Attachment II

to

Safety Review Update

Table 8.7-24. AE Reports With Nonserious Outcome (Other Than FDA Subgroups) for Migraine Use Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
1	MIB	458/154	06/19/95	Unk	Female	"No luck"	Lack of efficacy	Unknown	Unknown	Aspirin	Unknown
2	MIB	482/154	06/19/95	Unk	Female	Migraine headache pain not reduced	Lack of efficacy	Unknown	Unknown	Unknown	Unknown
3	MIB	336/154	02/09/94	56 yr	Male	Constipation	Constipation	1200 mg	1/94- continues	None	Unknown
4	MIB	418/154	02/03/95	39 yr	Female	Lack of effect (for headache) Vomiting Headache Nausea Chills Malaise for 48 hours Exceeded dosage	Lack of efficacy Vomiting Headache Nausea Chills Malaise Overdose NEC/NOS	Unknown	Unknown	Unknown	Unknown
5	AFP	0466536A	10/24/95	55 yr	Female	Does not work	No drug effect	400 mg, qid, po	10/95 1 day	Panadol\ prn	Unknown
6	NUP	1101/19012	12/01/95	21 yr	Female	Overdose No event	Overdose no signs of toxicity	2400 mg	Unknown	None	Unknown
7	NUP	1149/19012	04/09/96	Unk	Female	Did not relieve migraine headache	Lack of efficacy	Unknown	Unknown	Unknown	Unknown
8	MIB	0868999A	09/29/97	73 yr	Female	Blurred vision Difficulty focusing Optic migraine headache	Amblyopia Migraine	200 mg, prn, po	7/27/97-8/10/97 15 days	None	Unknown
9	MIB	0993583A	10/28/97	42 yr	Male	Did not help	No drug effect	Unknown dose, po	Unknown	Nasalcrom	Unknown
10	NUP	0899059A	12/02/97	65 yr	Female	Overdose Blisters on feet & hands Boils on feet and hands	Overdose Vesiculobullous rash Furunculosis	600 mg, tid, po	8 years	Procardia atenolol	Unknown
11	NUP	1017205A	08/05/98	53 yr	Female	Pressure in chest	Chest pain Nausea Allergic reaction	200 mg, qd, po	1/1/93-7/31/98 5 years	Propulsid	Unknown

a: MIB = Motrin® IB product, AFP = Arthritis Foundation™ product, NUP = Nuprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

Attachment III

to

Safety Review Update

Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
1	MIB	326/154	12/28/93	78 yr	Male	Convulsions Delirious Headache Chills Low grade fever Falls Irrational with prednisone	Convulsions major Delirium Headache Chills Fever Falling Irrational Death	200 mg	approx 9 months, interrupted	Prednisone, Unknown medications	Unknown	Death Life-threatening Hospitalization Disability Required intervention
2	NUP	774/19012	02/10/94	49 yr	Male	Gallbladder attack	Cholecystitis	200-800 mg	Approx 5 months	Tylenol	Unknown	Disability Partial recovery
3	MIB	351/154	03/14/94	26 yr	Male	Pancreatitis	Pancreatitis	Unknown	Unknown	Unknown	Unknown	Hospitalization Recovery
4	MIB	366/154	05/04/94	Unk	Unknown	Anxiety attacks	Anxiety	400-800 mg; 3 times daily	Unknown	Unknown	Unknown	Hospitalization
5	MIB	367/154 CTU #009959	05/17/94	61 yr	Male	Anaphylactic shock	Anaphylactic shock	Unknown	1 dose	Feosol Vibramycin	Unknown	Hospitalization Recovery
6	MIB	370/154 same as 839/19012	06/06/94	63 yr	Female	Perforated ulcer	Gastroduodenal ulcer with perforation	800 mg	Unknown	Nuprin tablets, Advil, Darvocet N-100, aspirin	Does not drink alcohol	Life-threatening Hospitalization Required intervention Recovery
7	NUP	846/19012	06/15/94	3 yr	Female	Accidental pediatric ingestion of 24 tablets Slight fever	Overdose with signs of toxicity Fever	4800 mg	1 day	None	Unknown	Required intervention Recovery

a: MIB = Motrin®IB product, AFP = Arthritis Foundation™ product, NUP = Nuprin® product, UNIB = Unknown ibuprofen product, MED = Mediprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
8	UNIB	0273590A	06/27/94	43 yr	Male	Nausea Stomach ulcer	Nausea Stomach ulcer	200 mg po tid	5/26/94-6/3/94; 7 days	None	Unknown	Hospitalization
9	MIB	374/154	06/29/94	72 yr	Male	Reduced hearing Ringing in ears	Diminution in hearing Tinnitus	800 mg	Unknown	None	Unknown	Disability
10	MIB	377/154	07/18/94	19 yr	Female	Lost ability to focus eyes Difficulty with speech Difficulty swallowing Loss of balance Vomiting Weakness	Blurred vision Trouble with speech Dysphagia Loss of balance Vomiting Weakness NOS	400 mg	1 dose	None	Unknown	Hospitalization Disability Partial recovery
11	NUP	895/19012	08/12/94	Unk	Male	Pancreatitis	Pancreatitis	Unknown	Unknown	Zantac, vitamin B	Unknown	Hospitalization
12	NUP	901/19012	08/18/94	33 yr	Female	Overdose Headache	Overdose NEC/NOS Headache	4800 mg	1 day	None	Unknown	Life-threatening Recovery
13	UNIB	0309383A	10/09/94	19 yr	Female	Cellulitis	Cellulitis	200 mg Q4H x 3 doses	12 hours, 10/3/94	One or more days between 10/3/94 and 10/9/94 Ortho Novum, Lortab, penicillin, Toradol, xylocaine 2% v/c, Fentanyl, Versed, Flagyl, ibuprofen, Peridex	Unknown	Hospitalization

