CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 078682Orig1s016s021

Name: Ibuprofen Capsules, 200 mg (OTC)

Sponsor: Bionpharma Inc.

Approval Date: March 24, 2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078682Orig1s016s021CONTENTS

Reviews / Information Included in this Review

Approval Letter	**X**
Tentative Approval Letter	
Labeling	
Labeling Review(s)	**X**
Medical Review(s)	
Chemistry Review(s)	
Pharm/Tox Review	
Bioequivalence Review(s)	
Statistical Review(s)	
Microbiology Review(s)	
Other Review(s)	
Administrative & Correspondence Documents	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078682Orig1s016s021

APPROVAL LETTER

ANDA 078682/S-016 and S-021

CHANGES BEING EFFECTED
APPROVAL

Bionpharma Inc.
600 Alexander Road
Suite 2-4B
Princeton, NJ 08540
Attention: Usha Sankaran
Associate Vice President, Regulatory Affairs

Dear Usha Sankaran:

This is in reference to your supplemental abbreviated new drug applications (sANDAs) received for review on August 28, 2017 (S-016) and November 6, 2018 (S-021), submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Ibuprofen Capsules, 200 mg (OTC).

These sANDAs, submitted as "Changes Being Effected," provide for:

S-016: labeling revisions to be in accordance with the reference listed drug (RLD) Advil® Liqui-Gels (Pain Reliever/Fever Reducver), NDA 020402/S-043, approved August 8, 2017.

S-021: new labeling for "Migraine Relief" in accordance with the RLD, Advil® Liqui-Gels (Migraine Relief), NDA 020402/S-043, approved August 8, 2017.

We have completed the review of these sANDAs and they are approved.

REPORTING REQUIREMENTS

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98 and at section 506I of the FD&C Act. The Office of Generic Drugs should be advised of any change in the marketing status of this drug or if this drug will not be available for sale after approval. In particular, under section 506I(b) of the FD&C Act, you are required to notify the Office of Generic Drugs in writing within 180 days from the date of this letter if this drug will not be available for sale within 180 days from the date of approval. As part of such written notification, you must include (1) the identity of the drug by established name and proprietary name (if any); (2) the ANDA number; (3) the strength of the drug; (4) the date on which the drug will be available for sale, if known; and (5) the reason for not marketing the drug after approval.

ANNUAL FACILITY FEES

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions [1] with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-

identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

Sincerely yours,

{See appended electronic signature page}

For CAPT Chi-Ann Wu, PharmD, MPH
Director
Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

[1] Some of these provisions were amended by the Generic Drug User Fee Amendments of 2017 (GDUFA II) (Public Law 115-52, Title III).

Theresa Liu

Digitally signed by Theresa Liu
Date: 2/21/2019 11:47:15AM
GUID: 508da70a00028d58911de18a598cda6f

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078682Orig1s016s021

LABELING REVIEW(s)

***** This document contains proprietary information that cannot be released to the public***v.40**

SUPPLEMENT LABELING REVIEW

Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs (OGD)
Center for Drug Evaluation and Research (CDER)

Date of this Review	2/1/2019
Review Cycle Number	2
ANDA(s) and Supplement Number(s)	078682/**S-020**, S-016 and S-021
Applicant Name	Bionpharma Inc.
Proprietary Name, Established Name, and Strength(s) [Add "(OTC)" after strength if applicable]	Ibuprofen Capsules, 200 mg (OTC)
Current Received Date	12/3/2018
Previous Received Date(s) of Proposed Supplement	S-020: 9/26/2018; 9/10/2018 S-016: 8/28/2017 S-021: 11/6/2018
Primary Labeling Reviewer	Oluwakemi O. Odesina
Secondary Labeling Reviewer	Refer to signature page

Review Conclusion

☒ ACCEPTABLE - No Comments.

☐ ACCEPTABLE - Include Post approval comments.

☐ Minor Deficiency* – Refer to Labeling Deficiencies and Comments for Letter to Applicant

☐ Major Deficiency† – Refer to Labeling Deficiencies and Comments for Letter to Applicant

†Theme - Choose an item.

Justification for Major Deficiency - Choose an item.

*Please Note: The Regulatory Project Manager (RPM) may change the recommendation from Minor Deficiency to Discipline Review Letter/Information Request (DRL/IR) if all other OGD reviews are acceptable. Otherwise, the labeling minor and major deficiencies will be included in the Complete Response Letter (CRL) letter to the applicant.

On Policy Alert List	☐ Yes	☒ No
Acceptable for Filing	☒ Yes	☐ No
Combined Insert/Outsert	☐ Yes	☒ No (If yes, indicate ANDA number)

☐ **For labeling supplement(s):**

This Changes Being Effected supplemental abbreviated new drug CLICK HERE

We have completed the review of this supplemental application. Choose an item. effective on the date of this letter. Choose an item.

OR

We have completed the review of your applications and have determined that we cannot approve these applications in their present form. We have described below our reasons for this action and, where possible, our recommendations to address

1. CONTAINER LABEL
2. CARTON LABELING
3. PRESCRIBING INFORMATION
4. MEDICATION GUIDE
5. STRUCTURED PRODUCT LABELING (SPL)

☒ **For combined supplement(s):**

.

The Division of Labeling Review has no comments. Labeling is acceptable.

Contents

1. ANDA REGULATORY INFORMATION:

Type of Supplement: PAS	
Are there any pending issues in DLR's SharePoint Drug Facts? If Yes, please explain:	**NO**
Is the drug product listed in the Policy Alert Tracker on DLRS SharePoint? If Yes, please explain:	**NO**
Is the drug product listed on the Susceptibility Test Interpretive Criteria web page? **https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm575163.htm**	NO

Reason for Submission:

- **12/3/2018 Ammendment:**

The below comments are from the C1 labeling review based on the submission dated 9/26/2018

To facilitate
container/carto
1, Section 1.1

Please refer t
changes.

The Applicant has made the requested revisions; we find it acceptable.

- **Original Submission:**

S-020 (PAS)

thi

S-021 (CBE)

As pe
Supp
consi
Migr

S-016 (CBE)

Bionpharma is hereby submitting a CBE-0 Labeling Supplement to revise the labeling for its Ibuprofen Capsules, 200 mg, to be in line with the revised labeling approved for the Reference Listed Drug, Advil® Liqui-Gels®, (NDA 020402, S-043) on August 8, 2017. The revised labeling is provided in m1 1.14.1.1. A side-by-side comparison of the revised labeling and the updated RLD labeling is provided in m1 1.14.1.2. The submission also includes the labeling history in m1 1.14.1.5 which summarizes the changes made to the labeling. As the labeling has been revised in line with the RLD, side-by-side comparison of the revised labeling with the previous approved labeling is not relevant and hence not included.

Is this supplement combined with another discipline?	**YES (S-020_**
Is this product an OTC product?	**YES**
Is this ANDA the RLD?	**NO**

2. MATERIAL ANALYSIS

The results for each material reviewed in this section provide the basis for the labeling comments to the Applicant and other review disciplines.

2.1 MATERIALS REVIEWED

Tables 1 and 2 provide a summary of recommendations for each material analyzed in this review.

Table 1: Review Summary of Container Label and Carton Labeling				
	Final or Draft or NA	**Packaging Sizes**	**Submission Received Date**	**Recommendation**
Container	Draft	S-016 (Pain Reliever/Fever Reducer)	08/28/2017 11/06/2018	Satisfactory

		• Blue Colored Capsules 8's, 20's, 200's, 240's, 300's Bottle Label • Orange Colored Capsules 8's, 20's, 200's, 240's 300's Bottle Label • Clear Capsules 8's 20's, 200's, 240's, 300's Bottle Label --- **S-021 (Migraine)** 20's Bottle Label --- **S-020 (Minis)** 8's, 300's Bottle Label	**12/3/2018**	
Pouch	Draft	**S-016 (Pain Reliever/Fever Reducer)** • Blue Colored Capsules 2's Pouch Label • Orange Colored Capsules 2's Pouch Label • Clear Capsules 2's Pouch Label	**08/28/2017**	Satisfactory
Carton	Draft	**S-016 (Pain Reliever/Fever Reducer)**	**08/28/2017** **11/06/2018**	Satisfactory

		• Blue Colored Capsules 4's Pouch Carton 20's Bottle Carton • Orange Colored Capsules 4's Pouch Carton 20's Bottle Carton • Clear Capsules 4's Pouch Carton 20's Bottle Carton --- **S-021 (Migraine)** 20 Capsules per Carton --- **S-020 (Minis)** 8 capsules per carton	12/3/2018	
(Other – specify)	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

Table 2 Review Summary of Prescribing Information and Patient Labeling

	Final or Draft or NA	Revision Date and/or Code	Submission Received Date	Recommendation
Prescribing Information	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Medication Guide	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Patient Information	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
SPL Data Elements	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

2.2 MODEL LABELING

The review model labels and labeling used for comparison to the submitted ANDA labeling are described in Table 3.

Table 3: Review Model Labeling for Prescribing Information, Patient Labeling, and Drug Facts Labeling (OTC) (Check the box used as the Model Labeling)

☒ **MOST RECENTLY APPROVED NDA MODEL LABELING**

(If NDA is listed in the discontinued section of the Orange Book, indicate whether the application has been withdrawn and if so, enter the most recently approved ANDA labeling information as applicable.)

