the DBL report
UPDATE

Update, April 1999

An Official Accompaniment to the Alberta Health Drug Benefit List (AHDBL)

The Expert Committee on Drug Evaluation and Therapeutics (ECDET)

produced by Alberta Blue Cross

Interchangeability of Levothyroxine Sodium Preparations

The levothyroxine sodium preparations, SYNTHROID and ELTROXIN have been designated as interchangeable since the first interchangeability designations in the AHDBL effective October 1, 1993. This was based on a recommendation by the Expert Committee on Drug Quality and Therapeutics following a review of data supplied by the manufacturers of SYNTHROID at that time (Boots Pharmaceuticals Ltd.) and ELTROXIN (Glaxo Canada Inc.) and consideration of similar decisions taken in other provinces.

In the April 1, 1999 AHDBL, the product LEVOTEC has also been designated as interchangeable with SYNTHROID and ELTROXIN; however, the product LEVO-T remains not interchangeable.

In reviewing the interchangeability of LEVOTEC, the Expert Committee considered new and comprehensive bioequivalence data comparing LEVOTEC and SYNTHROID, information provided by Knoll Pharma Inc. (current manufacturer of SYNTHROID) and information provided by Technilab Inc. (manufacturer of LEVOTEC).

The products LEVOTEC and SYNTHROID are bioequivalent. Bioequivalence study design requirements and standards for Narrow Therapeutic Range drugs as per the *Therapeutic Products Directorate Report C* and Directive *'Standards for Comparative Bioavailability Studies Involving Drugs with a Narrow Therapeutic Range - Oral Dosage Forms'* were met in all instances.

The active ingredient and absorbed moiety in levothyroxine sodium preparations is levothyroxine (T_4). In the determination of bioequivalence and interchangeability of drug products, consideration is given to differences in formulations and how differences in formulations affect absorption of the active ingredient.

Pharmacodynamic endpoints or clinical studies are used as surrogate measures of bioequivalence and interchangeability only if measurement of the absorbed moiety in plasma or urine cannot be made with sufficient accuracy and sensitivity. Although TSH measurement is recommended to determine if levothyroxine dosage is optimal *(Thyroid Testing Guidelines for Alberta Physicians),* it is not an appropriate parameter to measure differences between formulations as it is also a function of patient and disease factors and not solely formulation factors.

ABC 80103 / 40359 99/03