Lepr Rev (1987) **58** 249–255

Blister calendar packs for the implementation of multiple drug therapy in *DANIDA*-assisted leprosy control projects in India

G D GEORGIEV* & R W KIELSTRUP†
** 275 Turnpike Drive, Luton, Bedfordshire LU3 3RD, England; † Pharmanova, PO Box 10, Industriparken, DK-2750, Ballerup, Copenhagen, Denmark*

Accepted for publication 15 May 1987

Summary A brief description is given of leprosy control projects in Orissa, Madhya Pradesh and Tamil Nadu, set up by the Government of India and assisted by the Danish International Development Agency (DANIDA), as part of the Indian National Leprosy Eradication Programme. In view of the crucial importance of assuring the highest possible compliance to prescribed medication and regularity of clinic attendance over adequate periods of time, it was decided to use blister calendar packs for the dispensing of antileprosy drugs to patients with both paucibacillary and multibacillary forms of the disease. The projects cover a population of 12 million people with an estimated 130,000 leprosy patients. The packs are being manufactured by Pharmanova, Denmark, and over the next 4–5 years, approximately 1·7 million will be used in the four project areas.

The rationale for the use of blister calendar packs, the design requirements and the operational methodology are discussed in a separate publication.

This paper is concerned with the description, structure and technical specification of the packs to be used in India, illustrated with diagrams and photographs.

The operational benefits and cost-effectiveness of the use of such packs in leprosy control have still to be established, but the approach is worth consideration in view of the limited drugs available for leprosy and the paramount importance of regular drug supply and adequate treatment compliance.

In India, leprosy has been recognized as one of the foremost public health problems with far-reaching socio-economic implications.[1] It has been estimated that there are about 4 million leprosy patients in India, 20% of whom are infectious. Nearly 58% of the Indian population live in areas with a prevalence rate of over 5 per 1000 and are considered to be at high risk of contracting the disease.[2] The Government of India has expressed a clear and indisputable political determination to control leprosy and to ultimately eradicate it by the

0305-7518/87/058249+07 $01.00

turn of the century. During the past decade the expenditure on the National Leprosy Eradication Programme (NLEP) has been increased more than 14 times and its infrastructure and the facilities expanded to a great extent.[3] Multidrug therapy for leprosy, both paucibacillary and multibacillary, has been introduced in a phased manner in the hyperendemic districts and it is expected that the WHO multidrug regimens[4] will become standard treatment for leprosy by 1995.[2] In this rapid expansion of the multidrug treatment (MDT) programme, NLEP has established a close and most productive cooperation with the Voluntary Leprosy Agencies and the other International Organizations (WHO/SIDA/UNICEF/DANIDA). During the period 1982–86, 15 hyperendemic districts with prevalence of more than 10 per 1000 were brought under the umbrella of MDT and most of them have shown very encouraging results.[2,10].

The introduction of multiple drug therapy in leprosy control, particularly when on a large scale, necessitates a revision of the operational methodology adopted by monotherapy and the development of new strategies.[5] The need for efficient planning, management and monitoring, adequate infrastructure, appropriate training and active community involvement should now be widely accepted as being of crucial importance in leprosy control programmes. The operational strategy includes the origination, development, application and the evaluation of new technology to increase the effectiveness of control activities.[5,6] An important initiative in this direction has recently been taken by NLEP and assisted by the Danish International Development Agency (DANIDA). Four district MDT leprosy control projects have been set up, one each in Orissa and Tamil Nadu States, and two in Madhya Pradesh State, to monitor closely the whole range of control activities and to introduce and evaluate new control methodologies and technologies. These DANIDA-assisted projects cover a population of 12 million people and will take care of an estimated 130,000 leprosy patients.[7]