NDA#/Supplement# (S-000 if original): 020402/S-042; 020402/S-043

Supplement Approval Date: 03/08/2017; 08/08/2018

Proprietary Name: Advil Liqui-Gels Minis; Advil Liqui-Gels

Established Name: Solubilized Ibuprofen Capsules

Description of Supplement:

S-042

This "Prior Approval" supplemental new drug application proposes a new line extension product for a smaller liquid-filled capsule (identified as minis) as compared to the currently approved Advil® Liqui-Gels®.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We remind you to remove the 'NEW' flag from the statement "NEW Smaller Capsule" on the principal display panel 6 months after introduction to the marketplace.

S-043

This "Prior Approval" supplemental new drug application provides for the following changes:

- the addition of heart attack and stroke warning information to all Advil® LIQUI-GELS® and Advil® Migraine labels
- the addition of medication overuse headache warning information to the Advil® Migraine labels
- updates to the graphics on the principal display panel
- updates to the net quantity statement on the 2-count immediate container (pouch) label
- minor revisions to immediate container and carton labels (e.g., inactive ingredients revisions, update copyright and patent information)
- new bonus labeling (e.g., 100-, 180- child resistant, 180- non-child resistant count sizes)
- the addition of two instantly redeemable coupons for the Advil® Migraine 20- and 80-count cartons
- the removal of the 4-count carton (hang card), 8-count carton, 120-count carton, and 240-count immediate container (standalone bottle) labels approved in Supplement 025

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the following revisions listed below:

Delete [redacted] as a listed inactive ingredient within the Drug Facts labeling because it is not part of the final drug product.

Table 3: Review Model Labeling for Prescribing Information, Patient Labeling, and Drug Facts Labeling (OTC) (Check the box used as the Model Labeling)
****We note that the Applicant's proposed S-021 is to be in accordance with the RLD's S-043 and proposed S-020 is to be in accordance with the RLD's S-042. We note that approved RLD labeling for S-046 and S-047 approved on 8/2/2018 and 8/31/2018 respectively provide for: S-046 This "Prior Approval" supplemental new drug application proposes a new $1.00 instantly redeemable coupon (IRC) to be placed on the approved 40-count carton. We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. S-047 This "Prior Approval" supplemental new drug application provides for an alternate 8-count immediate container label to accompany previously approved small and large backer cards. We note that these supplements do not provide for changes to the Drug Facts Labeling.
☐ **MOST RECENTLY APPROVED ANDA MODEL LABELING** **ANDA#/Supplement# (S-000 if original):** Click here to enter text. **Supplement Approval Date:** Click here to enter text. **Proprietary Name:** Click here to enter text. **Established Name:** Click here to enter text. **Description of Supplement:** Click here to enter text.
☐ **TEMPLATE (e.g., BPCA, PREA, Carve-out):** Click here to enter text.
☐ **OTHER (Describe):** Click here to enter text.

Reviewer Assessment:

Is the NDA listed in the discontinued section of the Orange Book? **NO**
If yes, then comment below regarding the current model labeling.

Comment:

2.3 PATENTS AND EXCLUSIVITIES

The Orange Book was searched on 2/1/2019.

Are there any remaining unexpired patents or marketing exclusivities for Model Labeling? **NO**

If YES go to the Table 4 and assessments below.

Table 4 describes how the applicant certified to the Orange Book patent(s) for the Model Labeling (020402) and how this certification impacts the ANDA labels and labeling. For applications that have no patents N/A is entered in the patent number column.

Table 4: Impact of Model Labeling Patents on ANDA Labeling					
Patent Number	Patent Expiration	Patent Use Code	Patent Use Code Definition	Patent Certification	Labeling Impact ("Carve-out" or "None" or "Not addressed by firm")
NA					

Table 5 describes how the expiration of the Orange Book exclusivities for the Model Labeling impacts the ANDA labels and labeling. For applications that have no exclusivities N/A is entered in the Exclusivity Code column.

Table 5: Impact of Model Labeling Exclusivities on ANDA Labels and Labeling				
Exclusivity Code	Exclusivity Expiration	Exclusivity Code Definition	Exclusivity Statement	Labeling Impact ("Carve-out" or "None" or "Not addressed by firm")
NA				

Reviewer Assessment:

Are there any recently expired patents or exclusivities? **NO**
If yes, did these patents or exclusivities have any labeling impact? **N/A**

Comment:

2.4 UNITED STATES PHARMACOPEIA (USP) & PHARMACOPEIA FORUM (PF)

The USP was searched on 2/1/2019.

Table 6: USP				
	YES or NO	Date	Monograph Title (NA if no monograph)	Packaging and Storage/Labeling Statements (NA if no monograph)
Currently Official	NO		NA	NA
Not Yet Official	NO	NA	NA	NA

Reviewer Assessment:

Are the required USP recommendations and/or differences in test methods (e.g., dissolution, organic impurities, assay) reflected in the labels/labeling? **NA**

Comment:

2.5 HISTORY OF ANDA

We evaluated previously approved and pending supplements (Table 7) to determine if actions are needed for the current review.

Table 7: Labeling History of ANDA		
Original or Supplement	**Approval Date**	**What post approval changes were requested and were the changes addressed?**
S-012	07/31/2013	None
Are there any Pending Labeling Supplements for this ANDA that impact labeling? NO		
Pending Supplement	**Submission Date**	**Labeling Impact**

3. ASSESSMENT OF CURRENT SUPPLEMENT'S LABELING

3.1 CONTAINER AND CARTON LABELS

Reviewer Assessment:

Were container or carton labels submitted in this supplement? **YES**
If yes, state the reason for the submission, and comment below whether the proposed revisions are acceptable or deficient.

Comment:

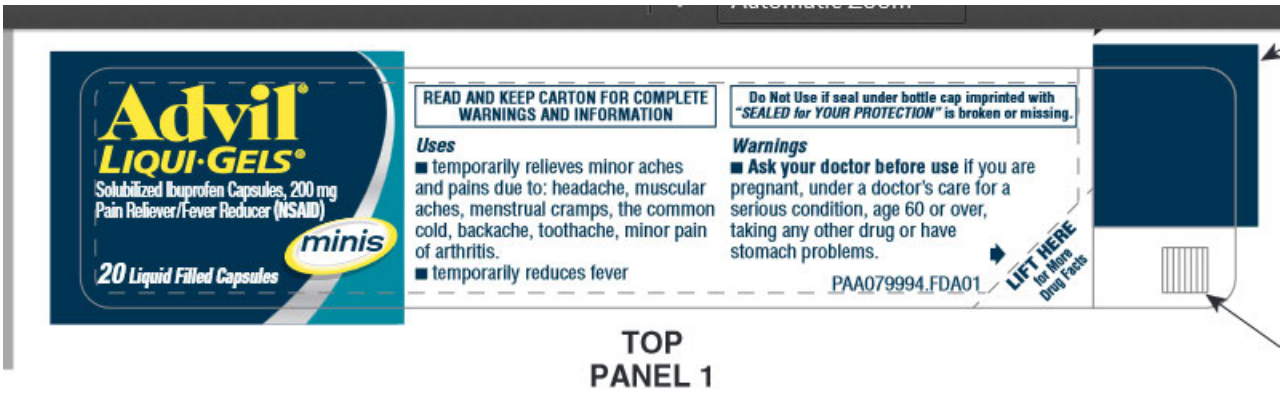
We note that this is an OTC drug product; the Applicant has submitted revised labeling in accordance with the RLD's approved S-042 and S-043; we find it acceptable.

3.1.1 MODEL CONTAINER LABELS

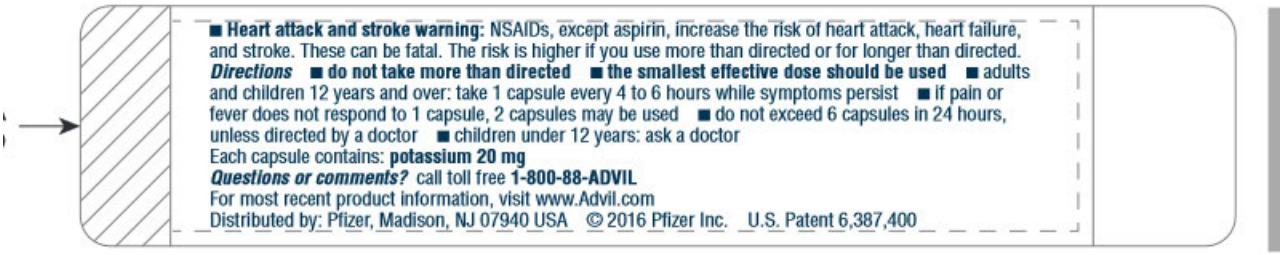
Please provide the reference listed drug labels if applicant submits container, blister, carton, etc.

