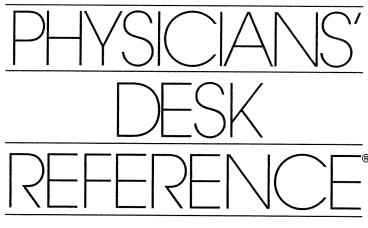


# GOODWIN BROGTER LLP LIBRARY

DEC 0 1 2005

RECEIVED



Senior Vice President, PDR Sales and Marketing: Dikran N. Barsamian Vice President, Product Management: William T. Hicks Vice President, Regulatory Affairs: Mukesh Mehta, RPh

Vice President, PDR Services: Brian Holland

Senior Directors, Pharmaceutical Solutions Sales: Chantal Corcos, Anthony Sorce

National Solutions Managers: Frank Karkowsky, Marion Reid, RPh Senior Solutions Managers: Debra Goldman, Elaine Musco, Warner Stuart, Suzanne E. Yarrow, RN

Solutions Managers: Eileen Bruno, Cory Coleman, Marjorie A. Jaxel, Kevin McGlynn, Lois Smith, Richard Zwickel

Sales Coordinators: Arlene Phayre, Janet Wallendal

Senior Director, Brand and Product Management: Valerie E. Berger Associate Product Managers: Michael Casale, Andrea Colavecchio Senior Director, Publishing Sales and Marketing: Michael Bennett Director, Trade Sales: Bill Gaffney Associate Director, Marketing: Jennifer M. Fronzaglia

Senior Marketing Manager: Kim Marich Direct Mail Manager: Lorraine M. Loening Manager, Marketing Analysis: Dina A. Maeder Promotion Manager: Linda Levine

Director of Operations: Robert Klein Director, PDR Operations: Jeffrey D. Schaefer Director of Finance: Mark S. Ritchin

Director, Client Services: Stephanie Struble Director, Clinical Content: Thomas Fleming, PharmD Director, Editorial Services: Bette LaGow

Drug Information Specialists: Michael DeLuca, PharmD, MBA; Kajal Solanki, PharmD; Greg Tallis, RPh Project Editors: Neil Chesanow, Harris Fleming Senior Editor: Lori Murray Senior Production Editor: Gwynned L. Kelly

Manager, Production Purchasing: Thomas Westburgh PDR Production Manager: Steven Maher Production Manager: Gayle Graizzaro Production Specialist: Christina Klinger Senior Production Coordinators: Gianna Caradonna, Yasmin Hernández Production Coordinator: Nick W. Clark Senior Index Editors: Noel Deloughery, Shannon Reilly Format Editor: Michelle G. Auffant Traffic Assistant: Kim Condon

Production Design Supervisor: Adeline Rich Senior Electronic Publishing Designer: Livio Udina Electronic Publishing Designers: Bryan C. Dix, Carrie Faeth, Monika Popowitz Production Associate: Joan K. Akerlind

Digital Imaging Manager: Christopher Husted Digital Imaging Coordinator: Michael Labruyere

DOCKE.

THOMSON Copyright © 2006 and published by Thomson PDR at Montvale, NJ 07645-1742. All rights reserved. None of the content of this publication may be reproduced, stored in a retrieval system, resold, redistributed, or transmitted in any form or by any means (electronic, mechanical,

 Indy Certonic, societ in a femeral system, resolution, redistributed, or transmitted in any form or by any means (electronic, mechanical, photocopying, recording, or otherwise) without the prior written permission of the publisher. Physicians' besk Reference®, PDR®, Pocket PDR®, PDR Family Guide to Prescription Drugs®, PDR Family Guide to Women's Health and Prescription Drugs®, and PDR Family Guide to Companion Guide, PDR® Pharmacopoeia, PDR® for Herbal Medicines, PDR® for Noprescription Drugs and Dietary Supplements, PDR® Nurse's Dictionary, PDR® Family Guide to Over-the-Counter Drugs, PDR® Family Guide to Natural Medicines and Healing Therapies, PDR® Family Guide to Common Ailments, PDR® Family Guide to Over-the-Counter Drugs, PDR® Family Guide to Nutritional Supplements, and PDR® Electronic Library are trademarks used herein under license. license.

