Louis A. Montgomery
6542 Hypoluxo Road, Suite 114
Lake Worth, FL 33467

August 23, 2005

Bundesinstitut für Arzneimittel und Medizinprodukte
Attn: Unit 71, Herrn Norbert Paeschke
VIA FACSIMILE: 49-(0)228-207 - 5207

Dear Herr Paeschke:

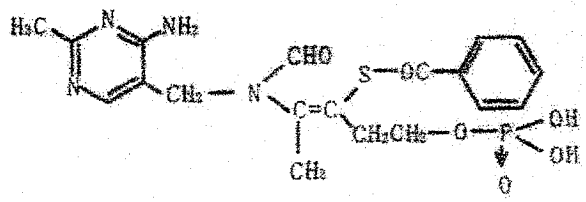
Please reference our telephone conversation earlier today.

I am assembling data from multiple sources to propose to the U.S. Food and Drug Administration (FDA) that the compound benfotiamin can reasonably be expected to be safe for human consumption.

If under the provisions of the U.S. Dietary Supplement Health and Education Act of 1994 (DSHEA 1994) the FDA determines that benfotiamin can reasonably be expected to be safe, I will be able to distribute benfotiamin as a dietary supplement in the United States.

Benfotiamin is distributed in Germany under the trade name Milgamma, in tablets of 50mg., 100mg. and 150mg., by Woerwag Pharma, GmbH, of Boeblingen. The chemical name for benfotiamine is: S-benzoylthiamine-O-monophosphate. The molecular formula and structure is depicted below:

White crystals or crystalline powder.
FORMULA: $C_{19}H_{23}N_4O_6PS$ MOLECULAR FORMULA: 466.45



MELTING POINT: about 200°C(with decomposition)

Tel. (561) 512-3719; Fax: (561) 641-0838; Email lou3551@aol.com

Louis A. Montgomery
6542 Hypoluxo Road, Suite 114
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The following information, if available, would be very useful to me:

1. The date benfotiamin began to be distributed in Germany.
2. The typical daily dose for benfotiamin.
3. The highest daily dose available/recommended for benfotiamin.
4. The gross number of doses sold annually in Germany.
5. Any adverse effects/events reported which could be associated with the use of benfotiamin.
6. The number of adverse effects/events as a percent of total users of benfotiamin.
7. An assessment by your institute as to the safety of benfotiamin for human use.
8. Any open source clinical data regarding the safety of benfotiamin you may be aware of and can supply or direct me to.

I of course would be pleased to reimburse your expenses for providing any or all of the requested information.

Don't hesitate to contact me if you require further explanation or clarification.

Mit Vielen Dank im Voraus,

Louis A. Montgomery

Tel. (561) 512-3719; Fax: (561) 641-0838; Email lou3551@aol.com

BfArM
Federal Institute for Drugs
and Medical Devices

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Your reference and letter of	Our reference (Please quote in your reply)	Telephone: +49-1888-307-	Bonn
August 23, 2005	715-3811-110211/05	3796	Sep. 22, 2005

Request for information on benfotiamine-containing drugs in Germany

Dear Mr Montgomery,

herewith I would like to answer your request concerning the marketing situation and other aspects of benfotiamine-containing drugs in Germany. Please apologize our delayed response – my attempt to respond to you via lou3551@aol.com has obviously failed.

ad Q1:
1978

ad Q2:
The typical daily benfotiamine-dose depends on respective indications and varies between different drugs (the below mentioned example represents typical dose recommendations):

- Prevention of Vitamin B1-deficiency: 1-2 x 50 mg dragee/week
- Treatment of Vitamin B1 deficiency: 1-3 x 50 mg dragee/day
- Treatment of polyneuropathy (caused by Vitamin B1 deficiency): up to 400 mg/day (first three weeks), afterwards up to 150 mg/day

ad Q3:

- 400 mg benfotiamine (enteral dosage forms)/day = highest daily dose of a marketed drug
- 900 mg benfotiamine (enteral dosage forms)/day = highest daily dose of a non-marketed but authorised drugs.

ad Q4:
This question cannot be answered exactly, since no respective data are available to us.