Model container/carton/blister labels [Source: Drugs@FDA]

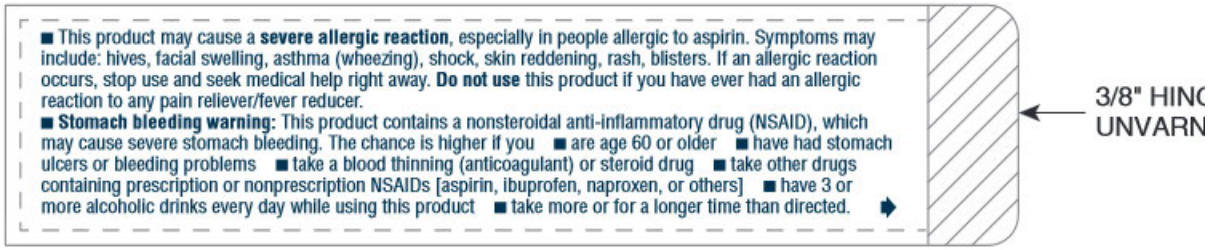
NDA 020402/S-042 approved on 03/08/2017

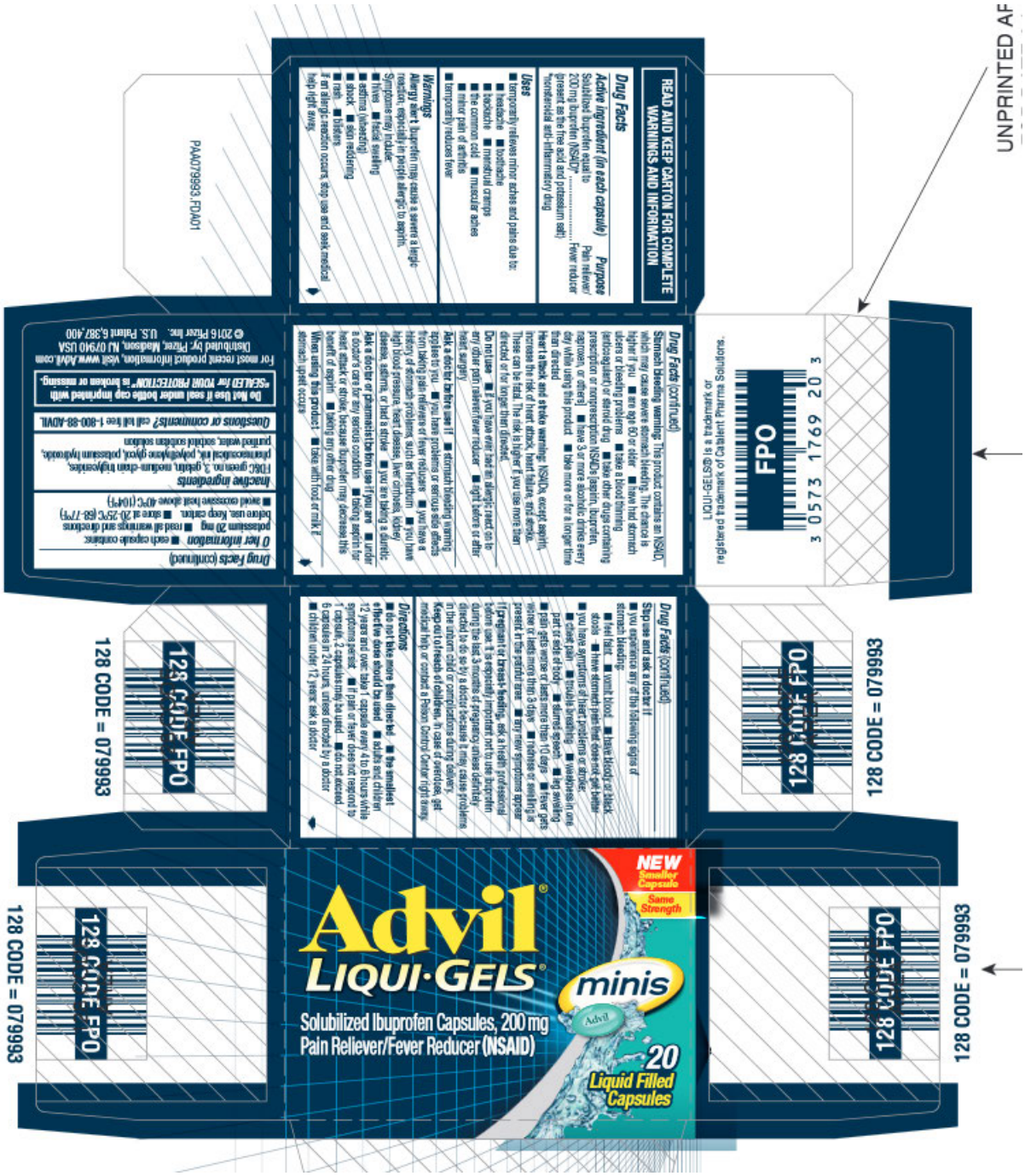


TOP
PANEL 1



BASE
PANEL 3

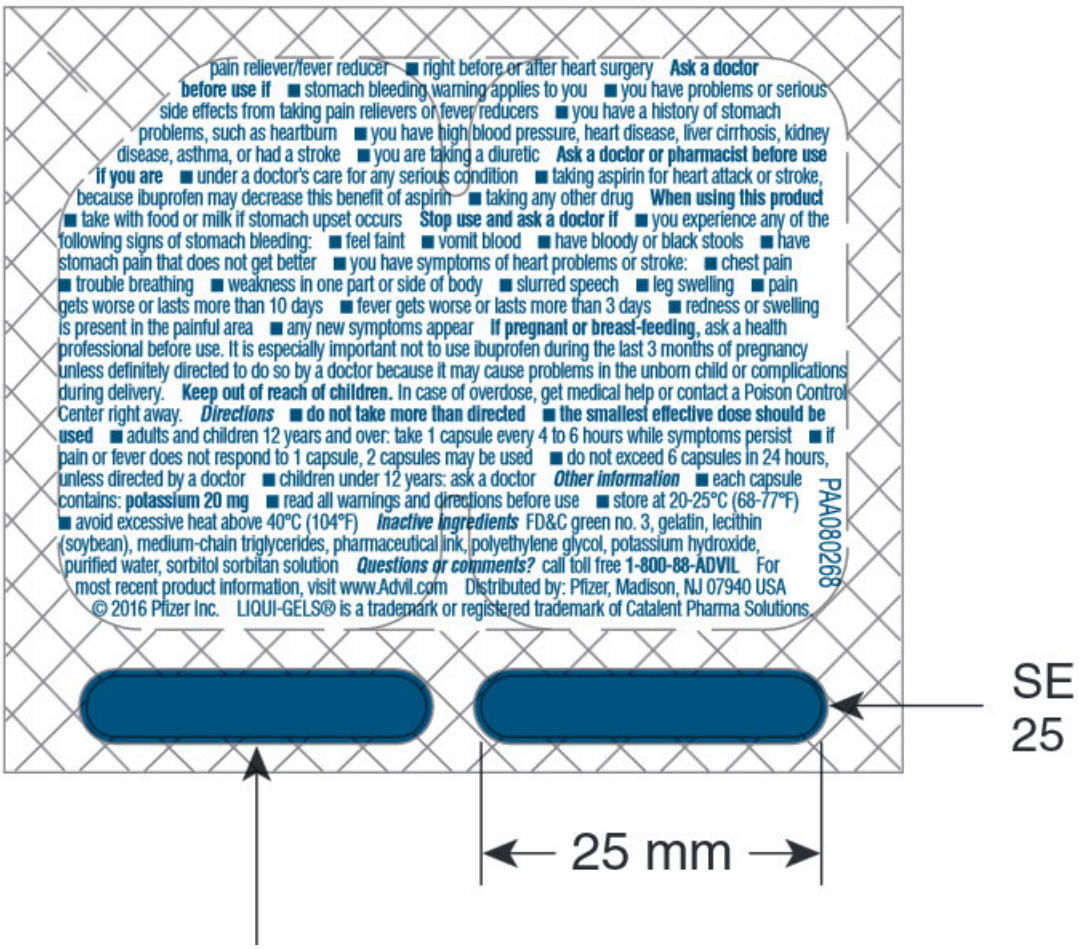




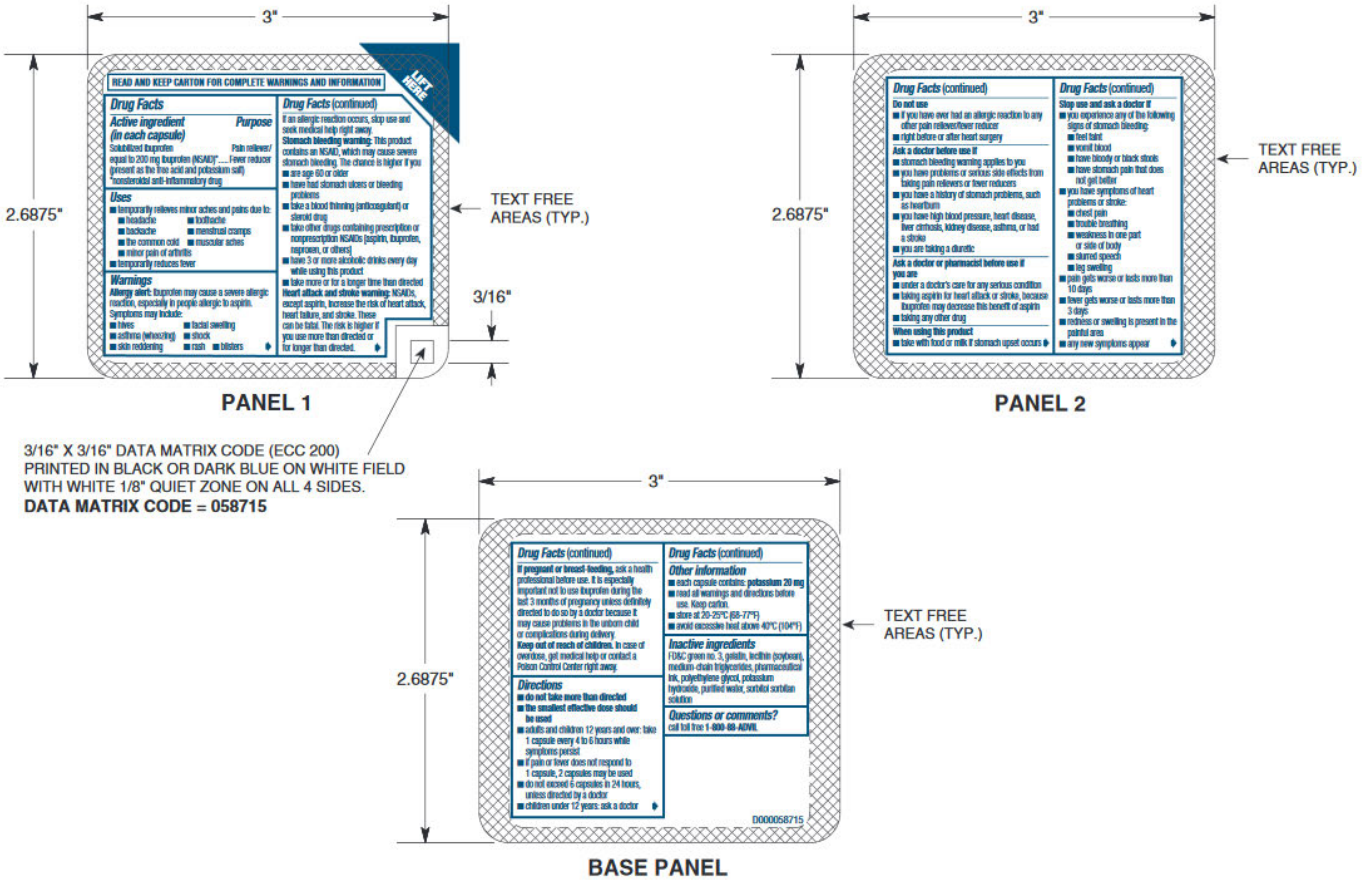
NDA 020402/S-043 approved on 08/08/2017

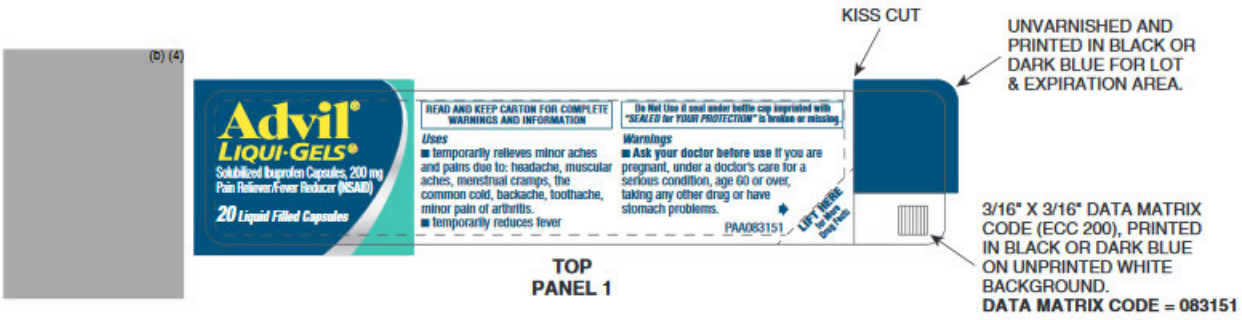

Advil®
LIQUI-GELS®
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
2 Liquid Filled Capsules
Active Ingredient (in each capsule)
Purpose
Solubilized ibuprofen equal to 200 mg (present as the free acid and potassium salt)
Pain reliever/ ibuprofen (NSAID)* .....Fever reducer
*nonsteroidal anti-inflammatory drug
Uses
■ temporarily relieves minor aches and pains due to: ■ headache ■ toothache ■ backache ■ menstrual cramps ■ the common cold ■ muscular aches ■ minor pain of arthritis
■ temporarily reduces fever
Warnings
Allergy alert: Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock ■ skin reddening ■ rash ■ blisters If an allergic reaction occurs, stop use and seek medical help right away. Stomach bleeding warning: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if you ■ are age 60 or older ■ have had stomach ulcers or bleeding problems ■ take a blood thinning (anticoagulant) or steroid drug ■ take other drugs containing prescription or nonprescription NSAIDs [aspirin, ibuprofen, naproxen, or others] ■ have 3 or more alcoholic drinks every day while using this product ■ take more or for a longer time than directed Heart attack and stroke warning: NSAIDs, except aspirin, increase the risk of heart attack, heart failure, and stroke. These can be fatal. The risk is higher if you use more than directed or for longer than directed. Do not use ■ if you have ever had an allergic reaction to any other
TO OPEN: FOLD BACK ON DOTTED LINE.
TEAR ON ARROW OR USE SCISSORS.
Do Not Use if pouch is broken or torn.
PAA080267

BACK

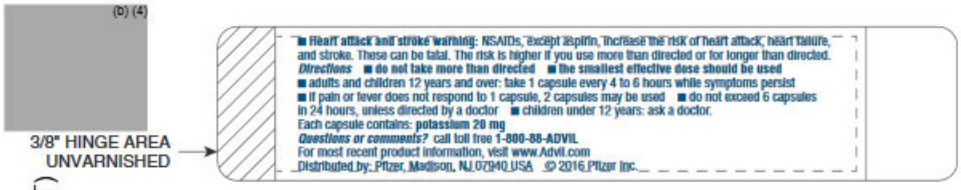

pain reliever/fever reducer ■ right before or after heart surgery **Ask a doctor before use if** ■ stomach bleeding warning applies to you ■ you have problems or serious side effects from taking pain relievers or fever reducers ■ you have a history of stomach problems, such as heartburn ■ you have high blood pressure, heart disease, liver cirrhosis, kidney