CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 20-812/S-007

Trade Name: Pediatric Advil Drops

Generic Name: Ibuprofen

Sponsor: Whitehall-Robins Healthcare

Approval Date: September 7, 2000

Supplement Changes: Changes to the allergy alert wording in the labeling

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-812/S-007

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-812/S-007

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-812/S-007

Whitehall-Robins Healthcare
Attention: Sharon Heddish
Vice President, Regulatory Affairs - Worldwide
Five Giralda Farms
Madison, NJ 07940-0871

SEP 7 2000

Dear Ms. Heddish:

Please refer to your supplemental new drug application dated October 26, 1999, received October 28, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pediatric Advil (ibuprofen) Drops, 100 mg/2.5 mL.

This "Changes Being Effected" supplemental new drug application provides for revised labeling to implement the allergy alert statements required by our September 15, 1998 letter.

We have completed the review of this supplemental new drug application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling submitted on October 26, 1999. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

We request that the labeling for this drug product be revised to comply with the requirements of 21 CFR 201.315 (sore throat warning) and 21 CFR 369.20 (general warning regarding accidental overdose by children) within 180 days or at the next printing, whichever comes first. In addition, please delete the period after the bulleted statement, "**Do not use**" on the bottle label.

We note that the labeling was not submitted in Drug Facts format consistent with the requirements of the March 17, 1999 FEDERAL REGISTER document "Over-the-Counter Human Drugs; Labeling Requirements; Final Rule" (64 FR 13254) (OTC labeling final rule), which has been incorporated into the regulations at 21 CFR 201.66. We remind you that the labeling of your product must be revised to reflect the Drug Facts format within the timeframes specified in the OTC labeling final rule.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we

ka 9/7/00

request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions regarding this application, please contact Thomas Parmelee, Pharm.D., Regulatory Project Manager, at 301-827-2271.

Sincerely,

Linda M. Katz, M.D., M.P.H.
Deputy Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Archival NDA 20-812
HFD-560/Div. Files
HFD-560/Ganley/Katz/Cook
HFD-560/~~Rothschild~~/Lumpkins/Mason/Neuner/Roberts/Pamelee
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-105/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFI-20/Press Office (with labeling)
HFD-400/OPDRA (with labeling)
HFD-613/OGD (with labeling)
HFD-095/DDMS-IMT (with labeling)
HFD-830/DNDC Division Director
DISTRICT OFFICE

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-812/S-007

LABELING

Labeling: ORIGINAL
NDA No: 20812 Rec'd. 10-28-99
Reviewed by: _____

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
Fever Reducer/Pain Reliever

Do not use if breakable ring on bottle cap is separated

Grape Flavor
SAMPLE-NOT FOR RETAIL SALE

For Ages 2-3

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Lasts up to 8 Hours

GRAPE-FLAVORED
DROPS
Alcohol Free

1/4 FL OZ (7.5 mL)

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Questions or Comments?
Call toll-free 1-800-88-ADVIL

Or ask your pharmacist, doctor or health care professional.

Other information
- store at 20°-25°C (68°-77°F)
- see bottom of box for lot number and expiration date

Inactive ingredients artificial flavor, carboxymethylcellulose sodium, citric acid, edetate disodium, FD&C Red No. 40, FD&C Blue No. 1, glycerin, microcrystalline cellulose, polysorbate 80, purified water, sodium benzoate, sorbitol solution, sucrose, xanthan gum.

Long Lasting: Up to 8 hours of fever relief.
Great Convenience:
Long duration means fewer doses needed per day.