a: MIB = Motrin®IB product, AFP = Arthritis Foundation™ product, NUP = Nuprin® product, UNIB = Unknown ibuprofen product, MED = Mediprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
14	NUP	955/19012	11/30/94	59 yr	Male	Acute gastritis	Gastritis	Unknown	1 dose	None	Unknown	Hospitalization Recovery
15	NUP	941/19012	03/22/95	18 yr	Female	Low blood pressure High blood sugar Sick to stomach Intentional overdose	Decreased blood pressure Hyperglycemia Upset stomach Intentional overdose	4800 mg	1 day	Prozac, Ditropan	Unknown	Hospitalization Required Intervention Recovery
16	NUP	1016/19012	07/18/95	60 yr	Female	Shock (following episode of severe vomiting) Event when taken with "Echinacea" Episode of severe vomiting Chest pain (after episode of severe vomiting)	Shock Miscellaneous drug interaction Vomiting Chest pain NOS	200-400 mg	27 days	"Echinacea"	Unknown	Hospitalization Partial recovery
17	UNIB	1044/19012	08/14/95	17 yr	Female	Intentional overdose Stomach pain	Intentional overdose Pains in stomach	2400 mg	1 dose	Unknown	Unknown	Hospitalization Recovery
18	MED	0451379A	09/15/95	17 yr	Male	Intentional overdose Lethargic Hypoprothrombinemia	Intentional overdose Somnolence Prothrombin decreased	98 gms orally	1 day	Diphenhydramine tablets	Unknown	Hospitalization Recovered
19	MED UNIB	0454419A 508/154[c]	09/25/95	6 yr	Male	Accidental overdose Shock Coma Metabolic acidosis	Accidental overdose Shock Coma Acidosis	Approx 6 gms, orally	1 dose	Unknown	Unknown	Life-threatening Hospitalization Required Intervention Recovered

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Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
20	MIB	494/154 submitted as 4784/17463	10/16/95	57 yr	Male	Perforated stomach	Gastric ulcer with perforation	200-400 mg	Unknown	Ibuprofen, atenolol, chlortalidone (Tenoretic)	Unknown	Recovery Required intervention Hospitalization
21	UNIB	0516874A	01/24/96	40 yr	Female	Death Asthma Unconscious Respiratory arrest	Death Asthma Coma Apnea	400 mg, one dose, orally	1 day	fenoterol metered-dose inhaler (MDI) on a prn basis	Unknown	Death Hospitalization
22	UNIB	529/154	02/16/96	17 yr	Male	Agranulocytosis	Agranulocytosis	400 mg	2/95	None	Unknown	Life-threatening Hospitalization Partial recovery
23	MIB	537/154	03/07/96	43 yr	Female	Anaphylactic shock Possible interaction between Motrin IB & tuna fish	Anaphylactic shock Food interaction	200 mg	1 dose	tuna fish	Unknown	Life-threatening Hospitalization Recovery
24	AFP	0582563A	04/25/96	Unk	Female	Severe toxic and allergic reaction	Allergic reaction	Dose Unknown	Unknown	Unknown	Unknown	Hospitalization
25	MIB	536/154	05/02/96	73 yr	Male	Allergic reaction Rash Itching Angina Bradycardia	Allergic reaction Rash Itching Angina pectoris Bradycardia	400 mg	1 dose	Unknown	Unknown	Life-threatening Hospitalization Required intervention Recovery
26	NUP	1172/19012	05/13/96	43 yr	Female	Blacked out/lost consciousness	Loss of consciousness	800 mg	2 doses	Unknown	Unknown	Hospitalization
27	UNIB	568/154	07/11/96	74 yr	Male	Grand mal seizure	Grand mal type seizure	400-1200 mg	Unknown	None	Unknown	Hospitalization Recovery

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Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
28	AFP	0691479A	10/21/96	49 yr	Female	Acute diverticulitis, extensive	Aggravation of existing disorder	Unknown	2-3 months	Pepcid Trilisate Carafate Maxide Voltaren	Unknown	Hospitalization
29	MIB	0783463A	04/18/97	18 yr	Female	Esophageal ulcer at the midesophagus	Esophageal ulcer	2 tablets, tid, po	Unknown	Unknown	Unknown	Hospitalization
30	MIB	0867526A	09/25/97	34 yr	Male	Neutropenia Overdose Weakness Malaise Confusion Hypotension	Leukopenia Overdose Asthenia Malaise Confusion Hypotension	More than 600 mg, tid, po	1 month	None	Unknown	Hospitalization Recovered
31	MIB	0934517A	02/10/98	23 yr	Female	Sudden swelling of lips and eyes Symmmetrical wheel formation on eyelids Tightening in chest Angioedema	Face edema Urticaria Chest pain Angioedema	200-600 mg, q4-6h pm, po	12/2/97; 1 day	acetaminophen acetaminophen with codeine; docusate sodium (12/2/97)	Unknown	Hospitalization Recovered
32	MIB	0976759A	05/06/98	55 yr	Female	Severe hemolytic anemia	Hemolytic anemia	200-800 mg/day, po	Unknown dates; over 2 years	Prevacid	Unknown	Life-threatening Hospitalization Recovered
33	MIB	0978560A	05/08/98	Adult	Male	Duodenal ulcer Anemia Syncope	Duodenal ulcer Anemia Syncope	600 mg, daily, po	Unknown	Unknown	Unknown	Hospitalization Recovered
34	MIB	0985394A	06/01/98	78 yr	Male	Syncope Confusion Agitation Working diagnosis of aseptic meningitis	Syncope Confusion Agitation Meningitis	400 mg, once, po	3/24/98; 1 dose	aspirin	Unknown	Hospitalization Recovered