Officers of Thomson Healthcare, Inc.: President and Chief Executive Officer: Kevin King: Chief Financial Officer: Paul Hilger; Chief Medical Officer: Rich Klasco, MD, FACEP; Executive Vice President, Medstat: Carol Diephuis; Executive Vice President, Micromedex: Jeff Reihl; Senior Vice President, Marketing: Timothy Murray; Senior Vice President, Technology: Michael Karaman; Vice President, Finance: Joseph Scarfone; Vice President, Human Resources: Pamela M. Bilash

GOOIBBN!145536355267ERLLP LIBRARY EXCHANCE PLACE BOSTON, MA 02109

**LUPIN EX. 1020** 

Find authenticated court documents without watermarks at docketalarm.com.

### BUPHENVL® bu'fen-al (sodium phenylbutyrate)

### BUPHENYL® (sodium phenylbutyrate) Powder Rx Only

### DESCRIPTION

Buphenyl® (sodium phenylbutyrate) Tablets for oral admin-istration and Buphenyl® (sodium phenylbutyrate) Powder for oral, nasogastric, or gastrostomy tube administration contain sodium phenylbutyrate. Sodium phenylbutyrate is an off-white crystalline substance which is soluble in water an on-white crystainle substance which is soluble in water and has a strong salty tasts. Sodium phenylbutyrate also is freely soluble in methanol and practically insoluble in ace-tone and diethyl ether. It is known chemically as 4-phenyl-butyric acid, sodium salt with a molecular weight of 186 and the molecular formula  $C_{10}H_{11}O_2Na$ . Chemical Structure:



Each tablet of BUPHENYL contains 500 mg of sodium phe Each ratice of BUFTEN 11 contains 500 mg of sodium phe-nylbutyrate and the inactive ingredients microcrystalline cellulose, magnesium stearate, and colloidal silicon dioxide. Each gram of BUPHENYL Powder contains 0.94 grams of sodium phenylbutyrate and the inactive ingredients cal-cium stearate, and colloidal silicon dioxide.

### CLINICAL PHARMACOLOGY

Sodium phenylbutyrate is a pro-drug and is rapidly metabolized to phenylacetate. Phenylacetate is a metabolically-active compound that conjugates with glutamine via acetylation to form phenylacetylglutamine. Phenylacetyl glutamine then is excreted by the kidneys. On a molar ba-sis, it is comparable to urea (each containing two moles of nitrogen). Therefore, phenylacetylglutamine provides an alternate vehicle for waste nitrogen excretion PHARMACOKINETICS

### General:

Pharmacokinetic studies have not been conducted in the primary patient population (neonates, infants, and chil-dren), but pharmacokinetic data were obtained from normal adult subjects.

#### Absorption

Peak plasma levels of phenylbutyrate occur within 1 hour after a single dose of 5 grams of sodium phenylbutyrate tablet with a  $C_{\rm max}$  of 218 µg/mL under fasting conditions; peak plasma levels of phenylbutyrate occur within 1 hour after a single dose of 5 grams of solium phenylbutyrate occur within 1 not ratter a single dose of 5 grams of solium phenylbutyrate powder with a  $C_{max}$  of 195 µg/mL under fasting conditions. The effect of food on phenylbutyrate's absorption is unknown.