Whitehall-Robins Healthcare
Madison, NJ 07940
Made in USA

SEP 7 2000

Important: **Read all product information before using. Keep this box for important information. This product is intended for use in children ages 2-3 years.**

Active ingredient	***Purposes***
Ibuprofen 100 mg per 2.5 mL	Fever reducer/pain reliever

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided. Do not discard dosing device.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
Under 24	Under 2	Consult Doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Warnings

Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use
- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- if your child has problems or serious side effects from taking fever reducers/pain relievers
- if your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea, or lack of fluid intake
- if breakable ring on bottle cap is separated

(See Side Panel for Additional Warnings)—>

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Warnings (continued)

Ask a doctor before use if your child
- is under a doctor's care for any serious condition or is taking any other drug
- has redness or swelling present in the painful area
- is taking any other product that contains ibuprofen, or any other pain reliever/fever reducer
- has stomach pain

Stop and ask a doctor if
- an allergic reaction occurs. Seek medical help right away
- fever or pain lasts for more than 3 days
- your child does not get any relief within the first day (24 hours) of treatment or pain or fever gets worse
- stomach upset gets worse or lasts
- sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting
- any new symptoms appear

Keep out of reach of children. In case of overdose, seek professional assistance or contact a poison control center right away.

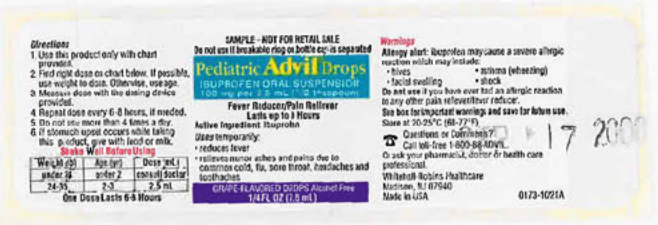
0173-10/30C

8

Labeling: ORIGINAL

NDA No: 20812 Rc'd. 10-28-99

Reviewed by: _____



Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
under 24	under 2	consult doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

SAMPLE - NOT FOR RETAIL SALE

Do not use if breakable ring on bottle cap is separated

Pediatric Advil Drops

IBUPROFEN ORAL SUSPENSION

100 mg per 2.5 mL / 5 teaspoons

Fever Reducer/Pain Reliever
Lasts up to 8 Hours

Active Ingredient Ibuprofen

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

GRAPE FLAVORED DROPS Alcohol Free

1/4 FL OZ (7.5 mL)

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

See box for important warnings and save for future use.

Store at 20-25°C (68-77°F).

Questions or Comments?
Call toll-free 1-800-88-ADVIL
Or ask your pharmacist, doctor or health care professional.

Wyeth-Ayerst Robins Healthcare
Madison, NJ 07940
Made in USA

0173-1021A

OCT 17 2000

Labeling: ORIGINAL
NDA No: 20812 Rec'd. 10-28-99
Reviewed by: _____

SEP 7 2000

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
Fever Reducer/Pain Reliever

Do not use if breakable ring on bottle cap is separated

Grape Flavor

For Ages 2-3

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Lasts up to 8 Hours

GRAPE-FLAVORED DROPS
Alcohol Free

1/2 FL OZ (15 mL)

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Questions or Comments?
Call toll-free 1-800-88-ADVIL.
Or ask your pharmacist, doctor or health care professional.

Other information
- store at 20-25°C (68-77°F)
- see bottom of box for lot number and expiration date

Inactive ingredients artificial flavor, carboxymethylcellulose sodium, citric acid, edetate disodium, FD&C Red No. 40, FD&C Blue No. 1, glycerin, microcrystalline cellulose, polysorbate 80, purified water, sodium benzoate, sorbitol solution, sucrose, xanthan gum.

Long Lasting: Up to 8 hours of fever relief.

Great Convenience: Long duration means fewer doses needed per day.