22-SEP-2005 14:46 BFARM ABT 7 +49 228 207 3515 S.01/02
Received Fax : Sep 22 2005 8:37 Fax Station : BENFOTIAMINE.NET, INC. p. 1

The distribution of benfotiamine-containing drugs in Germany is restricted to pharmacies. A medical prescription is not compulsory. Based on prescription data only, for example, in 2002, a total of 2.4 million defined daily dosages of one benfotiamine-containing drug (milgamma mono®) have been prescribed in Germany.

ad Q5:
Within the BfArM-database (spontaneous reports from Germany; reporting source: HCPs only) the following numbers of reports describing adverse reactions (ADRs) observed in association with use of benfotiamine-containing drugs have been identified (the reports were not differentiated with regard to the causal relationship between the drug and the reported ADRs).
Number of ADR-reports within the BfArM-database mentioning association with use of Benfotiamine-containing drugs:

- **Benfotiamine-containing monotherapeutics: n = 18** – per email
- **Benfotiamine-containing combination drugs: n = 92**

ad Q6:
No reporting rates can be calculated since no exact exposition data are available to us.

ad Q7:
With regard to benfotiamine routine pharmacovigilance has been performed using data from different sources (spontaneous ADR reports, periodic safety update reports, scientific literature); in doing so, no safety signals pertaining benfotiamine-containing drugs have been identified.

ad Q8:
Respectively, the following homepages may be of interest to you.
http://www.clinicaltrials.gov/
http://www.centerwatch.com/
http://controlledtrials.com/

We hope this information is of use to you. In case of further questions, please don't hesitate to contact me.

Yours sincerely
(on behalf of the BfArM)

Jörg Seebeck

22-SEP-2005 14:46 BFARM ABT 7 +49 228 207 3515 S.02/02
Received Fax : SEP 22 2005 8:37 Fax Station : BENFOTIAMINE.NET, INC. p. 2

Von Jörg Seebeck
An: lou1355@hotmail.com
Datum: 26.09.2005 09:19:51
Betreff: benfotiamine_BfArM

Dear Mr Montgomery,

with regard to the questions outlined in your last mail, please find here the follwing answers:
the number of ADR reports mentioned in my letter represent the total number of of reports received by the BfArM since 1978.

The second part of your "question 2" relates to the types of ADRs (hypersensitivity, etc) which have been received in association with use of benfotiamine. Please find attached a table of all reports describing cases in which benfotimaine was applied in the form of a monotherapeutic (n = 18 [and not 28 as falsely described in my previous letter]). Of these, the most important ones are those in which benfotiamine was considered by the reporter as "suspected" or "interacting" drug - these cases are indicated in the column "role" by the letters "s" or "i".

Hoping to be of assistance.
Yours sincerely

Jörg Seebeck

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Kind regards
Jörg

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Your reference	Our reference (please quote in your reply)	Tel: +49-1888-307-	Bonn
Dec. 30, 2005	715-3811-110211/05	-3796	Jan. 02, 2006

Re. request: benfotiamine/marketing status/Germany

Dear Mr Montgomery

Herewith I would like to answer the two questions outlined in your fax dated December 30, 2006.

ad 2)
The name benfotiamine (German: benfotiamin) refers to S-benzoylthiamine-O-monophosphate only and not its calcium or sodium salts.

ad 1)
The benfotiamine-containing drugs are marketed in Germany since 1978. From the beginning, these drugs were available via Pharmacies without the requirement of a medical prescription. In Germany benfotiamine-containing drugs (mono-therapeutics) are indicated for the prophylaxis and treatment of clinically/chemically-confirmed Vitamin-B1 deficiency disorders which cannot be treated sufficiently by dietary measures alone. In addition, benfotiamine is also a component of some multivitamin-preparations.

I hope this information is of use to you. In case of any questions, please do not hesitate to contact me.