#### Disposition:

Disposition: The overall disposition of sodium phenylbutyrate and its metabolites has not been characterized fully. However, the drug is known to be metabolized to phenylacetate and sub-sequently to phenylacetylglutamine. Following oral admin-istration of 5 grams (tablets), measurable plasma levels of phenylbutyrate and phenylacetylg. and phenylacetyl-glutamine was detected shortly thereafter. The pharmaco-kinetic parameters for phenylbutyrate for C<sub>max</sub> (µg/mL), T<sub>max</sub> (hours), and elimination half-life (hours) were 218, 1.35, and 0.77, respectively, and for phenylacetate were 48.5, 3.74, and 1.15, respectively. Following oral administration of 5 grams of the powder, measurable plasma levels of phenylbutyrate and phenylac-tively, and phenylacets of phenylbutyrate and phenylacetylglutamine was detected shortly thereafter. The pharmacokinetic parameters for phenylbu-tyrate for C<sub>max</sub> (µg/mL), T<sub>max</sub> (hours), and elimination half-life (hours) were 195, 100, and 0.76, respectively, and for phenylacetate were 45.3, 3.55, end 1.29, respectively. The major sites for metabolism of sodium phenylbutyrate are the liver and kidney. **Excretion:** A maiority of the administered compound (approximately 30 The overall disposition of sodium phenylbutyrate and its

A majority of the administered compound (approximately 80 - 100%) was excreted by the kidneys within 24 hours as the conjugation product, b) and actively utamine. For each gram of sodium phenylacetylglutamine. For each gram of sodium phenylbutyrate administered, it is estimated that between 0.12 - 0.15 grams of phenylacetylglutamine nitrogen are produced.

Pharmacodynamics: In patients with urea cycle disorders, BUPHENYL de-creases elevated plasma ammonia glutamine levels. It in-creases waste nitrogen excretion in the form of phenylacetylglutamine

#### Special Populations: Gender:

DOCKET

Significant gender differences were found in the pharmace kinetics of phenylbutyrate and phenylbutyrate and phenylbutyrate and phenylbutyrate pharmacokinetic parameters, (AUC and C<sub>max</sub>), for both plasma phenylbutyrate and phenylacetate were about 30 to 50 percent greater in females than in males

### Hepatic insufficiency:

In patients who did not have urea cycle disorders but had impaired hepatic function, the metabolism and excretion of

sodium phenylbutyrate were not affected. However, this in-formation was obtained from unvalidated, uncontrolled case R studies

# INDICATIONS AND USAGE

R

BUPHENYL is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornitine transcarbamylase (OTC), or argininosuc-cinic acid synthetase (AS). It is indicated in all patients with nearest deficience deficiency of the synthesis of the synthesi neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indi-cated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperanimonemic encephalopathy. It is impor-tant that the diagnosis be made early and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening

emergency. BUPHENYL must be combined with dietary protein restriction and, in some cases, essential amino acid supplementa-tion. (See Nutritional Supplementation subsection of the DOSAGE AND ADMINISTRATION section.)

DOSAGE AND ADMINISTRATION section.) Previously, neonatal-onset disease was almost universally fatal within the first year of life, even when treated with peritoneal dialysis and essential amino acids or their nitro-gen-free analogs. However, with hemodialysis, use of alter-native waste nitrogen excretion pathways (sodium phenyl-butyrate, sodium benzoate, and sodium phenylacetate), dietary protein restriction, and, in some cases, essential amino acid sumplementation the survival rate in powhereas amino acid supplementation, the survival rate in newb diagnosed after birth but within the first month of life is almost 80%. Most deaths have occurred during an episode of almost 80%. Most deaths have occurred during an episode of acute hyperammonemic encephalopathy. Patients with neo-natal-onset disease have a high nicidence of mental retar-dation. Those who had IQ tests administered had an inci-dence of mental retardation as follows: ornithine transcarbamylase deficiency, 100% (14/14 patients tested); argininosuccinic acid synthetase deficiency, 88% (15/17 pa-tients tested); and carbamyl phosphate systhetase defi-ciency, 57% (4/7 patients tested). Retardation was severe in the majority of the retarded patients. In patients diagnosed during gestation and treated prior to

