. Licensing by the EMEA (European equivalent of the FDA) is expected to be conditional on the introduction of risk management program to guarantee safety and to satisfy campaigners for the victims of thalidomide who sought a ban on thalidomide. This forms an integral part of the license application.

Thus, members who wish to prescribe thalidomide will have to conform with the Pharmion Risk Management Programme (PRMP). The programme is based on the STEPS programme for thalidomide in the USA where 79,000 patients have been successfully monitored over 5 years. The purpose of the programme is to help prevent the possibility of an unborn child being exposed to thalidomide. Under the programme, only physicians, pharmacies and patients, registered with the programme, who have agreed to accept and comply with the requirements, will respectively be able to prescribe, dispense and receive the drug.

Patients give a written agreement to comply by signing a consent form, after being fully informed of the risks and potential side effects including the death of a newborn child or severe deformities (if exposure occurs during pregnancy) and the precautions to be taken before during and after thalidomide therapy. Prescribing and dispensing are carefully managed to ensure compliance with the programme

- A physician who wants to start using thalidomide must first register with PRMP as a prescribing physician. A GMC number is required. Registration forms are available from the internet (<http://www.prmp.com>) or 0808 1563059. They will then receive a physician resource pack, including consent forms and patient education materials and once registered a unique identification number for use in future contacts with the PRMP.
- The Pharmacy must also register with the PRMP. A professional registration number is required. After registration the pharmacy will receive information on PRMP and a unique identification number.
- The physician performs all eligibility checks and then registers the patients with PRMP by faxing a copy of the Patient Registration/Informed Consent form to the Pharmion Risk Management Centre on 0801563058. Pharmion checks this and registers the patient and provides a unique identification for use in future contacts with PRMP. The confidentiality of this and the registration complies with Data protection law.
- The patient then has to phone the Risk Management Centre in order to complete a patient survey. The physician also needs to take part in a telephone survey to ensure all responsibilities for testing and monitoring are met. Once the surveys are complete the physician receives an authorisation number which has to be

written on the patient's prescription. The prescription can only be for 28 days supply and must be taken to the pharmacist within 7 days.

- The pharmacist must validate the authorisation number on every prescription by calling an interactive voice response system (IVRS) on 0808 156 3057, and obtain a confirmation number which must be written on the prescription.
- Thereafter there is a requirement for the physician to complete an IVRS call of about 45 seconds each month to gain further authorisation to write the next prescription.
- For women of childbearing age there is a requirement for monthly pregnancy tests, done on blood and two forms of contraception one of which must be highly effective. This includes sterilisation which alone is not considered sufficient. Men and children are included in the precautions with appropriate consent and patient information for all scenarios. Particularly male patients have thalidomide in semen and must use a barrier.
- The schedule for patient surveys is as follows,
 - Males (child and adult) – No survey with first prescription. Follow up survey required with each subsequent prescription.
 - Female adults NOT of child-bearing potential (hysterectomy or meet strictly defined menopause criteria) – Survey with first prescription. Follow up survey every 6 months
 - All other females (including children) – Survey with first prescription. Follow-up survey required with each subsequent prescription

At the outset this is obviously more time consuming and increases our workload, but having a mandatory system that is structured takes some of the effort out of the therapy and removes any chance of mistakes. The potentials for failure with voluntary measures have been alluded to in the literature^{1,2} and although our normal practice may appear to work it is not sufficient in the present climate. We are about to see measures for isotretinoin tightened up along similar lines and this will have a far greater impact on our clinics.

There has been significant dissent among members about having PRMP imposed, as we are well aware. We have discussed this with the company. They set out to be helpful in introducing this scheme and can be approached to help in situations where a lot of thalidomide is being used and the PRMP scheme is liable to disrupt services. It is acceptable to delegate the monthly registration survey to a trained nurse although responsibility remains with the doctor. The programme is kept under review and Pharmion welcome feedback on how it can be improved. We would like to hear your feedback and to relate these your comments to them, so please feel free to write especially about working problems and practicability. However, because of regulatory issues and the mandatory components, applied internationally, in many languages, we are not in a position to oppose those principles that are grounded in safety concerns and maintaining thalidomide as a viable treatment.

References

- 1 Chave TA, Finlay AY, Knight AG. Thalidomide usage in Wales: the need to follow guidelines. *British Journal of Dermatology* 2001;**144**:310-315
- 2 Holmes SC, Bankowska U, Mackie RM. The prescription of isotretinoin to women: is every precaution taken? *British Journal of Dermatology* 1998;**138**:450-455

December 2003