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Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
35	MIB	1014809A	07/29/98	17 yr	Female	CPK 577,200 u/L Pain	Creatine phosphokinase increased Pain	200-400 mg, q4-6h prn, po	5/18/98-5/21/98; 4 days	Depo-Provera Injection	Unknown	Hospitalization Recovered
36	MIB	1035465A	07/29/98	48 yr	Male	Numbness in mouth and throat Face became red Eyes swelled up Red blotches appeared all over body Feeling nauseous Allergic reaction	Paresthesia Vasodilatation Edema Rash Nausea Allergic reaction	400 mg, once, po	7/28/98; one dose	Unknown	Unknown	Hospitalization
37	MIB	1015600A	08/05/98	71 yr	Male	Necrotizing fasciitis Fever WBC count increased Edema Increase in serum creatinine	Cellulitis Fever Leukocytosis Edema Creatinine increased	200mg am, 400mg pm, po	Unknown	aspirin, cephalexin (completing 10 day course), cefazolin (before operation & postoperatively), ketorolac IV (during surgery), ketorolac po (2 doses postoperatively), morphine sulfate injections prn, droperidol	Unknown	Hospitalization Recovered
38	MIB	1039856A	09/22/98	49 yr	Male	Allergic reaction Hives Angioedema Decreased pulse rate Shock-like symptoms	Allergic reaction Urticaria Angiodema Bradycardia Anaphylactoid reaction	400 mg, once, po	9/21/98; 1 dose	aspirin 75mg nightly for the past year	Unknown	Hospitalization Recovered

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b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

Table 8.7-28 AE Reports With Serious Outcomes (Other Than FDA Subgroups) for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concommitant Meds	Alcohol Use	Outcome
39	MIB	1041375A	09/25/98	17 yr	Female	Couldn't see right, blurred	Amblyopia	200 mg, pm, po	9/21/98-9/24/98; 4 days	None	Unknown	Hospitalization
						Hearing was decreased	Deafness					
						Confused	Confusion					
						Myoclonic jerking	Convulsion					

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b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

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Attachment IV

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Table 8.7-32. Hepatic System (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
1	MIB	314/154	10/12/93	8 yr	Female	Cholestatic jaundice Serum sickness-like reaction	Cholestatic jaundice Serum sickness-like reactions, delayed hypersensitivity	800-1000 mg	3 days approx.	Unknown	Unknown	Treated with Rx drug Hospitalization Partial recovery
2	UNIB	0633909A	08/16/96	29 yr	Male	Cholestasis Severe reduction in the number of bile ducts	Cholestatic jaundice Biliary atresia	600 mg/day, po	3 weeks	Hypoallergenic injections (1/16/94-3/26/94) and weekly hyposensitization treatment to dust mite, mold, trees, grass, and wheat pollen	Unknown	Hospitalization
3	UNIB	1031739A	09/09/98	16 yr	Male	Intentional overdose Became extremely agitated Temperature 33.8 Celcius Combative behavior Respiratory depression Metabolic acidosis Elevated liver enzymes Unresponsive	Intentional overdose Agitation Hypothermia Hostility Hypoventilation Acidosis Liver function tests abnormal Coma	40 gm, once, po	Unknown	No ethanol, salicylate, acetaminophen, barbituates, benzodiazipines, or cocaine detected.	No ethanol	Hospitalization Recovered
4	UNIB	1040922A	09/24/98	44 yr	Male	A marked rise in hepatic transaminases	Liver function tests abnormal	600 mg, bid 4x/wk, po	Unknown	Unknown	None	Required intervention

a: MIB = Motrin®IB product, UNIB = Unknown Ibuprofen product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

Table 8.7-34. Hepatic System (FDA Subgroup) AE Reports With Nonserious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use
1	NUP	660/19012	10/06/93	28 yrs	Male	Fatigue	Fatigue	Unknown	Unknown	Depo-Medrol, Sterile Aqueous Solution, Erythromycin, Anaprox, Flexeril, Soma capsules, unspecified NSAID's, amitriptyline, Valium	Unknown
						Generalized aches and pains	Aches and pains in extremities				
						Fluctuating weight	Weight gain				
						Cuts on skin which don't heal	Healing impairment				
						Flaky skin on head, face, shoulders	Skin problem				
						Elevated liver enzymes	Elevated liver enzymes				
						Headaches	Headache				
						Stomach ulcers	Stomach ulcer NEC/NOS				
						Hair loss	Hair loss				
						Blisters on skin	Blisters				
						Events upon drug discontinuation	Event occurred after drug discontinued				
						Miscellaneous interactions between medications	Miscellaneous drug interaction				
2	NUP	996/19012	04/02/95	Unk	Male	Eyes and urine turned yellow	Jaundice	Unknown	Unknown	None	None
						Sweaty	Sweating				
						Chilly	Chills				
3	MIB	597/154	01/20/97	54 yrs	Female	Severe hepatocellular hepatitis	Hepatitis	Unknown	Unknown	Unknown	Unknown
						Upset	Reaction not specified				