disease, asthma, or had a stroke ■ you are taking a diuretic **Ask a doctor or pharmacist before use if you are** ■ under a doctor's care for any serious condition ■ taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin ■ taking any other drug **When using this product** ■ take with food or milk if stomach upset occurs **Stop use and ask a doctor if** ■ you experience any of the following signs of stomach bleeding: ■ feel faint ■ vomit blood ■ have bloody or black stools ■ have stomach pain that does not get better ■ you have symptoms of heart problems or stroke: ■ chest pain ■ trouble breathing ■ weakness in one part or side of body ■ slurred speech ■ leg swelling ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ redness or swelling is present in the painful area ■ any new symptoms appear **If pregnant or breast-feeding,** ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away. ***Directions*** ■ **do not take more than directed** ■ **the smallest effective dose should be used** ■ adults and children 12 years and over: take 1 capsule every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 capsule, 2 capsules may be used ■ do not exceed 6 capsules in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor ***Other information*** ■ each capsule contains: **potassium 20 mg** ■ read all warnings and directions before use ■ store at 20-25°C (68-77°F) ■ avoid excessive heat above 40°C (104°F) ***Inactive ingredients*** FD&C green no. 3, gelatin, lecithin (soybean), medium-chain triglycerides, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitol sorbitan solution ***Questions or comments?*** call toll free **1-800-88-ADVIL** For most recent product information, visit www.Advil.com Distributed by: Pfizer, Madison, NJ 07940 USA
© 2016 Pfizer Inc. LIQUI-GELS® is a trademark or registered trademark of Catalent Pharma Solutions.
PAA080268
SE
25
25 mm


(2) 2 ct PACKETS
Advil
LIQUI-GELS
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
4
Liquid Filled
Capsules
FPO
3 0573 1769 04 3
Do Not Use if the sealed child resistant
pouch is broken or torn.
For most recent product information, visit www.Advil.com
Pfizer, Madison, NJ 07940 USA © 2017 Pfizer Inc.
D000057830
128 CODE = 057830
FPO 128 CODE
AREA
AREA FOR LOT AND
EXPIRATION DATE
128 CODE = 057830
HIGH DENSITY CODE 128,