The effectiveness of the multiple drug therapy, and for that matter the effectiveness of leprosy control, crucially depends on the proper organization of leprosy clinics (treatment points), regular clinic attendance, compliance with domiciliary treatment and the constant availability of the necessary drugs in the field. This had been recognized and taken into account at an early stage of the projects' planning and particular attention had to be paid to drug supplies, the handling of antileprosy drugs by staff and their distribution to patients. It has been suggested that blister or calendar packs would be of value in the implementation of multiple drug therapy in leprosy (and possibly also in tuberculosis).[9] It was decided to dispense the drugs for the treatment of multibacillary as well as paucibacilliary patients in the above projects in blister calendar packs (BCP).[7] The rationale for their use, the possible operational advantages they may offer, the design requirements and the operational methodology are discussed in a separate publication.[8] The object of the present communication is to describe the design, structure and technical specifications of the packs which are developed and are to be used for both paucibacillary and

multibacillary leprosy patients in India. We hope that such information may be of benefit to others who are engaged in the treatment of leprosy patients and the control of leprosy, using WHO-recommended multidrug regimens.

Design and structure of BCP's

Separate BCP's for multibacillary (MB) and paucibacillary (PB) cases have been designed and it is expected that 1·7 million packs will be produced by Pharmanova in Copenhagen and used over a period of 4–5 years in the treatment of both adult and child patients. As the number of children who suffer from MB forms of leprosy is relatively low, it has not been cost-effective to produce BCP's for them and they will be treated with 'loose' tablets and capsules.

The initial design of a BCP requires careful consideration, since the capital outlay may be considerable. Combining one tablet and three other differently shaped products into one pack requires high technology and precision packing machinery. Changes in the design after field trials are also not easily undertaken because of the high cost of re-tooling for multiple product blisters. The pack design described here attempts to combine ease of handling for health staff with clarity and convenience for the patient. The upper part of the BCP contains the supervised clinic (or treatment point) dose of 2 capsules of rifampicin, each of 300 mg; 3 capsules of clofazimine, each of 100 mg; and 1 tablet of dapsone 100 mg (see Figures 1 and 2). After dispensing the drugs, the top of the pack is torn away along the perforated line and the rest of the pack containing the domiciliary treatment is given to the patient. The remaining pack can be folded vertically down the middle, thus protecting the vulnerable side of the aluminium foil and reducing the size. The arrangement of the drugs for home treatment is based on the lunar month in four weekly rows, making it easy for the patient to take his daily dose and for the staff to check the patient's compliance during home visits or at the clinic.

The MB-adult blister pack measures 122 mm × 146 m, Figures 1 and 2. After the top part is torn off at the clinic, the size of the remainder of the pack for home use measures 122 mm × 119 mm. This part folds along the middle, further reducing the size to 61 mm × 119 mm, so that the pack can easily be carried in the shirt pocket by the patient. The PB pack (Figure 3) measures 72 × 122 mm. After detaching the part for the monthly dose, it can also be folded to reduce the size.

The materials of which the BCP are made should provide optimal protection for the drugs against humidity and moisture, light and accidental physical damage. The blister body of the BCP is made of high-barrier tropicalized triplex laminate (TTL), a clear, rigid, triple layer of 328 micron thickness PVC. TTL has a weight of 461 g/m^2, which is considerably higher than the conventional mono PVC, giving optimal moisture protection for use in tropical conditions and adding extra strength and stability to the relatively large format blister packs.