In patients diagnosed during gestation and treated prior to any episode of hyperammonemic encephalopathy, survival is 100%, but even in these patients, most subsequently demonstrate cognitive impairment or other neurologic deficits. In late-onset deficiency patients, including females hetero-zygous for ornithine transcarbamylase deficiency, who recover from hyperammonemic encephalopathy and are then treated chronically with solium phenylbutyrate and dietary protein restriction, the survival rate is 98%. The two deaths in this group of patients occurred during episodes of hyper-ammonemic encephalopathy. However, compliance with the therapeutic regimen has not been adequately documented to allow evaluation of the potential for BUPHENYL and ditary protein restriction to prevent mental deterioration and recurrence of hyperammonemic encephalopathy if care-fully adhered to. The majority of these patients tested (30/46 or 65%) have IQs in the average to low average/ borderline mentally retarded range. Reversal of pre-existing neurophysic in protein set 11-3. neurologic impairment is not likely to occur with treatment and neurologic deterioration may continue in some patients. Even on therapy, acute hyperammonemic encephalopathy recurred in the majority of patients for whom the drug is indicated

BUPHENYL may be required life-long unless orthotopic liver transplantation is elected. (See CLINICAL PHARMACOLOGY, Pharmacodynamics subsection for the biochemical effects of BUPHENYL).

CONTRAINDICATIONS

BUPHENYL should not be used to manage acute hyperammonemia, which is a medical emergency.

### WARNINGS

Each BUPHENYL Tablet contains 62 mg of sodium (9.2% w/w) (corresponding to 124 mg of sodium per gram of so-dium phenylbutyrate [12.4% w/w]) and BUPHENYL Powdram pinely Bull, are 112.4% wW) and BUPHENTL Pow-der contains 11.7 grams of sodium per 100 grams of powder, corresponding to 125 mg of sodium per gram of sodium phe-nylbutyrate (12.4% w/w). BUPHENTL should be used with great care, if at all, in patients with congestive heart failure or severe renal insufficiency, and in clinical states in which there is sodium retention with edema.

Because BUPHENYL is metabolized in the liver and kidney, and phenylacetylghutamine is primarily excreted by the kid-ney, use caution when administering the drug to patients with hepatic or renal insufficiency or inborn errors of beta oxidation. Probenecid is known to inhibit the renal trans-pert of meny comparis encounded by the transformation. port of many organic compounds, including hippuric acid and may affect renal excretion of the conjugated product of BUPHENYL as well as its metabolite. Use of corticosteroids may cause the breakdown of body pro-

tein and increase plasma ammonia levels. PRECAUTIONS

Generat: BUPHENYL should not be administered to patients with known hypersensitivity to sodium phenylbutyrate or any component of this preparation. component of uns preparation. There have been published reports of hyperammonemia be ing induced by haloperidol and valproate. Neurotoxicity of phenylacetate in animals:

When given subcutaneously to rat pups, 190–474 mg/kg phenylacetate caused decreased proliferation and increased loss of neurons, and it reduced CNS myelin. Cerebral syn-

apse maturation was retarded, and the number of function-ing nerve terminals in the cerebrum was reduced, which resulted in impaired brain growth. Prenatal exposure of rat pups to phenylacetate produced lesions in layer 5 of the cor-tical pyramidal cells; dendritic spines were longer and thin-par then rearral and indications of the spines were longer and thinner than normal and reduced in number. Information for the Patients: The full text of the separate insert of information for pa-

tients is reprinted at the end of the labeling. Laboratory Tests: Plasma levels of ammonia, arginine, branched-chain amino

Plasma levels of ammonia, arginine, branched-chain amino acids, and serum proteins should be maintained within nor-mal limits, and plasma glutamine should be maintained at levels less than 1,000 µmol/L. Serum drug levels of phenyl-butyrate and its metabolites, phenylacetate and phen-ylacetylglutamine, should be monitored periodically. **Carcinogenesis, Mutagenesis, Impairment of Pertility:** Carcinogeneity, mutagenicity, and fertility studies of so-dium phenylbutyrate have not been conducted. **Preenance:** 

#### Pregnancy:

Pregnancy. Category C. Animal reproduction studies have not been conducted with BUPHENYL. It is also not known whether BUPHENYL can cause fetal harm when ad-ministered to a pregnant woman or can affect reproduction

capacity. BUPHENYL should be given to a pregnant woman only if clearly needed. Nursing Mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, cau-tion should be exercised when BUPHENYL is administered to a nursing woman. Pediatric Use:

Penarric use: The use of tablets for neonates, infants and children under the weight of 20 kg is not recommended. (See DOSAGE AND ADMINISTRATION

### ADVERSE REACTIONS

The assessment of clinical adverse events came from 206 patients treated with sodium phenylbutyrate. Adverse events (both clinical and laboratory) were not collected sys-tematically in these patients, but were obtained from pa-tient wisit reports by the 65 or investigation of courseling. tematically in these patients, but were obtained from pa-tient-visit reports by the 65 co-investigators. Causality of adverse effects is sometimes difficult to determine in this patient population because they may result from either the underlying disease, the patient's restricted diet, intercur-rent illness, or BUPHENYL. Furthermore, the rates may be under-estimated because they were reported primarily by parent or guarding and the patient parent or guardian and not the patient

# Clinical Adverse Events

In female patients, the most common clinical adverse event reported was amenorrhea/menstrual dysfunction (irregular menstrual cycles), which occurred in 23% of the menstruating patients.

Decreased appetite occurred in 4% of all patients. Body odor (probably caused by the metabolite, phenylacetate) and bad taste or taste aversion were each reported in 3% of patients. Other adverse events reported in 2% or fewer patients were: Gastrointestinal: abdominal pain, gastritis, nausea and vomiting; constipation, rectal bleeding, peptic ulcer disease, and pancreatitis each occurred in one patient.

Hematologic: aplastic anemia and ecchymoses each occurred in one patient.

Cardiovascular: arrhythmia and edema each occurred in one patient.

Renal: renal tubular acidosis Psychiatric: depression

Skin: rash

Miscellaneous: headache, syncope, and weight gain <u>Miscellaneous</u>: headache, syncope, and weight gain Neurotoxicity was reported in cancer patients receiving in-travenous phenylacetate, 250-300 mg/kg/day for 14 days, repeated at 4-week intervals. Manifestations were predom-inately somolence, fatigue, and lightheadedness; with less frequent headache, dysgeusia, hypoacusis, disorientation, impaired memory, and exacerbation of a pre-existing neu-ropathy. These adverse events were mainly mild in severity. The acute onset and reversibility when the phenylacetate infusion was discontinued suggest a drug effect. Laboratory Adverse Events

infusion was discontinued suggest a drug effect. Laboratory Adverse Events In patients with urea cycle disorders, the frequency of lab-oratory adverse events by body system were: <u>Metabolic</u> acidosis (14%), alkalosis and hyperchloremia (each 7%), hypophosphatemia (6%), hyperuricemia and hy-perphosphatemia (each 2%), and hypernatremia and hypokalemia (each 1%).

Nutritional: hypoalbuminemia (11%) and decreased total protein (3%).

Hepatic: increased alkaline phosphatase (6%), increased liver transaminases (4%), and hyperbilirubinemia (1%). <u>Hematologic:</u> anemia (9%), leukopenia and leukocytosis (cach 4%), thrombocytopenia (3%), and thrombocytosis (1%). The clinician is advised to routinely perform urinalysis, blood chemistry profiles, and hematologic tests. OVERDOSAGE

No adverse experiences have been reported involving overdoses of sodium phenylbutyrate in patients with urea cycle disorders.

In the event of an overdose, discontinue the drug and institute supportive measures Hemodialysis or peritoneal dialysis may be beneficial.

Continued on next page

Consult 2006 PDR® supplements and future editions for revisio

Find authenticated court documents without watermarks at docketalarm.com.

# Buphenyl-Cont.

#### DOSAGE AND ADMINISTRATION

For oral use only The use of BUPHENYL Tablets is indicated for children weighing more that 20 kg and for adults. The usual total daily dose of BUPHENYL Tablets and Powder for patients with urea cycle disorders is 450 – 600 mg/kg/day in patients weighing less than 20 kg, or 9.9 – 13.0 g/m<sup>2</sup>/day in larger patients. The tablets and powder are to be taken in equally divided amounts with each meal or feeding (i.e., three to six times per day). BUPHENYL Powder is indicated for oral use (via mouth.