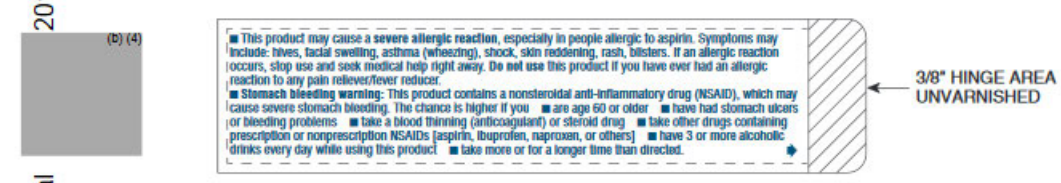

3"
2.6875"
READ AND KEEP CARTON FOR COMPLETE WARNINGS AND INFORMATION
LIFT HERE
Drug Facts
Active ingredient (in each capsule)
Purpose
Solubilized ibuprofen
Pain reliever/ equal to 200 mg ibuprofen (NSAID)* ..... Fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug
Uses
■ temporarily relieves minor aches and pains due to:
■ headache ■ toothache
■ backache ■ menstrual cramps
■ the common cold ■ muscular aches
■ minor pain of arthritis
■ temporarily reduces fever
Warnings
Allergy alert: ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin.
Symptoms may include:
■ hives ■ facial swelling
■ asthma (wheezing) ■ shock
■ skin reddening ■ rash ■ blisters
Drug Facts (continued)
If an allergic reaction occurs, stop use and seek medical help right away.
Stomach bleeding warnings: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if you
■ are age 60 or older
■ have had stomach ulcers or bleeding problems
■ take a blood thinning (anticoagulant) or steroid drug
■ take other drugs containing prescription or nonprescription NSAIDs (aspirin, ibuprofen, naproxen, or others)
■ have 3 or more alcoholic drinks every day while using this product
■ take more or for a longer time than directed
Heart attack and stroke warning: NSAIDs, except aspirin, increase the risk of heart attack, heart failure, and stroke. These can be fatal. The risk is higher if you use more than directed or for longer than directed.
TEXT FREE AREAS (TYP.)
3/16"
PANEL 1
3/16" X 3/16" DATA MATRIX CODE (ECC 200)
PRINTED IN BLACK OR DARK BLUE ON WHITE FIELD
WITH WHITE 1/8" QUIET ZONE ON ALL 4 SIDES.
DATA MATRIX CODE = 058715
3"
2.6875"
Drug Facts (continued)
Do not use
■ if you have ever had an allergic reaction to any other pain reliever/fever reducer
■ right before or after heart surgery
Ask a doctor before use if
■ stomach bleeding warning applies to you
■ you have problems or serious side effects from taking pain relievers or fever reducers
■ you have a history of stomach problems, such as heartburn
■ you have high blood pressure, heart disease, liver cirrhosis, kidney disease, asthma, or had a stroke
■ you are taking a diuretic
Ask a doctor or pharmacist before use if you are
■ under a doctor's care for any serious condition
■ taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin
■ taking any other drug
When using this product
■ take with food or milk if stomach upset occurs
Drug Facts (continued)
Stop use and ask a doctor if
■ you experience any of the following signs of stomach bleeding:
■ feel faint
■ vomit blood
■ have bloody or black stools
■ have stomach pain that does not get better
■ you have symptoms of heart problems or stroke:
■ chest pain
■ trouble breathing
■ weakness in one part or side of body
■ slurred speech
■ leg swelling
■ pain gets worse or lasts more than 10 days
■ fever gets worse or lasts more than 3 days
■ redness or swelling is present in the painful area
■ any new symptoms appear
TEXT FREE AREAS (TYP.)
PANEL 2
3"
2.6875"
Drug Facts (continued)
If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions
■ do not take more than directed
■ the smallest effective dose should be used
■ adults and children 12 years and over: take 1 capsule every 4 to 6 hours while symptoms persist
■ if pain or fever does not respond to 1 capsule, 2 capsules may be used
■ do not exceed 6 capsules in 24 hours, unless directed by a doctor
■ children under 12 years: ask a doctor
Drug Facts (continued)
Other information
■ each capsule contains: potassium 20 mg
■ read all warnings and directions before use. Keep carton
■ store at 20-25°C (68-77°F)
■ avoid excessive heat above 40°C (104°F)
Inactive ingredients
FD&C green no. 3, gelatin, lecithin (soybean), medium-chain triglycerides, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitol sorbitan solution
Questions or comments?
call toll free 1-800-88-ADVIL
D000058715
TEXT FREE AREAS (TYP.)
BASE PANEL