Whitehall-Robins Healthcare
Madison, NJ 07940
Made in USA

3 05730 17320 9

Important: **Read all product information before using. Keep this box for important information. This product is intended for use in children ages 2-3 years.**

Active Ingredient ***Purposes***
Ibuprofen 100 mg per 2.5 mL .....Fever reducer/pain reliever

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided. Do not discard dosing device.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
Under 24	Under 2	Consult Doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Warnings

Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use
- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- if your child has problems or serious side effects from taking fever reducers/pain relievers
- if your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea, or lack of fluid intake
- if breakable ring on bottle cap is separated

(See Side Panel for Additional Warnings)—>

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Warnings (continued)

Ask a doctor before use if your child
- is under a doctor's care for any serious condition or is taking any other drug
- has redness or swelling present in the painful area
- is taking any other product that contains ibuprofen, or any other pain reliever/fever reducer
- has stomach pain

Stop and ask a doctor if
- an allergic reaction occurs. Seek medical help right away
- fever or pain lasts for more than 3 days
- your child does not get any relief within the first day (24 hours) of treatment or pain or fever gets worse
- stomach upset gets worse or lasts
- sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting
- any new symptoms appear

Keep out of reach of children. In case of overdose, seek professional assistance or contact a poison control center right away.

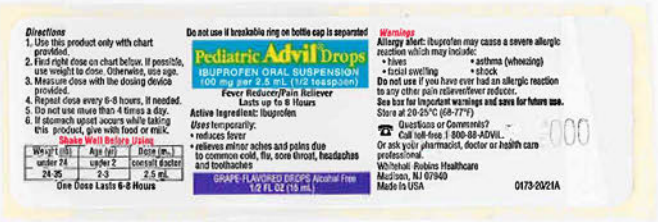
0173-20/30C

7

Labeling: ORIGINAL

NDA No: 20812 Rec'd. 10-28-99

Reviewed by: _____



Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
under 24	under 2	consult doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Do not use if breakable ring on bottle cap is separated

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)

Fever Reducer/Pain Reliever
Lasts up to 8 Hours

Active Ingredient: Ibuprofen

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

GRAPE-FLAVORED DROPS Alcohol Free
1/2 FL OZ (15 mL)

Warnings
Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.
See box for important warnings and save for future use.
Store at 20-25°C (68-77°F)

Questions or Comments?
Call toll-free 1 800-88-ADVIL
Or ask your pharmacist, doctor or health care professional.

Wyeth-Whitehall Robins Healthcare
Madison, NJ 07940
Made in USA

0173-20/21A

Labeling: Original

NDA No: 20812 Rc'd. 10-28-99

Reviewed by: _____

Pediatric Advil Drops

IBUPROFEN ORAL SUSPENSION

Fever Reducer/Pain Reliever

Do not use if breakable ring on bottle cap is separated

Fruit Flavor

SAMPLE-NOT FOR RETAIL SALE

For Ages 2-3

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION

100 mg per 2.5 mL (1/2 teaspoon)

Fever Reducer/Pain Reliever

Lasts up to 8 Hours

FRUIT-FLAVORED DROPS

Alcohol Free

1/4 FL OZ (7.5 mL)

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION

100 mg per 2.5 mL (1/2 teaspoon)

Fever Reducer/Pain Reliever

Questions or Comments? Call toll-free 1-800-88-ADVIL.

Or ask your pharmacist, doctor or health care professional.

Other information

- store at 20-25°C (68-77°F)
- see bottom of box for lot number and expiration date

Inactive ingredients artificial flavors, carboxymethylcellulose sodium, citric acid, edetate disodium FD&C Red No. 40, glycerin, microcrystalline cellulose, polysorbate 80, purified water, sodium benzoate, sorbitol solution, sucrose, xanthan gum.

Long Lasting: Up to 8 hours of fever relief.

Great Convenience: Long duration means fewer doses needed per day.