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

Table 8.7-36. Gastrointestinal Bleeding (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
1	Advil®	0184804A	10/04/93	42 yr	Male	Hematemesis Epigastric pain Dizzy Weak Headache Upper GI bleed	Hematemesis Abdominal pain Dizziness Asthenia Headache Upper gastrointestinal hemorrhage	200 mg	1 Dose	Consumed alcohol within the 10 days prior to admission	Alcoholism; consumes three-fifths of a gallon of wine and 2-3 cans of beer per day for 10 years	Hospitalization
2	NUP	738/19012	11/05/93	40 yr	Female	Dizzy Severe diarrhea Hallucinating Gastritis Drowsiness Gastrointestinal hemorrhage	Dizziness Diarrhea Hallucinations Gastritis Drowsiness Gastrointestinal bleeding	200 mg	1 Dose	Natalins Rx ethyl alcohol	Concomitant medication: ethyl alcohol; history of ethyl alcohol induced liver disease & coagulopathy	Required intervention Life-threatening Hospitalization Partial recovery
3	UNIB	0239033A	03/02/94	37 yr	Female	Melena Ulcer stomach Gastrointestinal hemorrhage	Melena Ulcer stomach Gastrointestinal hemorrhage	600 mg, 1200 mg, orally	2 Occasions	Unknown	Unknown	Hospitalization
4	MIB	363/154	04/29/94	42 yr	Male	Internal bleeding in stomach Vomiting (of blood)	Upper gastrointestinal hemorrhage Hematemesis	1200 mg	1 Day	None	Unknown	Hospitalization Disability Partial recovery
5	MIB	393/154	09/15/94	72 yr	Female	Acute gastrointestinal bleeding Gastritis	Gastrointestinal bleeding Gastritis	Intermit-antly took total 15 tablets	Unknown number of days	Dilantin Citracal Valium Didronel vitamin D Excedrin	Does not drink	Hospitalization Recovery
6	UNIB	439/154 0353307[c]	04/07/95 02/20/95	44 yr	Male	Gastrointestinal bleeding Mallory-Weiss tear	Gastrointestinal bleeding Mallory-Weiss syndrome	Unknown	Unknown	Unknown	Unknown	Hospitalization

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b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.

Table 8.7-36. Gastrointestinal Bleeding (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
7	AFP	0415824A	07/24/95	Adult	Male	Blood in stool	Melena	1 tablet/day, orally	6/95; 10-15 days	Arthritis Foundation NightTime caplets; vitamins	Unknown	Hospitalization Recovered
8	NUP	1122/19012	02/05/96	27 yr	Female	Bleeding ulcer	Bleeding ulcer	Unknown	Unknown	Unknown	Unknown	Hospitalization
9	MIB	581/154	06/18/96	80 yr	Male	GI hemorrhage	Gastrointestinal bleeding	200 mg	9 days	warfarin, potassium chloride, digoxin	Unknown	Hospitalization Recovered
10	MIB	0782985A	04/18/97	20 yr	Male	Shallow midesophageal ulcer oozing blood Antral gastritis Mild duodenitis Microcytic anemia	Esophageal ulcer Gastritis Duodenitis Microcytic anemia	6 doses, po	Unknown dates; 2 days	aspirin	Unknown	Hospitalization Recovered
11	UNIB	0808330A	05/22/97	72 yr	Male	Bleeding rectally	Rectal hemorrhage	200 mg, bid, po	Unknown dates	Pepcid AC 10 mg famotidine tablets Isoptin Lanoxin Hydrea Zocor Prinivil allopurinol	Unknown	Hospitalization Recovered
12	MIB	0834516A	07/11/97	46 yr	Female	Bleeding from large ulcer	Hematemesis Peptic ulcer hemorrhage	Unk dose, more than qid	Unknown	Unspecified iron pill	Unknown	Hospitalization Recovered

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Table 8.7-36. Gastrointestinal Bleeding (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
13	NUP	0934619A	01/29/98	Adult	Male	Expired Liver failure Hepatic encephalopathy Gastrointestinal bleed secondary to gastric ulcer	Death Liver failure Acute brain syndrome Stomach ulcer hemorrhage	Unknown dose, po	7/14/94	Advil	Unknown	Death Hospitalization

a: NUP = Nuprin® product, UNIB = Unknown Ibuprofen product, MIB = Motrin®IB product, AFP = Arthritis Foundation™ product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.

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Table 8.7-38. Gastrointestinal Bleeding (FDA Subgroup) AE Reports With Nonserious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use
1	MIB	442/154	04/06/94	Unk	Female	Made me sick Gastrointestinal bleeding/threw up blood	Nausea Gastrointestinal bleeding	Unknown	1 Week	Unknown	Unknown
2	NUP	885/19012	07/26/94	Unk	Female	Rectal bleeding in stool	Blood in stool	Unknown	Unknown	Premarin Uro-Mag	Unknown
3	MIB	387/154	09/08/94	78 yr	Female	Blood in stool	Blood in stool	200 mg	2 Days	Ecotrin	Unknown
4	NUP	960/19012	12/29/94	Unk	Male	Throwing up "Runs" with blood in it	Vomiting Bloody diarrhea	Unknown	Unknown	None	Unknown
5	MIB	428/154	02/15/95	37 yr	Female	Exacerbation of psoriasis (burning) Gastrointestinal bleeding	Exacerbation skin disorder Gastrointestinal bleeding	1200 mg	12 Days	None	Unknown
6	MIB	440/154	03/29/95	62 yr	Male	Upper gastrointestinal bleeding Mallory-Weiss Tear	Gastrointestinal bleeding Mallory-Weiss Syndrome	Unknown	Unknown	Unknown	Unknown
7	NUP	998/19012	04/03/95	Unk	Female	Caused bowels to be really black	Melena	Unknown	Unknown	None	Unknown
8	NUP	1035/19012	07/10/95	Unk	Female	Ulcer Possible internal bleeding	Peptic ulcer Bleeding ulcer	1200 mg	Unknown	Unknown	Unknown
9	MIB	544/154	03/15/96	45 yr	Male	Rectal bleeding	Rectal bleeding	400 mg	1 Dose	None	Unknown
10	NUP	1162/19012	04/22/96	74 yr	Female	Blood in the stool (aggravated ulcerated proctitis)	Exacerbation gastrointestinal disorder	Unknown	Unknown	Ecotrin, metoprolol	Unknown
11	NUP	1191/19012	07/01/96	66 yr	Male	Rectal bleeding	Rectal bleeding	Unknown	Unknown	Ecotrin, Zyloprim	Unknown
12	AFP	0688917A	10/21/96	Adult	Male	Caused internal bleeding	Hemorrhage	Total of 4 tablets, po	Unknown dates	Unknown	Unknown

a: MIB = Motrin® IB product, NUP = Nuprin® product, AFP = Arthritis Foundation™ product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