The body of the blister pack is backed with a moisture impervious, 20 micron,

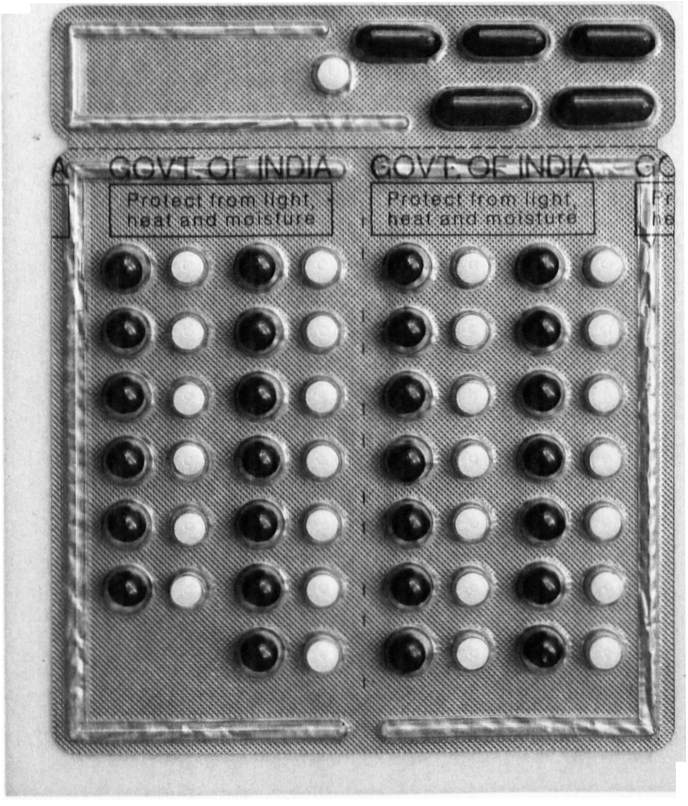

Figure 1. Photograph of the pack for multibacillary (MB) leprosy, showing the side with elevated 'blisters' or 'bubbles' containing the supervised, monthly dose (top right) and the tablets of dapsone and capsules of clofazimine for daily unsupervised dosage at home. The weeks are arranged in vertical columns and numbered on the reverse (flat) side of the pack. Once the supervised drugs have been given, this part of the pack can be broken off (and discarded) along the horizontal line above 'Govt of India'. The remainder of the pack is then taken home by the patient and it can be folded to fit into a pocket along the vertical line at the centre. Actual dimensions, 122 × 146 mm.

aluminium foil covering. The protection against humidity and moisture is further enhanced by one layer of a heavily reinforced PVdC, resulting in significantly improved barrier protection for the TTL, having a moisture vapour transmission rate (MVTR) of 0·06 g/m^2/24 h under tropical conditions of 38°C and 90% relative humidity. This compares very favourably with conventional mono PVC 250 micron, the MVTR rate for which is 3·1 g/m^2/24 h. (DIN 53122) or approximately 5 times that of the TTL. Under less rigorous storage conditions of 20°C/85% rh., the MVTR rate of the TLL is as low as 0·07 g/m^2/24 h. The MVTR rates given are those of the finished blister, i.e. after standard thermoforming.