TOP PANEL 1



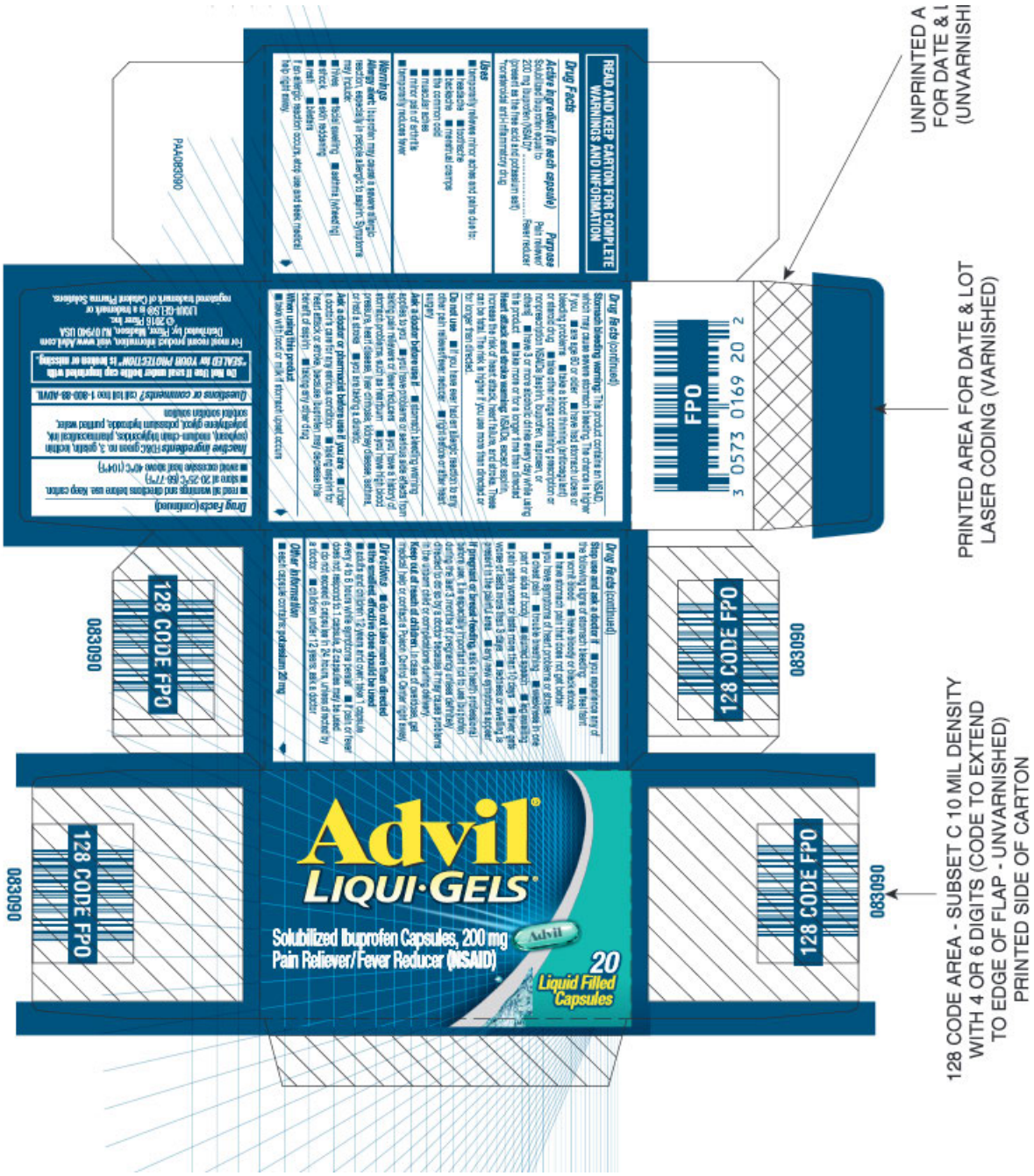
BASE PANEL 3

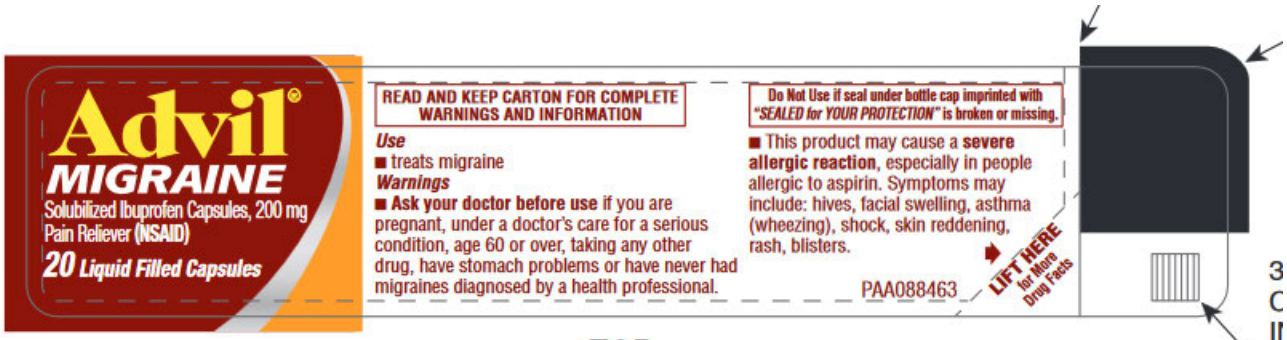


RELEASED BACK PANEL 2

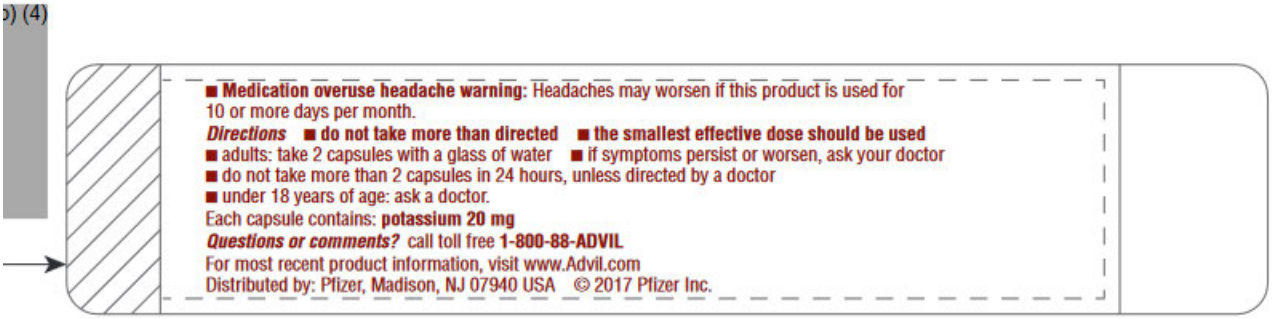
2017 16:06 (GMT)

al\Final

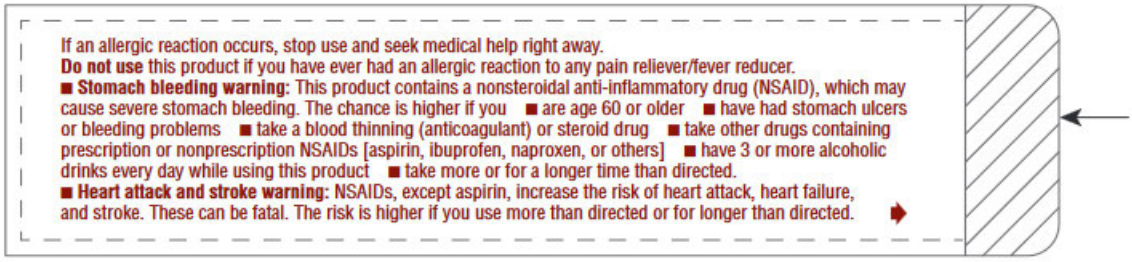

UNPRINTED A
FOR DATE & L
(UNVARNISH
PRINTED AREA FOR DATE & LOT
LASER CODING (VARNISHED)
128 CODE AREA - SUBSET C 10 MIL DENSITY
WITH 4 OR 6 DIGITS (CODE TO EXTEND
TO EDGE OF FLAP - UNVARNISHED)
PRINTED SIDE OF CARTON
Advil
LIQUI-GELS
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
20
Liquid Filled
Capsules
128 CODE FPO
083090
FPO
READ AND KEEP CARTON FOR COMPLETE WARNINGS AND INFORMATION
Drug Facts
Uses
Warnings
Drug Facts (continued)
Other information
PA4083090



TOP PANEL 1



BASE



RELEASED BACK PANEL 2

020402Orig1s043lbl.pdf

020402s042lbl.pdf

3.1.2 RX PRESCRIBING INFORMATION, PATIENT LABELING, & DRUG FACTS LABELING (OTC)

Reviewer Assessment:

Was labeling submitted in this supplement? **YES**
Are the Prescribing Information or Drug Facts Labeling (OTC) contained in the submission the same as the review model labeling (not including allowable differences under 21 CFR 314.94(a)(8))? **YES**
Is the Prescribing Information shared by other ANDAs? **NO** (If yes please list ANDA numbers).
Are the specific requirements for format met under 21 CFR 201.57 (new), or 201.80 (old), or 201.66 (OTC)? **YES**

Comment:

Acceptable

3.1.3 DESCRIPTION, HOW SUPPLIED, MANUFACTURED BY STATEMENT

[For OTC products, please include the inactives in Table 8; package sizes being marketed in Table 9; and drug product manufacturer/distributor statement in Table 10.]

Reviewer Assessment:

Are there changes to the inactives in the DESCRIPTION section or OTC labeling? **YES**
Are there changes to the dosage form description(s) or package size(s) in HOW SUPPLIED section or OTC package sizes? **YES**
Are there changes to the manufacturer/distributor/packer statements? **YES**
If yes, then comment below in Tables 8, 9, and 10.

Table 8: Comparison of DESCRIPTION Section or Inactive Ingredients Subsection (OTC)		
Previous Labeling Review	**Currently Proposed**	**Assessment**
nactive ingredients gelatin, pharmaceutical nk, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol	FD&C Blue #1, gelatin, (b) (4) pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol	We note that the Applicant has different colors for their respective proposed drug products; we find it acceptable.

Table 9: Comparison of HOW SUPPLIED Section or Packaging Sizes for OTC Products		
Previous Labeling Review	**Currently Proposed**	**Assessment**

Table 9: Comparison of HOW SUPPLIED Section or Packaging Sizes for OTC Products		
Packaging sizes of 20s, 40s, 80s, 120s	S-016 (Pain Reliever/Fever Reducer) • Blue Colored Capsules 8's, 20's, 200's, 240's, 300's Bottle Label • Orange Colored Capsules 8's, 20's, 200's, 240's 300's Bottle Label • Clear Capsules 8's 20's, 200's, 240's, 300's Bottle Label --- S-021 (Migraine) 20's Bottle Label --- S-020 (Minis) 8's, 300's Bottle Label	We note that there are different additional packaging sizes for the Applicant's new proposed packaging, we find it acceptable.

Table 10: Manufacturer/Distributor/Packer Statements		
Previous Labeling Review	Currently Proposed	Assessment
Distributed by: McNeil Consumer Healthcare Division of McNEIL-PPC, Inc. Fort Washington, PA 19034 USA	Manufactured for: Bionpharma Inc. 600 Alexander Road, Princeton, NJ 08540	We note that application was transferred to Bionpharmac Inc per the 12/4/2015 Administrative Change/Applicant cover letter; we find it acceptable.

4. SPECIAL CONSIDERATIONS

Please include other information that may pertain to your drug product application.

Oluwakemi Odesina

Digitally signed by Oluwakemi Odesina
Date: 2/01/2019 02:04:41PM
GUID: 5423006c00721f6b43db6c5df1f43327

Theresa Liu

Digitally signed by Theresa Liu
Date: 2/04/2019 01:17:48PM
GUID: 508da70a00028d58911de18a598cda6f

***** This document contains proprietary information that cannot be released to the public***v.40**

SUPPLEMENT LABELING REVIEW

Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs (OGD)
Center for Drug Evaluation and Research (CDER)

Date of this Review	11/13/2018
Review Cycle Number	1
ANDA(s) and Supplement Number(s)	078682/**S-020**, S-016 and S-021
Applicant Name	Bionpharma Inc.
Proprietary Name, Established Name, and Strength(s) [Add "(OTC)" after strength if applicable]	Ibuprofen Capsules, 200 mg (OTC)
Current Received Date	S-020: 9/26/2018 S-016: 8/28/2017 S-021: 11/6/2018
Previous Received Date(s) of Proposed Supplement	S-020: 9/10/2018
Primary Labeling Reviewer	Oluwakemi O. Odesina
Secondary Labeling Reviewer	Refer to signature page

Review Conclusion

☐ ACCEPTABLE - No Comments.

☐ ACCEPTABLE - Include Post approval comments.

☒ Minor Deficiency* – Refer to Labeling Deficiencies and Comments for Letter to Applicant

☐ Major Deficiency† – Refer to Labeling Deficiencies and Comments for Letter to Applicant

†Theme - Choose an item.

Justification for Major Deficiency - Choose an item.

*Please Note: The Regulatory Project Manager (RPM) may change the recommendation from Minor Deficiency to Discipline Review Letter/Information Request (DRL/IR) if all other OGD reviews are acceptable. Otherwise, the labeling minor and major deficiencies will be included in the Complete Response Letter (CRL) letter to the applicant.

On Policy Alert List	☐ Yes	☒ No
Acceptable for Filing	☒ Yes	☐ No
Combined Insert/Outsert	☐ Yes	☒ No (If yes, indicate ANDA number)

☐ **For labeling supplement(s):**

This Changes Being Effected supplemental abbreviated new drug CLICK HERE

We have completed the review of this supplemental application. Choose an item. effective on the date of this letter. Choose an item.

OR

We have completed the review of your applications and have determined that we cannot approve these applications in their present form. We have described below our reasons for this action and, where possible, our recommendations to address

1. CONTAINER LABEL
2. CARTON LABELING
3. PRESCRIBING INFORMATION
4. MEDICATION GUIDE
5. STRUCTURED PRODUCT LABELING (SPL)

☒ **For combined supplement(s):**

.