Yours sincerely
by order

Jörg Seebeck

Jörg Seebeck

Arch

Line listing mit Bewertung

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-04011841	Inland	Spontaneous report		44 Year	m		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 tavanic 250	s	17-SEP-2004	20-SEP-2004	Oral	250.	possible
#2 insuman rapid	c			Subcutaneous		
#3 zocor	c			Oral	040	
#4 norvasc	c			Oral	010	
#5 lantus	c			Subcutaneous		
#6 beloc zok	c			Oral	001	
#7 atacand	c			Oral	024	
#8 plavix	c			Unknown	001	
#9 adalat	c			Unknown		
#10 resonium a	c			Unknown		
#11 isomol	c			Unknown	002	
#12 vioxx	c			Unknown	025	
#13 milgamma mono	c			Unknown	150	
#14 renagel	c			Unknown	2.4	
#15 renavil	c			Unknown	001	
#16 furorese	c			Unknown	500	
#17 danoprox	c			Unknown	100	
#18 motilium	c			Oral		
#19 calciumacetat nefro	c			Unknown	2.8	
#20 tilidolor	c			Unknown		
#21 bikalm	c			Unknown		
#22 novalgin	c			Rectal	001	
#23 neurontin	c			Unknown		
#24 pantozol	c			Unknown	002	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes		Marked restlessness	19-SEP-2004	Unknown
		Confusion	19-SEP-2004	Unknown

2

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-04003161	Inland	Report from study		56 Year	f	51	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 lonafarnib	s	16-APR-2003		Oral	200	possible
#2 phenprocoumon	c	JUL-2003		Oral		
#3 hydromorphone	c	JUL-2003		Oral	008	
#4 carboplatin	s	16-APR-2003	30-JUL-2003	Intravenous (not otherwise specified)		possible
#5 benfotiamine	c	29-JUL-2003		Oral	300	
#6 paclitaxel	s	16-APR-2003	30-JUL-2003	Intravenous (not otherwise specified)		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes	hospitalization	Anaemia	08-AUG-2003	recovered/resolved
		Weakness generalized	08-AUG-2003	recovered/resolved

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-04003105	Inland	Spontaneous report		58 Year	m		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 extraneal	s	MAY-2001		intraperitoneal	002	possible
#2 unat 200	c			Unknown		
#3 ass 100	c			Unknown		
#4 silibene	c			Unknown		
#5 physioneal 1.36%	c			Unknown		
#6 rocaltrol	c			Unknown		
#7 melotazone	c			Unknown		
#8 benfotiamine	c			Unknown		
#9 lantus	c			Unknown		

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes	hospitalization	Peritonitis	MAY-2001	recovered/resolved

3

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-02003111	Inland	Report from study		70 Year	f	68	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 milgamma mono	s	30-JAN-2002	26-FEB-2002	Oral	600	possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes	hospitalization	Cerebral vascular disturbance	19-FEB-2002	recovered/resolved
		Syncope	26-FEB-2002	recovered/resolved

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Received Fax : 04-OKT-2005 15:06 BFARM ABT 7 +49 228 207 3515 S.05/11
Oct 04 2005 8:57 Fax Station : BENFOTIAMINE-NEI INC. P. 5

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_Int
DE-BFARM-01009602	Inland	Spontaneous report		66 Year	m		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 zocor 40 mg	s	JUL-2001	06-NOV-2001	Oral	001	possible
#2 sandimmun	c			Oral	050	
#3 lendormin	c			Oral	001	
#4 imurek	c			Oral	100	
#5 captopril	c			Oral	100	
#6 furorese	c			Oral	080	
#7 pyridoxine hydrochloride	c			Oral	200	
#8 sandimmun 100 mg	c			Oral	002	
#9 insulin human	c			Unknown	032	
#10 benfotiamine	c			Oral	200	
#11 prednisolone	c			Unknown	005	
#12 aspirin	c			Oral	100	
#13 diamox	c			Oral		

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes	hospitalization	Rhabdomyolysis	06-NOV-2001	recovered/resolved
		Creatine kinase increased	06-NOV-2001	recovered/resolved
		CPK increased	06-NOV-2001	recovered/resolved
		Myoglobin urine	06-NOV-2001	recovered/resolved
		Alanine aminotransferase increase	06-NOV-2001	recovered/resolved
		Strength loss of	06-NOV-2001	recovered/resolved
		Aspartate aminotransferase increase	06-NOV-2001	recovered/resolved
		BUN increased	06-NOV-2001	recovered/resolved