Table 8.7-38. Gastrointestinal Bleeding (FDA Subgroup) AE Reports With Nonserious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use
13	NUP	1255/19012	11/27/96	56 yr	Male	Blood in stool	Blood in stool	prescribed 2400 mg by MD	2 days	None	Unknown
14	NUP	0875668A	10/10/97	Adult	Male	Gastrointestinal bleeding Hematocrit 31	Gastrointestinal hemorrhage Anemia	Unknown dose, daily, po	Unknown	None	Unknown
15	NUP	0905329A	12/12/97	9 yr	Male	Vomiting Blood in stool	Vomiting Melena	400-800 mg daily, po	2 days	None	Unknown

a: MIB = Motrin® IB product, NUP = Nuprin® product, AFP = Arthritis Foundation™ product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

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Table 8.7-40. Kidney Failure (FDA Subgroup) AE Reports With Serious Outcome for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
1	MED	0185395A	10/04/93	12 yr	Female	Flank pain BUN increased Creatinine increased	Back pain BUN increased Creatinine increased	Unknown	Unknown	meperidine acetamino-phen	Unknown	Hospitalization
2	MIB	356/154	03/29/94	32 yr	Male	Malignant hypertension Interstitial nephritis More headaches	Malignant hypertension Interstitial nephritis Exacerbation headache	400 mg q4hr prn	Approx 1 year	Advil	Unknown	Life-threatening Hospitalization Disability Required intervention Chronic condition
3	UNIB	0253881A	04/18/94	14 yr	Female	Acute severe bilateral Flank pain Acute kidney failure	Back pain Acute kidney failure	600 mg, orally	2 weeks prior to event	None	Unknown	Hospitalization
4	UNIB	0392412A 479/154[c,e]	06/02/95 08/17/95	2 yr	Male	Accidental overdose Nonoliguric renal insufficiency Mild metabolic acidosis Moderate microscopic hematuria	Accidental overdose Kidney function abnormal Acidosis Hematuria	640 mg/kg, (40 tablets), po	Unknown	Child did not have access to any other medications	Unknown	Hospitalization Recovered
5	UNIB	0634596A	08/12/96	45 yr	Male	Membranous nephropathy	Nephrosis	Less than 1200 mg/day	Unknown; 1 month	Unknown	Unknown	Hospitalization Recovered
6	UNIB	0635155A	08/12/96	50 yr	Male	Membranous nephropathy	Nephrosis	1200 mg/day, po	Unknown; 4 months	Unknown	Unknown	Hospitalization Recovered
7	UNIB	0635225A	08/12/96	49 yr	Male	Membranous nephropathy	Nephrosis	800 mg, qod, po	Unknown; 9 months	Unknown	Unknown	Recovered

a: MED = Medipren® product, MIB = Motrin® IB product, UNIB = Unknown ibuprofen product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Submitted to FDA by P&U as a listing in an index of non-15-day foreign reports.
e: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

Table 8.7-40. Kidney Failure (FDA Subgroup) AE Reports With Serious Outcome for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
8	UNIB	1238/19012	10/15/96	21 yr	Female	Massive overdose lead to renal toxicity Renal toxicity	Overdose with signs of toxicity Renal toxicity	100,000 mg	1 Day	Unknown	Unknown	Hospitalization Recovery
9	UNIB	0683683A	11/05/96	21 yr	Female	Metabolic acidosis Hypotension Respiratory depression Acute renal failure Disseminated intravascular coagulation Adult respiratory distress syndrome Ingestion of a massive amount	Acidosis Hypotension Hypoventilation Acute kidney failure Coagulation disorder Respiratory disorder Intentional overdose	Massive ingestion	Unknown	Unknown	Unknown	Hospitalization Recovered
10	UNIB	0790207A	04/30/97	42 yr	Female	Acute renal papillary necrosis Severe bilateral flank pain, colicky in nature & radiating to groin Passage of blood-stained "mucous-like" material Overdose	Papillary kidney necrosis Back pain Urine abnormality Overdose[e]	4800 mg for 3 days	Unknown dates; 3 days	Zoloft	Unknown	Hospitalization Recovered
11	UNIB	0823635A 623/154[c]	06/25/97 06/14/97	29 yr	Male	Acute renal failure Rhabdomyolysis Drug interaction	Acute kidney failure Myopathy Drug interaction	200 mg then 400 mg,per MD	Until 4/29/95; few days only	Ciprofibrate	Unknown	Hospitalization Recovered

a: MED = Medipren® product, MIB = Motrin® IB product, UNIB = Unknown ibuprofen product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Submitted to FDA by P&U as a listing in an index of non-15-day foreign reports.
e: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

Table 8.7-40. Kidney Failure (FDA Subgroup) AE Reports With Serious Outcome for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use	Outcome
12	UNIB	0936425A	02/18/98	34 yr	Female	Acute interstitial nephritis Aching Swelling Blood in urine Protein in urine	Nephritis Malaise Pain Edema Hematuria Albuminuria	Unknown dose, regularly	Up to onset of symptoms	Prednisolone, azathioprine, cyclosporine, DF118 (dihydroco-deine)	Unknown	Hospitalization Recovered

a: MED = Medipren® product, MIB = Motrin® IB product, UNIB = Unknown ibuprofen product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Submitted to FDA by P&U as a listing in an index of non-15-day foreign reports.
e: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