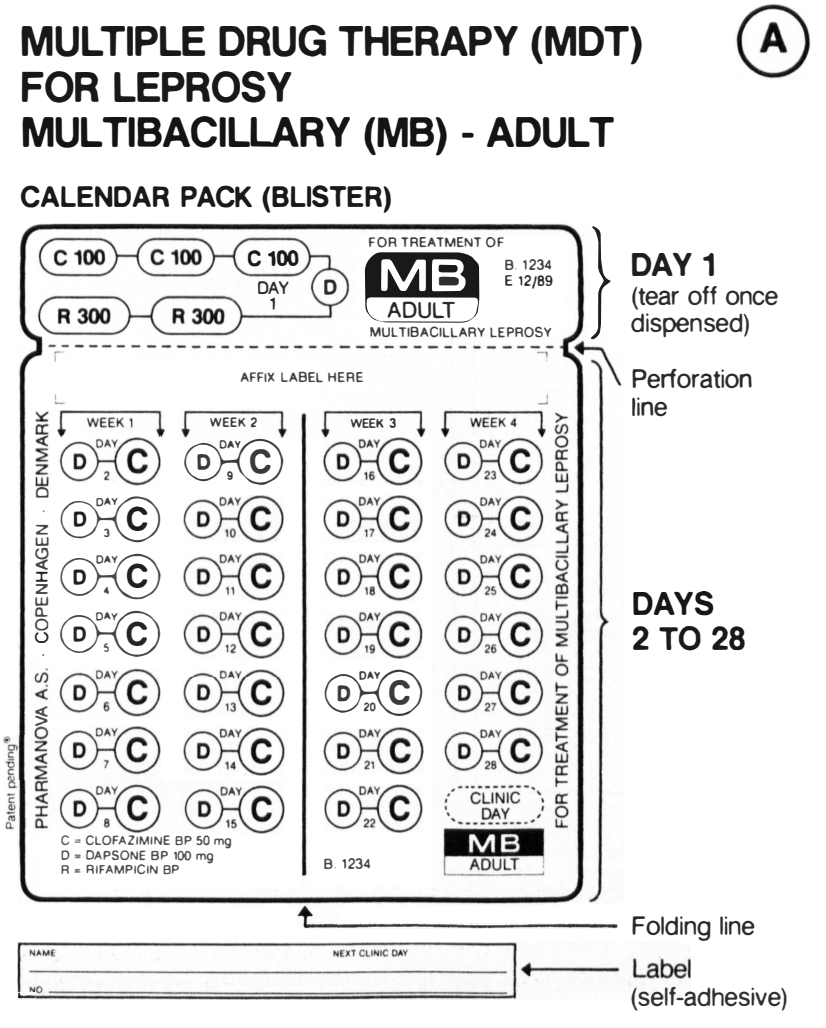

Figure 2. Diagram of the flat side of the pack for multibacillary (MB) leprosy. Actual dimensions 122 × 146 mm.

The light protective (and child resistant) properties of the calendar blister could be enhanced by employing fully coloured or white opaque laminate, but this should be weighed against the disadvantage of obscuring the blister contents from the view of patients having no prior experience or dexterity in the handling of such packs.

The packs for these projects in India have been produced in three different

Figure 3. Diagram of the flat side of the pack for paucibacillary (PB) leprosy. Actual dimensions, 70 × 122 mm.

colours: red for adult MB cases, green for adult PB cases and blue for child PB cases (no pack has been produced for child MB cases for the reasons already stated). It is also intended to provide written directions for patients and staff, on paper of corresponding colours; thus the clinical grouping into PB or MB, the drug regimen and the directions for use, will be clearly linked. Finally, it is also intended to give each patient a non-transparent PVC pack holder which will provide additional protection against moisture, light and physical damage. This will accommodate the pack itself, the instructions and the patient's identification/

treatment card, whilst at the same time affording a degree of privacy for those who are sensitive about the association of BCP's with leprosy.

The operational benefits and cost-effectiveness of BCP's in the treatment of leprosy have yet to be defined. However, in view of the limited number of drugs currently available for the treatment of this disease and the extreme importance of assuring compliance to prescribed regimens, together with regularity of attendance for adequate periods of time, many avenues must be explored. What appears at first consideration to be expensive and inappropriate may, in the long run, be of decisive value. We hope that this communication will provide useful information to those who wish to consider this approach in the implementation of MDT in leprosy.

Acknowledgments

We would like to record our appreciation to the Government of India for permission to publish and Mr N Dabelstein of DANIDA for his enthusiastic support for the introduction of blister packs. We also wish to express our thanks to Patrica Sutherland for invaluable help in the preparation of this manuscript.

References

[1] Guidelines for Multidrug Treatment in Endemic Districts. Leprosy Division, Directorate General of Health Services, Nirman Bhawan, New Delhi, India, 1987.

[2] Leprosy Status Report 1985–86. Leprosy Division, Directorate General of Health Services, Nirman Bhawan, New Delhi, India, 1986.

[3] Rao CK *et al.* Voluntary Agencies and Leprosy Control in India. *Lepr Rev*, 1987; **58:** 1.

[4] WHO Study Group. *Chemotherapy of leprosy for control programmes.* Technical Report Series No. 675. WHO: Geneva, 1982.

[5] Georgiev, GD, McDougall AC. Operational Strategy of Multidrug Treatment Leprosy Control. In preparation.

[6] Fleischer K. Keynote Address. Symposium on Multidrug Therapy in Leprosy, Würzburg, W. Germany. *Lepr. Rev*, 1986; **57:** suppl 3, 7.

[7] Georgiev GD. Operational Plan of Danida-assisted MDT Projects of National Leprosy Eradication Programme. Danish International Development Agency (1986). Asiatisk Plads 2, DK 1448 Copenhagen K, Denmark.

[8] Georgiev GD, McDougall AC. Blister calendar Packs for Multiple Drug Therapy in Leprosy: Rationale, Principles of Design and Use in Control Programmes. In preparation.

NEWS AND NOTES

XIIIth International Leprosy Congress, 11–17 September, 1988, The Hague, The Netherlands

Full details of the sessions have already been printed in this journal; see Number 1, **58,** 1986.