Labeling deficiencies determined on 11/16/2018, based on your submissions received on 9/26/2018

1. CONTAINER LABEL

Revise the expression of the established name to remove the term “Mini” (e.g. Ibuprofen Capsules). Instead, the term “Mini” should be used as a modifier, in accordance with the reference listed drug (RLD).

2. CARTON LABELING

We recommend adding the statement “Smaller Capsule Same Strength” to the principal display panel (PDP), in accordance with the RLD.

Contents

1. ANDA REGULATORY INFORMATION:

Type of Supplement: PAS	
Are there any pending issues in DLR's SharePoint Drug Facts? If Yes, please explain:	**NO**
Is the drug product listed in the Policy Alert Tracker on DLRS SharePoint? If Yes, please explain:	**NO**
Is the drug product listed on the Susceptibility Test Interpretive Criteria web page? **https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm575163.htm**	NO

Reason for Submission:

S-020 (PAS)

(b) (4)

thı

S-021 (CBE)

As pe
Supp
consi
Migr

S-016 (CBE)

Bionpharma is hereby submitting a CBE-0 Labeling Supplement to revise the labeling for its Ibuprofen Capsules, 200 mg, to be in line with the revised labeling approved for the Reference Listed Drug, Advil® Liqui-Gels®, (NDA 020402, S-043) on August 8, 2017. The revised labeling is provided in m1 1.14.1.1. A side-by-side comparison of the revised labeling and the updated RLD labeling is provided in m1 1.14.1.2. The submission also includes the labeling history in m1 1.14.1.5 which summarizes the changes made to the labeling. As the labeling has been revised in line with the RLD, side-by-side comparison of the revised labeling with the previous approved labeling is not relevant and hence not included.

Is this supplement combined with another discipline?	**YES (S-020_**
Is this product an OTC product?	**YES**

Is this ANDA the RLD?	NO

2. MATERIAL ANALYSIS

The results for each material reviewed in this section provide the basis for the labeling comments to the Applicant and other review disciplines.

2.1 MATERIALS REVIEWED

Tables 1 and 2 provide a summary of recommendations for each material analyzed in this review.

Table 1: Review Summary of Container Label and Carton Labeling

	Final or Draft or NA	Packaging Sizes	Submission Received Date	Recommendation
Container	Draft	**S-016 (Pain Reliever/Fever Reducer)** • Blue Colored Capsules 8's, 20's, 200's, 240's, 300's Bottle Label • Orange Colored Capsules 8's, 20's, 200's, 240's 300's Bottle Label • Clear Capsules 8's 20's, 200's, 240's, 300's Bottle Label --- **S-021 (Migraine)** 20's Bottle Label --- **S-020 (Minis)** 8's, 300's Bottle Label	08/28/2017 11/06/2018 9/10/2018	Revise
Pouch	Draft	**S-016 (Pain Reliever/Fever Reducer)** • Blue Colored Capsules	08/28/2017 11/06/2018 9/10/2018	Satisfactory

		2's Pouch Label • Orange Colored Capsules 2's Pouch Label • Clear Capsules 2's Pouch Label		
Carton	Draft	**S-016 (Pain Reliever/Fever Reducer)** • Blue Colored Capsules 4's Pouch Carton 20's Bottle Carton • Orange Colored Capsules 4's Pouch Carton 20's Bottle Carton • Clear Capsules 4's Pouch Carton 20's Bottle Carton --- **S-021 (Migraine)** 20 Capsules per Carton --- **S-020 (Minis)** 8 capsules per carton	**08/28/2017** **11/06/2018** **9/10/2018**	Revise
(Other – specify)	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

Table 2 Review Summary of Prescribing Information and Patient Labeling

	Final or Draft or NA	Revision Date and/or Code	Submission Received Date	Recommendation

Prescribing Information	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Medication Guide	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
Patient Information	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.
SPL Data Elements	Click here to enter text.	Click here to enter text.	Click here to enter text.	Click here to enter text.

2.2 MODEL LABELING

The review model labels and labeling used for comparison to the submitted ANDA labeling are described in Table 3.

Table 3: Review Model Labeling for Prescribing Information, Patient Labeling, and Drug Facts Labeling (OTC)
(Check the box used as the Model Labeling)

☒ **MOST RECENTLY APPROVED NDA MODEL LABELING**

(If NDA is listed in the discontinued section of the Orange Book, indicate whether the application has been withdrawn and if so, enter the most recently approved ANDA labeling information as applicable.)

NDA#/Supplement# (S-000 if original): 020402/S-042; 020402/S-043

Supplement Approval Date: 03/08/2017; 08/08/2018

Proprietary Name: Advil Liqui-Gels Minis; Advil Liqui-Gels

Established Name: Solubilized Ibuprofen Capsules

Description of Supplement:

S-042

This "Prior Approval" supplemental new drug application proposes a new line extension product for a smaller liquid-filled capsule (identified as minis) as compared to the currently approved Advil® Liqui-Gels®.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We remind you to remove the 'NEW' flag from the statement "NEW Smaller Capsule" on the principal display panel 6 months after introduction to the marketplace.

S-043

This "Prior Approval" supplemental new drug application provides for the following changes:

- the addition of heart attack and stroke warning information to all Advil® LIQUI-GELS® and Advil® Migraine labels
- the addition of medication overuse headache warning information to the Advil® Migraine labels
- updates to the graphics on the principal display panel
- updates to the net quantity statement on the 2-count immediate container (pouch) label
- minor revisions to immediate container and carton labels (e.g., inactive ingredients revisions, update copyright and patent information)
- new bonus labeling (e.g., 100-, 180- child resistant, 180- non-child resistant count sizes)
- the addition of two instantly redeemable coupons for the Advil® Migraine 20- and 80-count cartons
- the removal of the 4-count carton (hang card), 8-count carton, 120-count carton, and 240-count immediate container (standalone bottle) labels approved in Supplement 025

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the following revisions listed below:

Delete (b) (4) as a listed inactive ingredient within the Drug Facts labeling because it is not part of the final drug product.

Table 3: Review Model Labeling for Prescribing Information, Patient Labeling, and Drug Facts Labeling (OTC) (Check the box used as the Model Labeling)
****We note that the Applicant's proposed S-021 is to be in accordance with the RLD's S-043 and proposed S-020 is to be in accordance with the RLD's S-042. We note that approved RLD labeling for S-046 and S-047 approved on 8/2/2018 and 8/31/2018 respectively provide for: S-046 This "Prior Approval" supplemental new drug application proposes a new $1.00 instantly redeemable coupon (IRC) to be placed on the approved 40-count carton. We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text. S-047 This "Prior Approval" supplemental new drug application provides for an alternate 8-count immediate container label to accompany previously approved small and large backer cards. We note that these supplements do not provide for changes to the Drug Facts Labeling.
☐ **MOST RECENTLY APPROVED ANDA MODEL LABELING** **ANDA#/Supplement# (S-000 if original):** Click here to enter text. **Supplement Approval Date:** Click here to enter text. **Proprietary Name:** Click here to enter text. **Established Name:** Click here to enter text. **Description of Supplement:** Click here to enter text.
☐ **TEMPLATE (e.g., BPCA, PREA, Carve-out):** Click here to enter text.
☐ **OTHER (Describe):** Click here to enter text.

Reviewer Assessment:

Is the NDA listed in the discontinued section of the Orange Book? **NO** If yes, then comment below regarding the current model labeling.

Comment:

2.3 PATENTS AND EXCLUSIVITIES

The Orange Book was searched on 11/13/2018.

Are there any remaining unexpired patents or marketing exclusivities for Model Labeling? **NO**

If YES go to the Table 4 and assessments below.

Table 4 describes how the applicant certified to the Orange Book patent(s) for the Model Labeling (020402) and how this certification impacts the ANDA labels and labeling. For applications that have no patents N/A is entered in the patent number column.

Table 4: Impact of Model Labeling Patents on ANDA Labeling					
Patent Number	Patent Expiration	Patent Use Code	Patent Use Code Definition	Patent Certification	Labeling Impact ("Carve-out" or "None" or "Not addressed by firm")
NA					

Table 5 describes how the expiration of the Orange Book exclusivities for the Model Labeling impacts the ANDA labels and labeling. For applications that have no exclusivities N/A is entered in the Exclusivity Code column.

Table 5: Impact of Model Labeling Exclusivities on ANDA Labels and Labeling				
Exclusivity Code	Exclusivity Expiration	Exclusivity Code Definition	Exclusivity Statement	Labeling Impact ("Carve-out" or "None" or "Not addressed by firm")
NA				

Reviewer Assessment:

Are there any recently expired patents or exclusivities? **NO**
If yes, did these patents or exclusivities have any labeling impact? **N/A**

Comment:

2.4 UNITED STATES PHARMACOPEIA (USP) & PHARMACOPEIA FORUM (PF)

The USP was searched on 11/13/2018.

Table 6: USP				
	YES or NO	Date	Monograph Title (NA if no monograph)	Packaging and Storage/Labeling Statements (NA if no monograph)
Currently Official	NO		NA	NA
Not Yet Official	NO	NA	NA	NA

Reviewer Assessment:

Are the required USP recommendations and/or differences in test methods (e.g., dissolution, organic impurities, assay) reflected in the labels/labeling? **NA**

Comment:

2.5 HISTORY OF ANDA

We evaluated previously approved and pending supplements (Table 7) to determine if actions are needed for the current review.