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Table 8.7-42. Kidney Failure (FDA Subgroup) AE Reports With Nonserious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use
1	NUP	1242/19012	10/22/96	37 yr	Female	Kidneys are inflamed and bleeding Retained fluid throughout entire body Severe reaction to Nuprin Caplets	Changes in kidney function Fluid retention Reaction NOS	Unknown	Unknown	None	Unknown
2	NUP	0864229A	03/21/97	79 yr	Male	Digoxin blood level elevated Urine flow has been cutting down	Drug level increased Oliguria	400-600 mg/day, po	Unknown	Casodex, Lanoxin, Medrol Tablets, Imdur	Unknown

a: NUP = Nuprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

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Table 8.7-44. Concomitant Alcohol Use or Abuse (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use	Outcome
1	Advil	0184804A	10/04/93	42 yr	Male	Hematemesis Epigastric pain Dizzy Weak Headache Upper GI bleed	Hematemesis Abdominal pain Dizziness Asthenia Headache Upper gastrointestinal hemorrhage	200 mg	1 dose	consumed alcohol within the 10 days prior to admission	Alcoholism; consumes three-fifths of a gallon of wine and 2-3 cans of beer per day for 10 years	Hospitalization
2	NUP	738/19012	11/05/93	40 yr	Female	Dizzy Severe diarrhea Hallucinating Gastritis Drowsiness Gastrointestinal hemorrhage	Dizziness Diarrhea Hallucinations Gastritis Drowsiness Gastrointestinal bleeding	200 mg	1 dose	Natalins Rx, ethyl alcohol	Concomitant medication listed as ethyl alcohol; history of ethyl alcohol induced liver disease & coagulopathy	Hospitalization Required Intervention Life-threatening Partial recovery

a: NUP = Nuprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

Table 8.7-44. Concomitant Alcohol Use or Abuse (FDA Subgroup) AE Reports With Serious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use	Outcome
3	NUP	906/19012[c] submitted as 4662/17463[c]	08/30/94	Birth	Male	Tonic-clonic seizures	Seizures (PED-NEO)	unknown	7 days	Motrin 600 mg, erythromycin	Minimal alcohol consumption	Hospitalization Disability Congenital anomaly Required intervention
						Hypoxic-ischemic encephalopathy	Encephalopathy congenital (PED-NEO)					
						Loss of brain volume/cortical infarctions	Brain malformation NEC/NOS (PED-NEO)					
						Microencephalic	Microencephaly (PED-NEO)					
						Fetal distress	Fetal distress (PED-NEO)					
						Meconium found in posterior pharnyx	Meconium aspiration (PED-NEO)					
						Premature closure of ductus arteriosis	Closure of ductus arteriosis (PED-NEO)					
						Limp at birth with heart rate below 100	Neonatal flaccidity (PED-NEO)					
						Third trimester exposure in utero	Exposure in utero-3rd trimester (PED-NEO)					
						Below average APGAR scores	Low APGAR score (PED-NEO)					

a: NUP = Nuprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case submitted to FDA by two different manufacturers.

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Table 8.7-46. Concomitant Alcohol Use or Abuse (FDA Subgroup) AE Reports With Nonserious Outcomes for Uses Other Than Migraine Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Ref. No.	Received Date	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Meds	Alcohol Use
1	NUP	871/19012	07/15/94	15 yr	Male	Took Nuprin with alcohol Hangover	Alcohol interaction Hangover	400 mg	1 dose	Theophylline Alcohol	Consumed 7 beers and 1/2 pint of liquor
2	NUP	1190/19012	06/25/96	39 yr	Female	Seizure I am taking Prozac® Drank some alcohol	Seizures Antidepressant interaction Alcohol interaction	400 mg 3 times daily	Unknown	Prozac® Alcohol	Consumed alcohol
3	NUP	0866588A	04/17/97	21 yr	Male	Dizzy	Dizziness	Unknown	Unknown	Unspecified alcohol	Reported drinking some alcohol after taking Nuprin Caplets

a: NUP = Nuprin® product.
b: Event Term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).

Attachment V

to

Safety Review Update

Table 8.8-3 Reports of Ibuprofen Overdose With Serious Outcomes Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use	Outcome
1	NUP	846/19012	06/15/94	3 yr	Female	Accidental pediatric ingestion of 24 tablets Slight fever	Overdose with signs of toxicity Fever	4800 mg	1 day	None	Unknown	Required intervention Recovery
2	NUP	901/19012	08/18/94	33 yr	Female	Overdose Headache	Overdose NEC /NOS Headache	4800 mg	1 day	None	Unknown	Life-threatening Recovery
3	NUP	941/19012	03/22/95	18 yr	Female	Low blood pressure High blood sugar Sick to stomach Intentional overdose	Decreased blood pressure Hyperglycemia Upset stomach Intentional overdose	4800 mg	1 day	Prozac Ditropan	Unknown	Hospitalization Required intervention Recovery
4	UNIB	0392412A 479/154[c]	06/02/95 08/17/95	2 yr	Male	Accidental overdose Nonoliguric renal insufficiency Mild metabolic acidosis Moderate microscopic hematuria	Accidental overdose Kidney function abnormal Acidosis Hematuria	640 mg/kg,(40 tablets),po	Unknown	The child did not have access to any other medications.	Unknown	Hospitalization Recovered
5	NUP	1044/19012	08/14/95	17 yr	Female	Intentional overdose Stomach pain	Intentional overdose Pains in stomach	2400 mg	1 dose	Unknown	Unknown	Hospitalization Recovery
6	MED	0451379A	09/15/95	17 yr	Male	Intentional overdose Lethargic Hypoprothrombinemia	Intentional overdose Somnolence Prothrombin decreased	98 gms, orally	1 day	Diphenhydramine tablets	Unknown	Hospitalization Recovered
7	MED UNIB	0454419A 508/154[c]	09/25/95 11/20/95	6 yr	Male	Accidental overdose Shock Coma Metabolic acidosis	Accidental overdose Shock Coma Acidosis	Approx 6 gms, orally	1 dose	Unknown	Unknown	Life-threatening Hospitalization Required intervention Recovered

a: NUP = Nuprin® product, UNIB = Unknown ibuprofen product, MED = Mediprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