The Congress Location and Hotel Accommodation: The 13th ILA Congress will be held in The Netherlands Congress Centre, The Hague, The Netherlands, from 11–17 September 1988. Hotel accommodation will be provided in several price categories ranging from ca. Dfl. 50,-to Dfl. 250,- and more. *Congress Bureau*: For all information concerning the congress, please contact the Congress Bureau: QLT Convention Services, Keizersgracht 792, 1017 EC Amsterdam, The Netherlands. Tel. +31 (0)20-26 1372, Tlx. 31578 inter nl att qlt. This Meeting is co-sponsored by the World Health Organization.

XIIth International Congress for Tropical Medicine and Malaria, September 1988

This congress will be held in the International Congress Center RAI in Amsterdam from 18–24 September 1988, immediately after the International Leprosy Congress (above).

Information can be obtained at: Organisatie Bureau, Amsterdam, Europaplein 12, 1078 GZ Amsterdam, The Netherlands. Tel. +31 (0)20-440807, Tlx. 13499.

Meeting of the International Society of Dermatology, Oxford, September 1988

A joint meeting of this Society with the International Society of Dermatopathology will take place in Oxford, UK, 4–8 September, 1988. There will be at least two sessions on leprosy, including histopathology, together with exhibits and demonstrations, one of which will come from the Wellcome Institute of Tropical Medicine in London. Further details; Mrs Christine Cherry, Department of Dermatology, the Slade Hospital, Headington, Oxford, OX3 7JH, England.

Chinese Journal of Dermatology

We are most grateful for the continued flow of medical journals from the People's Republic of China, including this one on dermatology. Some material on leprosy still appears in this publication and the latest (February 1987) contains an interesting article by Dr Ji Baohong *et al.* on 'Experimental therapeutic activity against *M. leprae* of cyclopentylrifamycin'.

Thesis in French from Dakar on Erythema Nodosum Leprosum

Dr J Millan, Institut de Léprologie Appliquée de Dakar, BP 11023 CD Annexe, Dakar, Sénégal, Africa, kindly sent a copy of a thesis 'Manifestations Cliniques et Perturbations Biologiques au cours des Erythemes Noueux Lépreux' (Clinical Manifestations and Biological Changes in the Course of Erythema Nodosum Leprosum), by Waldemar Daluz, presented for the degree of Doctor of Medicine (Diplome d'Etat), July 1986, in the University of Dakar. This is a document of considerable length; 129 pages, A4 size, plus appendices, covering the entire subject under the following headings: evolution of ideas; etiopathology; clinical manifestations; clinical forms; biological signs; histopathology; differential diagnosis; treatment of the reactional state; prognosis; personal study. There are 74 references. We congratulate Dr Daluz and the Institute on this valuable contribution to the study of a perplexing and all too common condition.

CBM/LEPRA Ophthalmic Course, Karigiri, India, March 1987

A four-day ophthalmic teaching course was held at the Schieffelin Leprosy Research and Training Centre, Karigiri from 2 to 5 March 1987. It was designed to give instruction to leprologists on the detection and management of the ocular complications of leprosy by means of a series of lectures, clinical and surgical demonstrations, videos and slide–tape presentations. The course was run by Dr Margaret Brand from Carville USA, and Mr Timothy ffytche from St Thomas's Hospital, London, and there were contributions from Dr N Suryawanshi and Dr Mary Jacob of Karigiri.

Teaching included presentations on basic anatomy, physiology and pathology of the eye with special emphasis on leprosy; in addition there were lectures on the clinical signs and management of lagophthalmos, intra-ocular inflammation, corneal ulcers and infiltrative lesions together with a discussion on global aspects of blindness in leprosy.

There were twelve participants on the course which was sponsored jointly by the Christoffel Blindenmission and LEPRA who together with the staff of Karigiri and The Leprosy Mission are to be congratulated on their support for this important contribution to teaching. Further enquiries: Mr T ffytche, Consultant Ophthalmologist, Department of Ophthalmology, St Thomas's Hospital, Lambeth Palace Road, London SE1 7EH.