gastrostomy, or nasogastric tube) only. The powder is to be mixed with food (solid or liquid). Sodium phenylbutyrate mixed with food (solid or induid). Solidum pinenyibultyrate is very soluble in water (5 grams per 10 mL). When BUPHENYL Powder is added to a liquid, only sodium phe-nyibultyrate will dissolve, the excipients will not. The effect of food on sodium phenyibultyrate has not been determined. Each level tenspoon (enclosed) dispenses 3.2 grams of powder and 3.0 grams of sodium phenylbutyrate. Each level tablespoon (enclosed) dispenses 9.1 grams of powder and 8.6 grams of sodium phenylbutyrate. Shake lightly before use.

The safety or efficacy of doses in excess of 20 grams (40 Tab-lets) per day has not been established. NUTRITIONAL MANAGEMENT

# To promote growth and development, plasma levels of am-monia, arginine, branched-chain amino acids, and serum protein should be maintained within normal limits while plasma glutamine is maintained at levels less that 1,000 µmol/L. Minimum daily protein intake for a patient of a particular age should be taken from, for example, "Recommended Dietary Allowances", 10th ed., Food and Nutrition Board, National Academy of Sciences, 1989. The allocation of dietary nitrogen into natural protein and essential aming

of dietary nitrogen into natural protein and essential amino acids is a function of age, residual urea-cycle enzyme activ-ity, and the dose of sodium phenylbutyrate. At the recommended dose of sodium phenylbutyrate, it is suggested that infants with neonatal - onset CPS and OTC deficiencies initially receive a daily dietary protein intake detciencies initially receive a daily dietary protein intake limited to approximately 1.6 g/kg/day for the first 4 months of life. If tolerated, the daily protein intake may be in-creased to 1.9 g/kg/day during this period. Protein tolerance will decrease as the growth rate decreases, requiring a re-duction in dietary nitrogen intake. From 4 months to 1 year of age, it is recommended that the infaint receive at least 1.4g/kg/day but 1.7g/kg/day is advisable. From 1 to 3 years of age, the protein intake should not be less than 1.2 g/kg/ day 1.4 g/kg/day is advisable during this period. For neona-tion-set patients with carbamy/hopshate synthetizes defiday i. A graphay is advisable during this period. For neon-tal-onset ptatients with carbamylphosphate synthetizes defi-ciency or ornithine transcarbamylase deficiency who are at least 6 months of age, it is recommended that the daily pro-tein intake be equally divided between natural protein and supplemental essential amino acids. Patients with argininosuccinic acid synthetase deficiency

and those with late-onset disease (partial deficiencies, in-cluding females heterozygous for ornithine transcarbamylase), initially may receive a diet containing the age-determined minimal daily natural protein allowance. The protein intake may be increased as tolerated and determined by plasma glutamine and other amino acid levels. However many patients with partial deficiencies avoid dietary

Citrulline supplementation is required and recommended for patients diagnosed with neonatal-onset deficiency of car-bamylphosphate synthetase or ornithine transcarbamylase; citrulline daily intake is recommended at 0.17 g/kg/day or

3.8  $g/m^2/day$ . The free-base form of arginine may be used instead of citrulline in patients with milder forms of carbamylphosphate synthetase and orinthine transcarbamylase deficiency (daily intake is recommended at 0.17 g/kg/day or 3.8 g/m<sup>2</sup>/ day)

Arginine supplementation is needed for patients diagnosed with deficiency of argininosuccinic acid synthetase; arginine (free base) daily intake is recommended at 0.4 - 0.7 g/kg/day or 8.8 - 15.4 g/m<sup>2</sup>/day. If calorie supplementation is indicated, a protein-free prod-

uct is recommended. Caloric intake should be based upon the "Recommended Dietary Allowances", 10th ed., Food and Nutrition Board, National Research Council, National Academy of Sciences, 1989.