Table 8.6-3 Reports of Ibuprofen Overdose With Serious Outcomes Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use	Outcome
8	UNIB	1238/19012	10/15/96	21 yr	Female	Massive overdose lead to renal toxicity Renal toxicity	Overdose with signs of toxicity Renal toxicity	100,000 mg	1 day	Unknown	Unknown	Hospitalization Recovery
9	UNIB	0683683A	11/05/96	21 yr	Female	Metabolic acidosis Hypotension Respiratory depression Acute renal failure Disseminated intravascular coagulation Adult respiratory distress syndrome Ingestion of a massive amount	Acidosis Hypotension Hypoventilation Kidney failure acute Coagulation disorder Respiratory disorder Intentional overdose	Massive ingestion	Unknown	Unknown	Unknown	Hospitalization Recovered
10	UNIB	0790207A	04/30/97	42 yr	Female	Acute renal papillary necrosis Severe bilateral flank pain, colicky in nature & radiating to groin Passage of blood-stained "mucous-like" material Overdose	Papillary kidney necrosis Back pain Urine abnormality Overdose[d]	Avg of 4800 mg for 3 days	Unknown dates; 3 days	Zoloft	Unknown	Hospitalization Recovered
11	MIB	0867526A	09/25/97	34 yr	Male	Neutropenia Overdose Weakness Malaise Confusion Hypotension	Leukopenia Overdose Asthenia Malaise Confusion Hypotension	More than 600 mg, tid, po	1 month	None	Unknown	Hospitalization Recovered

a: NUP = Nuprin® product, UNIB = Unknown ibuprofen product, MED = Mediprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

Table 8.8-3 Reports of Ibuprofen Overdose With Serious Outcomes Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use	Outcome
12	MIB	1031739A	09/09/98	16 yr	Male	Intentional overdose Became extremely agitated Temperature 33.8 Celcius Combative behavior Respiratory depression Metabolic acidosis Elevated liver enzymes Unresponsive	Intentional overdose Agitation Hypothermia Hostility Hypoventilation Acidosis Liver function tests abnormal Coma	40 gm, once, po	Unknown	No ethanol, salicylate, acetaminophen, barbituates, benzodiazipines, or cocaine detected	No ethanol	Hospitalization Recovered

a: NUP = Nuprin® product, UNIB = Unknown ibuprofen product, MED = Mediprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Single case from the published literature submitted to FDA by two different manufacturers.
d: Original manufacturer's report does not code an overdose term, but the reported event describes an overdose.

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Table 8.8-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
1	NUP	659/19012	10/05/93	1 yr	Female	Inadvertent pediatric ingestion (overdose) Lazy eye Very tired	Overdose with signs of toxicity Eye disorders NEC/NOS Fatigue and tiredness	Unknown	1 dose	Unknown	Unknown
2	NUP	790/19012	02/16/94	3 yr	Male	Accidental pediatric ingestion (overdose) Subsequent stomach ache Loose stools	Overdose with signs of toxicity Pains in stomach Loose stools	1400 mg	Unknown	Unknown	Unknown
3	NUP	791/19012	03/07/94	Unk	Female	Drowsy Overdose	Drowsiness Overdose with signs of toxicity	1800 mg	Unknown	None	Unknown
4	MIB	361/154	04/28/94	46 yr	Male	Accidental overdose Upset stomach Severe indigestion	Overdose NEC/NOS Upset stomach Indigestion	1800-2400 mg	1 day	Polycitrate	Unknown
5	NUP	834/19012	04/29/94	Pediatric	Male	Accidental pediatric ingestion Looks flushed	Overdose with signs of toxicity Flushing skin	Unknown	Unknown	None	Unknown
6	NUP	861/19012	05/05/94	Pediatric	Male	Baby boy may have swallowed one tablet Looks a little sleepy eyed	Overdose with signs of toxicity Sleepiness	200 mg	5/94	None	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.

Table 8.8-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
7	NUP	874/19012	07/15/94	21 mo	Female	Accidental pediatric ingestion Very drowsy	Overdose with signs of toxicity Drowsiness	400 mg	1 day	None	Unknown
8	NUP	878/19012	07/18/94	13 yr	Female	Overdose (13-year-old took 4 tablets) Dizzy	Overdose with signs of toxicity Dizziness	800 mg	1 dose	None	Unknown
9	NUP	898/19012	08/10/94	Unk	Female	Overdose Drowsy	Overdose with signs of toxicity Drowsiness	3 gm	1 day	None	Unknown
10	MIB	415/154	12/21/94	24 yr	Male	Flunked drug test Chronic overdose of several ibuprofen products	Laboratory test abnormalities NEC/NOS Chronic overdose[c]	2400-7200 mg/day	September 1994 through 11/26/94	Sudafed Coricidin Drixoral Other medications for congestion/ sinus infection	Unknown
11	Excedrin IB	39/173	01/26/95	Unk	Female	Overdose Hallucinations	Overdose NEC/NOS Hallucinations	Unknown	Unknown	Unknown	Unknown
12	MIB	418/154	02/03/95	39 yr	Female	Lack of effect (for headache) Vomiting Headache Nausea Chills Malaise for 48 hours Exceeded dosage	Lack of efficacy Vomiting Headache Nausea Chills Malaise Overdose NEC/NOS	Unknown	Unknown	Unknown	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.