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BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-01003601	Inland	Spontaneous report		66 Year	m	97	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 milgamma mono 150	s	02-APR-2001	04-APR-2001	Oral	001	possible
#2 marcumar	c			Unknown		
#3 siofor 850	c			Oral	002	
#4 glibenclamid 3,5mg	c			Oral	002	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Erythema	04-APR-2001	recovered/resolved
		Itching	04-APR-2001	recovered/resolved

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-98901069	Inland	Report from study		60 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Hernia NOS	22-MAR-1999	Unknown
		Aggravation of existing disorder	22-MAR-1999	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003251	Inland	Report from study		21 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	30-JAN-1996	Unknown

6

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003250	Inland	Report from study		36 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	16-JAN-1996	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003249	Inland	Report from study		30 Year	m		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	16-JAN-1996	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003248	Inland	Report from study		20 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	16-JAN-1996	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003247	Inland	Report from study		28 Year	m		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	31-JAN-1996	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003246	Inland	Report from study		23 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	17-JAN-1996	Unknown

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-96003245	Inland	Report from study		26 Year	f		

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 benfotiamin	s			Oral		possible

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Headache	31-JAN-1996	Unknown

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BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-92006791	Inland	Spontaneous report		50 Year	m	72	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 kafadolon kapseln	s	22-MAY-1991	22-MAY-1991	Oral		possible
#2 benfotiamine	c	17-APR-1991		Oral	003	
#3 doxepin	c	25-AUG-1989		Oral	025	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
		Urticaria	22-MAY-1991	recovered/resolved
		Rash maculo-papular	22-MAY-1991	recovered/resolved

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-92005052	Inland	Spontaneous report		72 Year		98	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 tensobon	s	MAY-1992	22-JUN-1992	Oral	063	possible
#2 accupro	s	23-JUN-1992	06-JUL-1992	Oral	013	possible
#3 insulin	c			Subcutaneous	070	
#4 triazolam	c			Unknown		
#5 benfotiamin	c			Oral	100	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes		Cough	JUN-1992	recovered/resolved

8

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-92003142	Inland	Report from study		51 Year	m	57	

DRUG identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 pankreatin	c	25-SEP-1991		Oral	600	
#2 delix 1,25	s	09-OCT-1991	12-OCT-1991	Oral	1.3	possible
#3 delix 2,5	s	13-OCT-1991	16-OCT-1991	Oral	2.5	possible
#4 bufedil forte	c	23-SEP-1991		Oral	600	
#5 cyanocobalamin	c	23-SEP-1991		Unknown	750	
#6 benfotiamine	c	23-SEP-1991		Oral	150	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes		Hyperkalaemia	14-OCT-1991	Unknown

90

BfArM Ref. no.	Country	Source Report type	Literature	Patient Age	Sex	Weight (kg)	Pregnancy_int
DE-BFARM-91010278	Inland	Spontaneous report		64 Year	f	60	

DRUG Identification Drug name	Role	Start	End	Route of Administration	Dosage Daily dose	Assessment Bewertung BfArM
#1 zofran	i	16-SEP-1991	16-SEP-1991	Intravenous (not otherwise specified)		
#2 metoclopramide	i			Unknown		
#3 prednisolon	c			Unknown	010	
#4 prazosin	c			Unknown	002	
#5 allopurinol	c			Oral	300	
#6 talinolol	c			Unknown	100	
#7 benfotiamine	c			Oral	100	
#8 indometacin	c			Unknown	200	
#9 glibenclamide	c			Unknown		
#10 daunorubicin	c	16-SEP-1991	16-SEP-1991	Intravenous (not otherwise specified)		
#11 cytarabine	c	16-SEP-1991	16-SEP-1991	Intravenous (not otherwise specified)		
#12 lidocaine	c	16-SEP-1991	16-SEP-1991	Unknown		
#13 cyanocobalamin	c			Oral	050	

Seriousness Serious	Seriousness criteria	REACTION Reaction MedDRA	Onset	Outcome
Yes	lifethreatening	Cardiac arrest	16-SEP-1991	recovered/resolved
		Respiratory depression	16-SEP-1991	recovered/resolved