### HOW SUPPLIED

BUPHENYL Tablets are available in 250 cc bottles, which contain 250 sodium phenylbutyrate tablets (NDC 62592-496-03). The bottles are equipped with thild resistant caps. Each tablet is off-white, oval, and embossed with "UCY 500". Each tablet contains 500 mg of sodium phenylbu-tyrate. STORE AT ROOM TEMPERATURE 15°C-30°C (59°F-86°F). AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED. BUPHENYL Powder is available in 500 cc bottles, which bold 266 grams of powder, containing 250 grams of sodium phenylbutyrate (NDC 62592-188-64). The bottles are equipped with child-resistant caps. Measurers are provided. equipped with child-resistant caps. Measurers are provided. Each level teaspoon (enclosed) dispenses 3.2 grams of pow-der and 3.0 grams of sodium phenylbutyrate. Each level ta-blespoon (enclosed) dispenses 9.1 grams of powder and 8.6 grams of sodium phenylbutyrate. STORE AT 15°C-39°C (59°F-86°F). AFTER OPENING, KEEP BOTTLE TIGHTLY CLOSED.

US Patent number 4 457.942

DOCKE'

Manufactured for: Ucyclyd Pharma, Inc., Scottsdale, AZ 85258

By: Pharmaceutics International, Inc. Hunt Valley, MD 21031

NDC 62592-496-03 bottle of 500 mg tablets NDC 62592-188-64 bottle containing 250g of sodium phenylbutyrate powder. Prescribing Information as of August 2003

49603-08A

# Unicity International THE MAKE LIFE BETTER COMPANY 1201 NORTH 800 EAST OREM, UT 84097

Direct Inquiries to:

(801) 226 2600 www.makelifebetter.com

science@unicity.net

Products of Unicity International, The Make Life Better Company are distributed through independent distributors.

### **BIOSLIFE 2**®

bi-os lif 2 **Advanced Fiber and Nutrient Drink** 

#### DESCRIPTION

BiosLife 2 is a nutrient-rich fiber drink mix that contains a patented complex of soluble and insoluble fibers, vitamins, and minerals

# BENEFITS AND RESEARCH

BioLife 2 —a good source of dietary fiber — when included as part of a healthy diet, may help lower your blood choles-terol levels and reduce your risk of heart disease. Eight weeks of BiosLife 2 showed a significant reduction in LDL-c compared to placebo. The mechanism of BiosLife 2 in cho lesterol reduction is though bile-acid sequestration.

### SUGGESTED USE

First users: dissolve the contents of one packet into 8 to 10 fl. oz. of liquid (water or juice), stir vigorously and drink im-mediately 5 to 10 minutes before the main meals. After fiber adjustment use as directed above up to three times daily before every meal. CONTENTS

One packet of BiosLife 2 contains 4.5 gram fiber, comprising of 4 grams of soluble fiber. Added to this fiber mix are optimal daily levels and bio-available forms of several vitamins, and chromium (as ChromeMate<sup>TM</sup>). BiosLife 2 is available in Natural, Original, and Tropical Fruit flavors. For detailed dietary information, please see www.unicity.net

#### SAFETY AND WARNINGS

BiosLife 2 is well accented. Some users report mild gastro intestinal discomfort after first use. This is a normal effect of increased fiber intake and normally disappears within 30 days. Taking this product without adequate liquid can re-sult in complications. If you are a diabetic, consult a physi-cian for proper use of this product, as the chromium may reduce the need for medication.

### HOW SUPPLIED

Conveniently packaged in single-serving packets or bulk canisters.

#### REFERENCES

Sprecher, DL and Pearce GL (2002), Metabolism 51: 1166-

70. Verdegem, PJE; Freed, S and Joffe D (2005), American Di-abetes Assocation 65<sup>th</sup> Scientific Sessions, San Diego. US Patent 4,883,788 and US Patent 4,824,672. "HESE STATEMENTS HAVE NOT BEEN EVALUATED

BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT CURE, OR PREVENT ANY DISEASE.