Whitehall-Robins Healthcare
Madison, NJ 07940
Made in USA

SEP 7 2000

Important: **Read all product information before using. Keep this box for important information. This product is intended for use in children ages 2-3 years.**

Active ingredient ***Purposes***

Ibuprofen 100 mg per 2.5 mL ..... Fever reducer/pain reliever

Uses temporarily:

- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

Directions

1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided. Do not discard dosing device.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
Under 24	Under 2	Consult Doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Warnings

Allergy alert: ibuprofen may cause a severe allergic reaction which may include:

- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use

- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- if your child has problems or serious side effects from taking fever reducers/pain relievers
- if your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea, or lack of fluid intake
- if breakable ring on bottle cap is separated

(See Side Panel for Additional Warnings)—>

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION

100 mg per 2.5 mL (1/2 teaspoon)

Fever Reducer/Pain Reliever

Warnings (continued)

Ask a doctor before use if your child

- is under a doctor's care for any serious condition or is taking any other drug
- has redness or swelling present in the painful area
- is taking any other product that contains ibuprofen, or any other pain reliever/fever reducer
- has stomach pain

Stop and ask a doctor if

- an allergic reaction occurs. Seek medical help right away
- fever or pain lasts for more than 3 days
- your child does not get any relief within the first day (24 hours) of treatment or pain or fever gets worse
- stomach upset gets worse or lasts
- sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting
- any new symptoms appear

Keep out of reach of children. In case of overdose, seek professional assistance or contact a poison control center right away.

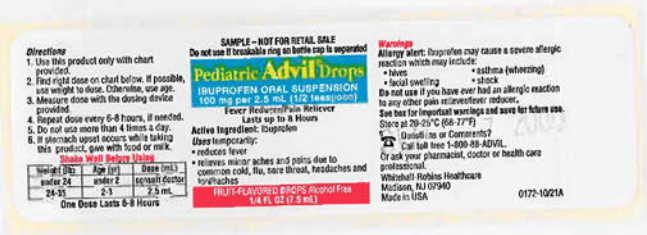
0172-10/30C

7

Labeling: ORIGINAL

NDA No: 20812 Rc'd. 10-28-99

Reviewed by: _____



Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lbs)	Age (yr)	Dose (mL)
under 24	under 2	consult doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

SAMPLE – NOT FOR RETAIL SALE
Do not use if breakable ring on bottle cap is separated

Pediatric Advil Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever
Lasts up to 8 Hours

Active Ingredient: Ibuprofen
Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

FRUIT-FLAVORED DROPS Alcohol Free
1/4 FL OZ (7.5 mL)

Warnings
Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.
See box for important warnings and save for future use.
Store at 20-25°C (68-77°F)
Questions or Comments?
Call toll free 1-800-88-ADVIL
Or ask your pharmacist, doctor or health care professional.
Whitehall-Robins Healthcare
Madison, NJ 07940
Made in USA

0172-10/21A

Labeling: ORIGINAL
NDA No: 20812 Rec'd. 10-28-99
Reviewed by: _____

SEP 7 2000

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
Fever Reducer/Pain Reliever

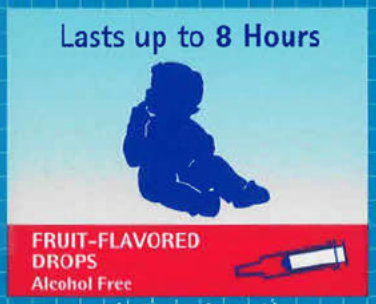
Do not use if breakable ring on bottle cap is separated

Fruit Flavor

For Ages 2-3

Pediatric Advil® Drops

IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever



1/2 FL OZ (15 mL)

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Questions or Comments? Call toll-free 1-800-88-ADVIL.
Or ask your pharmacist, doctor or health care professional.

Other information
- store at 20-25°C (68-77°F)
- see bottom of box for lot number and expiration date

Inactive ingredients artificial flavors, carboxymethylcellulose sodium, citric acid, edetate disodium, FD&C Red No. 40, glycerin, microcrystalline cellulose, polysorbate 80, purified water, sodium benzoate, sorbitol solution, sucrose, xanthan gum.

Long Lasting: Up to 8 hours of fever relief.

Great Convenience: Long duration means fewer doses needed per day.