Table 8.8-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
13	NUP	1010/19012	05/18/95	5 yr	Female	Red, bumpy rash on neck After pediatric ingestion of two tablets (overdose)	Erythematous rash Overdose with signs of toxicity	400 mg	1 dose	Unknown	Unknown
14	MIB	477/154	08/23/95	51 yr	Female	Menstrual period for 8 weeks Chronic overdose	Menorrhagia (prolonged), excessive menstruation Chronic overdose	2000-2800 mg	1991-continues	None	Unknown
15	NUP	1050/19012	08/24/95	17 yr	Female	Overdose Upset stomach Left bad taste in mouth	Overdose with signs of toxicity Upset stomach Taste alterations	2400 mg	1 dose	Tums	Unknown
16	NUP	1074/19012	10/01/95	Unk	Female	Got sick Took 20 caplets at one time	Reaction not specified Overdose with signs of toxicity	4000 mg	1 dose	Unknown	Unknown
17	NUP	1072/19012	10/04/95	8 mo	Male	Infant ate 3 Nuprin tablets Vomited	Overdose with signs of toxicity Vomiting	600 mg	1 dose	Unknown	Unknown
18	NUP	1139/19012	03/19/96	18 yr	Female	Suicide attempt (overdose) Major stomach pains Major stomach cramps	Intentional overdose Pains in stomach Stomach cramps	4800 mg	1 dose	None	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.

Table 8.8-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1995 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
19	NUP	1137/19012	03/21/96	37 yr	Male	"Very vivid dreams" Overdose	Dream abnormalities Overdose with signs of toxicity	2400 mg	Unknown	None	Unknown
20	NUP	1183/19012	06/11/96	Unk	Male	Has the shakes (Dose exceeds recommended daily maximum)	Shakiness Overdose with signs of toxicity	2400 mg	Unknown	Unknown	Unknown
21	NUP	1231/19012	09/23/96	16 yr	Female	Stomach ache Following overdose	Pains in stomach Overdose with signs of toxicity	7200 mg	1 dose	Tylenol Ritalin	Unknown
22	NUP	1245/19012	10/31/96	57 yr	Male	Takes 9 tablets a day Now left heel is numb Also stomach discomfort after the medication was discontinued	Overdose with signs of toxicity Numbness Epigastric discomfort after drug discontinued	1800 mg	Unknown	Synthroid Zantac	Unknown
23	MIB	592/154	12/30/96	2 yr	Female	Possible overdose Acting tired (O) Cap wasn't childproof	Overdose with signs of toxicity Fatigue and tiredness Product complaint	800 mg	1 dose	Tylenol	Unknown
24	NUP	1267/19012	01/22/97	Approx 24 mo	Male	My 2 year old son just swallowed one of my Nuprin caplets and now he is acting funny	Overdose with signs of toxicity Change in behavior	200 mg	1 dose	None	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.

Table 8.6-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
25	MIB	600/154	02/06/97	50 yr	Male	Daily dose of 3200 to 4000 mg for ten days Resulted in positive drug screen (opiates/can)	Overdose with signs of toxicity Laboratory test abnormalities NEC/NOS	3200-4000 mg	10 days	Naprelan Norgesic forte Carisoprodol hydrocodone Propacet lorazepam	Unknown
26	NUP	0864328A	03/31/97	Adult	Male	Take 24 tablets daily Light headed	Overdose Dizziness	4800 mg, daily, po	Unknown	Unknown	Unknown
27	NUP	0866985A	06/03/97	44 yr	Female	Overdose Visual disturbances	Overdose Vision abnormal	600 mg, 6 times daily, po	Since 10/96 Interrupted use	metoclopramide Trazodone Zoloft Tegretol	Unknown
28	NUP	0866972A	06/06/97	24 yr	Female	Overdose Hallucinate	Overdose Hallucinations	1200 mg, tid, po	Unknown	None	Unknown
29	MIB	0844041A	07/31/97	39 yr	Male	False positive test for codeine & morphine	Lab test abnormal Overdose	3200 mg/day, po	Unknown	over-the-counter and prescription Nasalcrom Sudafed Tavist-D 2 weeks prior	Unknown
30	NUP	0893995A	11/17/97	55 yr	Female	Overdose Hands itch	Overdose Pruritus	1600 mg/day, po	Unknown	None	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.

Table 8.8-5. Reports of Ibuprofen Overdose With a Nonserious Outcome and Symptoms or Signs Received by McNeil From October 1, 1993 Through September 30, 1998 for McNeil OTC Adult Ibuprofen Products or Unknown OTC Adult Ibuprofen Products

Case No.	Product Form[a]	Mfr. Report No.	Date Received	Age	Sex	AE Verbatim	Event Term[b]	Daily Dose	Duration	Concomitant Medications	Alcohol Use
31	NUP	0894632A	11/19/97	Adult	Female	Overdose Legs became swollen	Overdose Peripheral edema	400 mg, q6h, po	11/8/97-11/10/97; 3 days	Beconase AQ Inhaler Nasalcrom Inhaler bid	Unknown
32	NUP	0899059A	12/02/97	65 yr	Female	Overdose Blisters on feet & hands Boils on feet & hands	Overdose Vesiculobullous rash Furunculosis	600 mg, tid, po	8 years	Procardia atenolol	Unknown
33	NUP	0964688A	04/13/98	42 yr	Male	Overdose Red itchy rash	Overdose Rash	600 mg, qid prn, po	3/6/98-4/10/98, 4/13/98-cont	None	Unknown
34	NUP	0972352A	04/29/98	35 yr	Female	Overdose Joint aches Joint inflammation	Overdose Arthralgia Arthritis	400-800 mg, q4-6h, po	3/7/98-3/11/98; 5 days	Claritin, Desogen	Unknown
35	NUP	1025267A	08/20/98	51 yr	Female	Overdose Systemic red raised itchy rash all over itchy rash	Overdose Rash Pruritus	400 mg, qid, po	7/29/98-8/19/98; 21 days	allopurinol Dyazide Tenormin Provera (10 days/month)	Unknown

a: NUP = Nuprin® product, MIB = Motrin® IB product.
b: Event term is a standard coding dictionary term for adverse events from one of the following dictionaries: COSTART or UMED (Upjohn Medical Event Dictionary).
c: Original manufacturer's report does not code an overdose term, but the reported event describes a chronic overdose of several ibuprofen products.