#### CARDIOESSENTIALS® Caring for your heart

#### DESCRIPTION

CardioEssentials is Unicity's superior heart product. Benefits and research

CardioEssentials provides nutrients for the heart muscle and supports healthy heart function. The combination of Learnithine, L-taurine, and Coenzyme Q10 has been shown to benefit congestive heart failure patients in a clinical study. In this study, left ventricular size was reduced in CHF patients, giving them a better prognosis. These ingredients are known to be important in providing adequate en ergy for the heart muscle. CardioEssentials provides ade-quate amounts of these ingredients, i.e. 100 mg of CoQ10. Hawthorn extract is traditionally used in supporting the heart function

### SUGGESTED USE

Take six capsules daily with food.

# PHYSICIANS' DESK REFERENCE

Contents CardioEssentials features a proprietary blend of Learning thine, L-taurine, and Hawthorn, combined with 100 mg at Contents dietary information, please detailed For www.makelifebetter.com

SAFETY AND WARNINGS SAFETY AND water and a set of the set of the

# HOW SUPPLIED

Available in bottles of 180 tablets.

\*THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT REFERENCES

Jeejeebhoy, F et al (2002), American Heart Journal 143 1092-1100.

#### CM PLEX™ AND CM PLEX™ CREAM [CM plěks]

Proprietary fatty acid blend to help alleviate symptoms of osteo arthritis\*

OTC

#### DESCRIPTION

OTC

CM Plex and CM Plex Cream are a softgel, and topical cream product respectively, combining fatty acids, in a pro-prietary blend of cetyl myristate, cetyl myristoleate, and other cetyl esters.

### Benefits and research

Cetyl myristoleate and related fatty acids have been proven to improve joint health, through their anti-inflammatory of to improve joint nearth, through their anti-inflammatory ef-fects. A clinical study indicated that subjects exhibited im-provements in knee flexion compared to placebo. A second study indicated the study indicated the cream is effective for improving knee range of motion, improving ability to climb stairs, rise from a chair, and walk, and improving balance, strength, and endurance.<sup>8</sup>

#### SUGGESTED USE

Softgels: Take one or two softgels three times daily with meals. Cream: Apply generously onto clean skin and gently massage until the cream disappears. Repeat 3 to 4 times daily as necessary. For maximum results combine both products. Contents

# CM Plex contains a proprietary blend of cetyl myristate, ce-tyl myristoleate, and other cetyl esters. For detailed dietary information, please see www.unicity.net.

Safety and Warnings CM Plex Softgels and Cream are well accepted. Some gas-trointestinal discomfort may be experienced with CM Plex Softgels as with any dietary supplement.

### HOW SUPPLIED

CM Plex is available in both cream and soft gels. REFERENCES

Hesslink, R et al (2002), Journal of Rheumatology 29: 1708-1712

Kraem er, WJ et al (2004), Journal of Rheumatology 31. 767-774.

\*THESE STATEMENTS HAVE NOT BEEN EVALUATED BY THE FOOD AND DRUG ADMINISTRATION. THIS PRODUCT IS NOT INTENDED TO DIAGNOSE, TREAT CURE, OR PREVENT ANY DISEASE.

#### VISUTEIN® vis-u-ten

Clinically proven to support healthy eyes and vision.\*

# DESCRIPTION

VISUtein is Unicity's product providing key nutrients for the eye.

# Benefits and research

The carotenoids lutein and zeaxanthin play an important role in eye health. Low concentrations of these phytonutric ents in the retina have been associated with age related macula degeneration (AMD). Studies have shown, that sup-plementations with kink hard back and a supermacula degeneration (AMD). Studies have shown, that sup-plementation with high levels of lutein, as present in VISUtein, can restore the lutein concentration in the retina-The product further features important vitamins, and carot-enoids that are important in preserving overall eye health and supporting clear vision. Nacetyl cysteine is added to boost the glutathion levels in the retina. Low glutathion levels have been shown to reduce protection of the eye against oxidative stress. A recent clinical study with VISUtein has shown that AMD patients experience clear improvements in visual acuity, contrast sensitivity, and recovery from 8 feash.\* flash.<sup>4</sup>

Take two capsules per day with a meal.

VISUtein provides 18 mg of lutein, along with 200 mg of N-acetyl cystein, and 60 mg anthocyanidins from bilberry

отс

OTC

# SUGGESTED USE