Whitehall-Robins Healthcare
Madisen, NJ 07940
Made in USA

3 05730 17220 2

***Important:* Read all product information before using. Keep this box for important information. This product is intended for use in children ages 2-3 years.**

Active ingredient ***Purposes***
Ibuprofen 100 mg per 2 5mL..... Fever reducer/pain reliever

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

Directions
1. Use this product only with chart provided.
2. Find right dose on chart below. If possible, use weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided. Do not discard dosing device.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
Under 24	Under 2	Consult Doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Warnings

Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use
- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- if your child has problems or serious side effects from taking fever reducers/pain relievers
- if your child is dehydrated (significant fluid loss) due to continued vomiting, diarrhea, or lack of fluid intake
- if breakable ring on bottle cap is separated

(See Side Panel for Additional Warnings)—>

Pediatric Advil® Drops
IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)
Fever Reducer/Pain Reliever

Warnings (continued)

Ask a doctor before use if your child
- is under a doctor's care for any serious condition or is taking any other drug
- has redness or swelling present in the painful area
- is taking any other product that contains ibuprofen, or any other pain reliever/fever reducer
- has stomach pain

Stop and ask a doctor if
- an allergic reaction occurs. Seek medical help right away
- fever or pain lasts for more than 3 days
- your child does not get any relief within the first day (24 hours) of treatment or pain or fever gets worse
- stomach upset gets worse or lasts
- sore throat is severe, lasts for more than 2 days or occurs with fever, headache, rash, nausea or vomiting
- any new symptoms appear

Keep out of reach of children. In case of overdose, seek professional assistance or contact a poison control center right away.

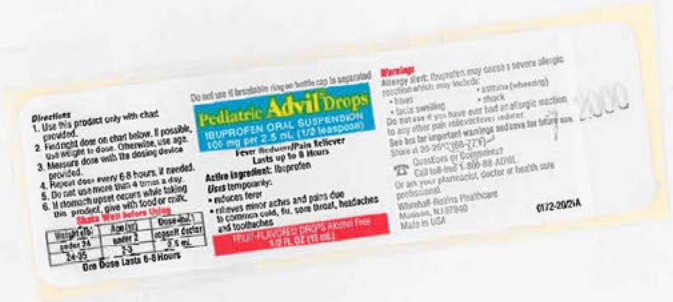
10

0172-20/30C

Labeling: ORIGINAL

NDA No: 20812 Rec'd. 10-28-99

Reviewed by: _____



Directions
1. Use this product only with chart provided.
2. Find child's dose on chart below. If possible, use child's weight to dose. Otherwise, use age.
3. Measure dose with the dosing device provided.
4. Repeat dose every 6-8 hours, if needed.
5. Do not use more than 4 times a day.
6. If stomach upset occurs while taking this product, give with food or milk.

Shake Well Before Using

Weight (lb)	Age (yr)	Dose (mL)
under 24	under 2	ask a doctor
24-35	2-3	2.5 mL

One Dose Lasts 6-8 Hours

Do not use if breakable ring on bottle cap is separated

Pediatric Advil Drops

IBUPROFEN ORAL SUSPENSION
100 mg per 2.5 mL (1/2 teaspoon)

Fever Reducer/Pain Reliever
Lasts up to 6 Hours

Active ingredient: Ibuprofen

Uses temporarily:
- reduces fever
- relieves minor aches and pains due to common cold, flu, sore throat, headaches and toothaches

TRUIT FLAVORED DROPS Alcohol Free
1.0 FL OZ (15 mL)

Warnings
Allergy Alert: Ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.
See box for important warnings and save for future use.
Store at 20-25°C (68-77°F)

Questions or Comments?
Call toll-free 1-800-88-ADVIL
Or ask your pharmacist, doctor or health care professional.

Wyeth-Ayerst Pharmaceuticals
Madison, NJ 07940
Made in USA

0172-20/2A

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-812/S-007

LABELING REVIEW

8.1 9.1

DEC 15 1999

Labeling Review of NDA Supplement

NDA: 20-812/S-007	**Submission Date**: October 26, 1999 **Received**: October 28, 1999 **Review Date**: November 12, 1999
Applicant:	Whitehall-Robins Five Giralda Farms Madison, NJ 07940-0871 973-660-5753
Applicant's Representative:	Sharon C. Heddish Vice President Regulatory Affairs – Worldwide
Drug:	Pediatric Advil Drops (Ibuprofen, 100 mg/2.5mL)
Pharmacologic Category:	Fever reducer/pain reliever
Submitted:	Special Supplement – CBE - Final printed Color labeling/diskette
Reviewer:	Stephanie A. Mason

The sponsor submitted 20 copies of final printed labeling for the following to be in compliance with the Agency's September 15, 1998 letter which provides for the required allergy alert and two additional warnings:

1. Pediatric Advil Drops (ibuprofen) Oral Suspension Grape/Fruit flavor ¼ oz carton/label.

2. Pediatric Advil Drops (ibuprofen) Oral Suspension Grape/Fruit flavor ½ oz carton/label.

Reviewer's comments: Implementation of the required allergy alert, and two additional warnings is acceptable. For the bottle label, the sponsor should delete the period after the bulleted statement under **Do not use**, and include the sore throat warning in the labeling at the time of the next printing or within six months.

In addition, it is noted that the submitted labeling is outdated and does not include: (1) the required **Drug Facts** format per the final rule for OTC Labeling Requirements, (2) the amended warning regarding accidental

overdose (§ 369.20), and (3) the required sore throat warning as stated in § 201.315.

An **Acknowledgement and Retain letter** should be sent to the sponsor. The sponsor should also be reminded of the deficiencies stated above.

Stephanie A. Mason, IDS
Reviewer

Debbie L. Lumpkins, B.S., Microbiologist
Team Leader 3

cc:
NDA 20-812
HFD-560/Div. File
HFD-560/K.Rothschild
HFD-560/S.Mason
HFD-560/D.Lumpkins:12/14/99
HFD-560/L.Katz 12/15/99
HFD-560/C.Ganley
R/D:S.Mason:11/12/99
F/T:S.Mason:12/ /99
20812s7.doc

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 20-812/S-007

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ORIGINAL

Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940-0871
Telephone (973) 660-5500
Website address: http://healthfront.com

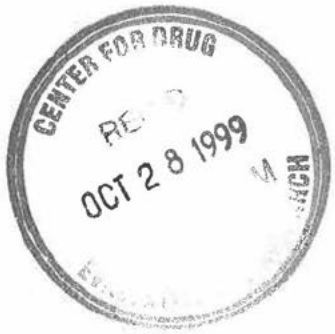
WHITEHALL ROBINS

NDA NO. 20812 REF NO. 007
NDA SUPPL FOR SLR

October 26, 1999

NDA 20-812
Pediatric Advil® Drops
(ibuprofen 100 mg/2.5 mL)

Special Supplement - Changes Being Effected
(Allergy Alert Warning)



Charles J. Ganley, M.D., Director
Division of OTC Drug Products **(HFD-560)**
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20857

Dear Dr. Ganley:

Reference is made to NDA 20-812 for Pediatric Advil® Drops (ibuprofen 100 mg/2.5 mL), sponsored by Whitehall-Robins Healthcare ("Whitehall-Robins"), a division of American Home Products Corporation. Reference is also made to your letter of September 15, 1998, regarding revised class-labeling for potential allergic reactions (attached).

This letter directed Whitehall-Robins to update the labeling of this product to comply with the required warning statements and submit final printed labeling (FPL) in the form of a SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED as described under 21 CFR 314.70(c). Enclosed herewith are 20 copies of the final printed labeling, ten of which are mounted on heavy weight paper for the products covered under this NDA. The following label components are enclosed:

Pediatric Advil® Drops Ibuprofen Oral Suspension Grape Flavor ¼ oz Carton
Pediatric Advil® Drops Ibuprofen Oral Suspension Grape Flavor ¼ oz Label
Pediatric Advil® Drops Ibuprofen Oral Suspension Grape Flavor ½ oz Carton
Pediatric Advil® Drops Ibuprofen Oral Suspension Grape Flavor ½ oz Label

Pediatric Advil® Drops Ibuprofen Oral Suspension Fruit Flavor ¼ oz Carton
Pediatric Advil® Drops Ibuprofen Oral Suspension Fruit Flavor ¼ oz Label
Pediatric Advil® Drops Ibuprofen Oral Suspension Fruit Flavor ½ oz Carton
Pediatric Advil® Drops Ibuprofen Oral Suspension Fruit Flavor ½ oz Label

In addition an image of the labeling for the carton and label of the product is included on diskette in PDF format.

If you have any questions or comments regarding this submission, please contact the undersigned at (973) 660-5753 or Mary Davis at (973) 660-5825.

Sincerely,

WHITEHALL-ROBINS HEALTHCARE

Mary H Davis

Sharon C. Heddish
Vice President
Regulatory Affairs - Worldwide

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-589/NDA 20-812

Whitehall-Robins Healthcare
Attention: Sharon Heddish
Vice President, Regulatory Affairs
Five Giralda Farms
Madison, New Jersey 07940-0871

SEP 15

Sept 15, 1998 MHD

Dear Ms. Heddish:

Please refer to your new drug applications for Children's Advil (Grape) Suspension (ibuprofen), 100mg/5mL (NDA 20-589), and Pediatric Advil (Fruit) Drops (ibuprofen oral suspension), 100 mg/2.5 mL.

In an effort to improve the consistency of labeling for OTC drug products containing analgesic active ingredients, the Agency has reevaluated class labeling issues relating to these drug products. Included among the issues under evaluation were warnings relating to potential allergic reactions to these products, including those in aspirin-sensitive individuals.

We have completed our evaluation and have concluded that the following warning statements are required.

Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
- hives
- facial swelling
- asthma (wheezing)
- shock

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Stop use and ask a doctor if an allergic reaction occurs. Seek medical help right away.

Of note, for pediatric drug products bearing allergy warning statements under the heading of "Aspirin Sensitive Children"; this heading will no longer be used. In addition, for products with drug fact format labeling, the last two warning statements must be placed under their respective subheadings as the first bulleted statement.

At this time, the Agency is requesting that the applicants of approved new drug applications for OTC internal analgesic drug products update the labeling of these products to comply with the labeling stated above. Please submit final printed labeling exactly as specified above in the form of "SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED" as described under 21 CFR 314.80(c). Please incorporate all previous revisions consistent with the most recently approved labeling. However, please do not include any other labeling changes in this supplemental new drug application. To facilitate review of your submission, please provide a highlighted or marked-up copy of the labeling that shows the changes being made.

The labeling changes must be implemented within 6 months or at the next printing, whichever comes first.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 31.81 for an approved NDA.

If you have any questions concerning this request, please contact Stephanie Mason, Acting Project Manager, at (301)-827-2275.

Sincerely yours,

Debra L. Bowen, M.D.
Acting Director
Division of OTC Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-812/S-007

NOV 1 1999

Whitehall Robins Healthcare
5 Giralda Farm
Madison, NJ 17940

Attention: Sharon C. Heddish
Vice President Regulatory Affairs-Worldwide

Dear Ms. Heddish:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Pediatric® Adivl Drop® (ibuprofen) 100mg/2.5ml Suspension

NDA Number: 20-812

Supplement Number: S-007

Date of Supplement: October 26, 1999

Date of Receipt: October 28, 1999

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on December 27, 1999 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Food and Drug Administration
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Attention: Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

for

Maria Rossana R. Cook, M.B.A.
Chief, Project Management Staff
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Original NDA 20-812/S-007
HFD-560/Div. Files
HFD-560/CSO/K. Rothschild

SUPPLEMENT ACKNOWLEDGEMENT