Table 7: Labeling History of ANDA		
Original or Supplement	**Approval Date**	**What post approval changes were requested and were the changes addressed?**
S-012	07/31/2013	None
Are there any Pending Labeling Supplements for this ANDA that impact labeling? NO		
Pending Supplement	**Submission Date**	**Labeling Impact**

3. ASSESSMENT OF CURRENT SUPPLEMENT'S LABELING

3.1 CONTAINER AND CARTON LABELS

Reviewer Assessment:

Were container or carton labels submitted in this supplement? **YES**
If yes, state the reason for the submission, and comment below whether the proposed revisions are acceptable or deficient.

Comment:

We note that this is an OTC drug product; the Applicant has submitted revised labeling in accordance with the RLD's approved S-042 and S-043; we do not find the labeling to be acceptable. We will issue the following comments to the Applicant:

1. CONTAINER LABEL

Revise the expression of the established name to remove the term "Mini" (e.g. Ibuprofen Capsules). Instead, the term "Mini" should be used as a modifier, in accordance with the reference listed drug (RLD).

2. CARTON LABELING

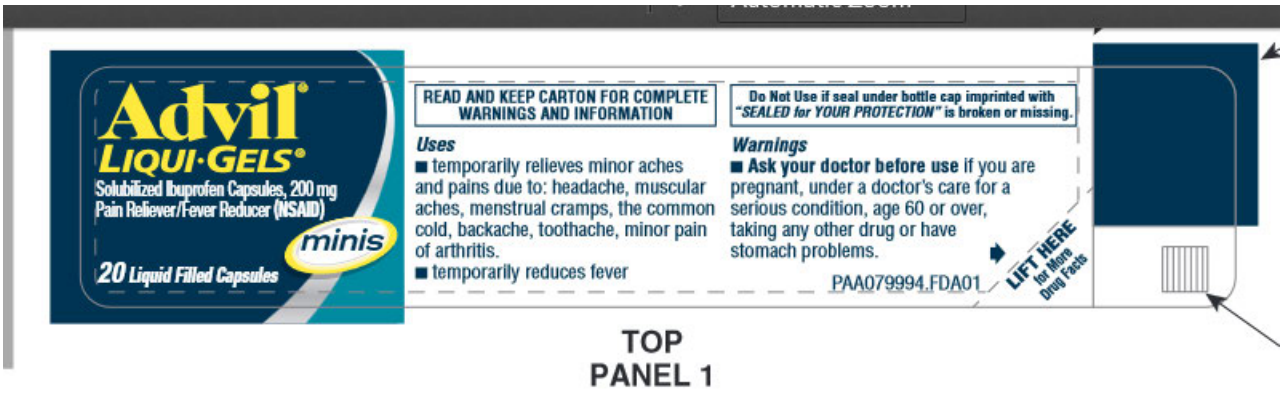
We recommend adding the statement "Smaller Capsule Same Strength" to the principal display panel (PDP), in accordance with the RLD.

3.1.1 MODEL CONTAINER LABELS

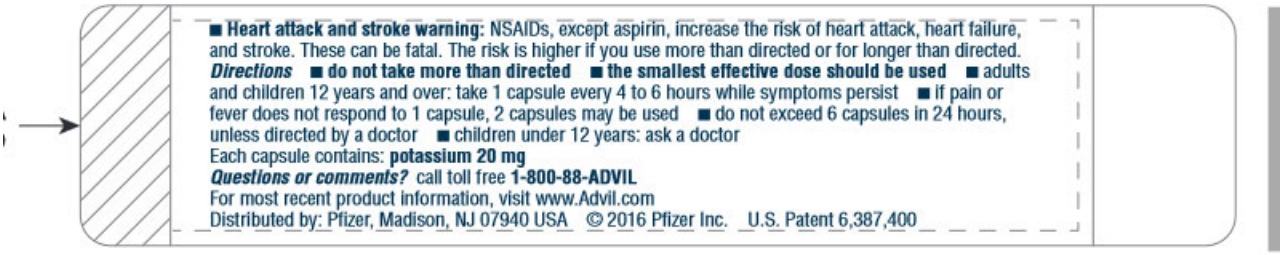
Please provide the reference listed drug labels if applicant submits container, blister, carton, etc.

Model container/carton/blister labels [Source: Drugs@FDA]

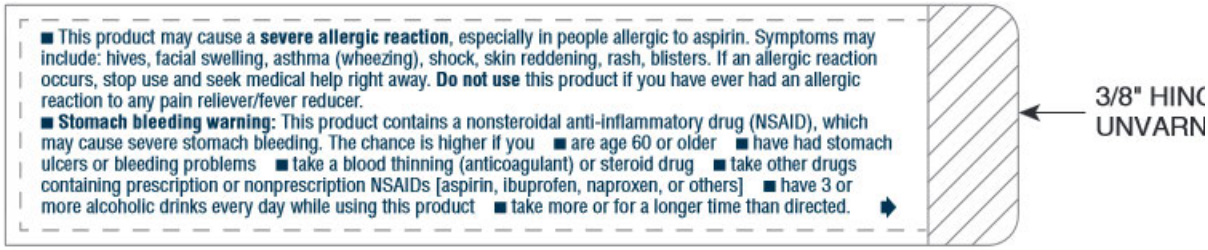
NDA 020402/S-042 approved on 03/08/2017

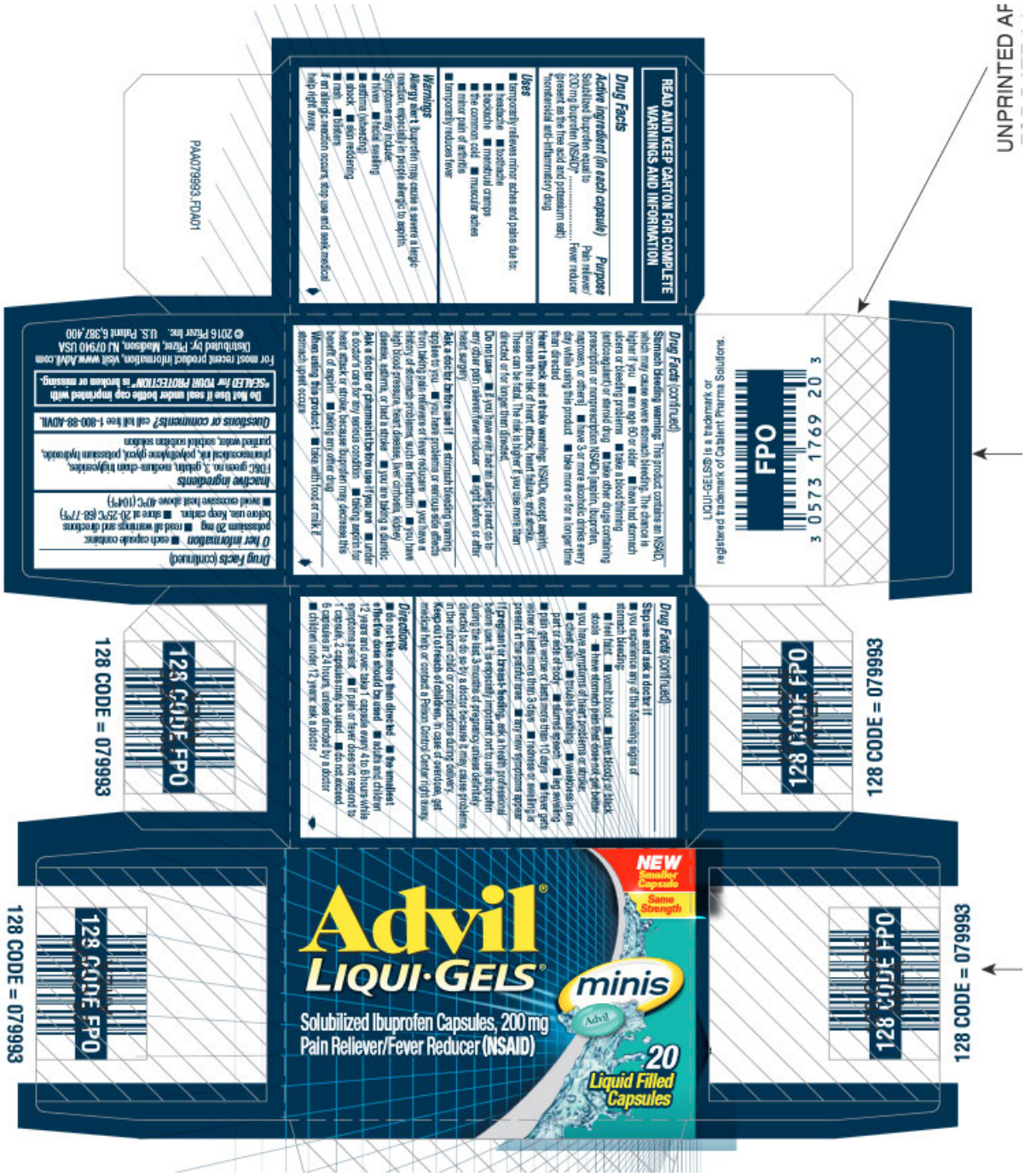


TOP
PANEL 1



BASE
PANEL 3

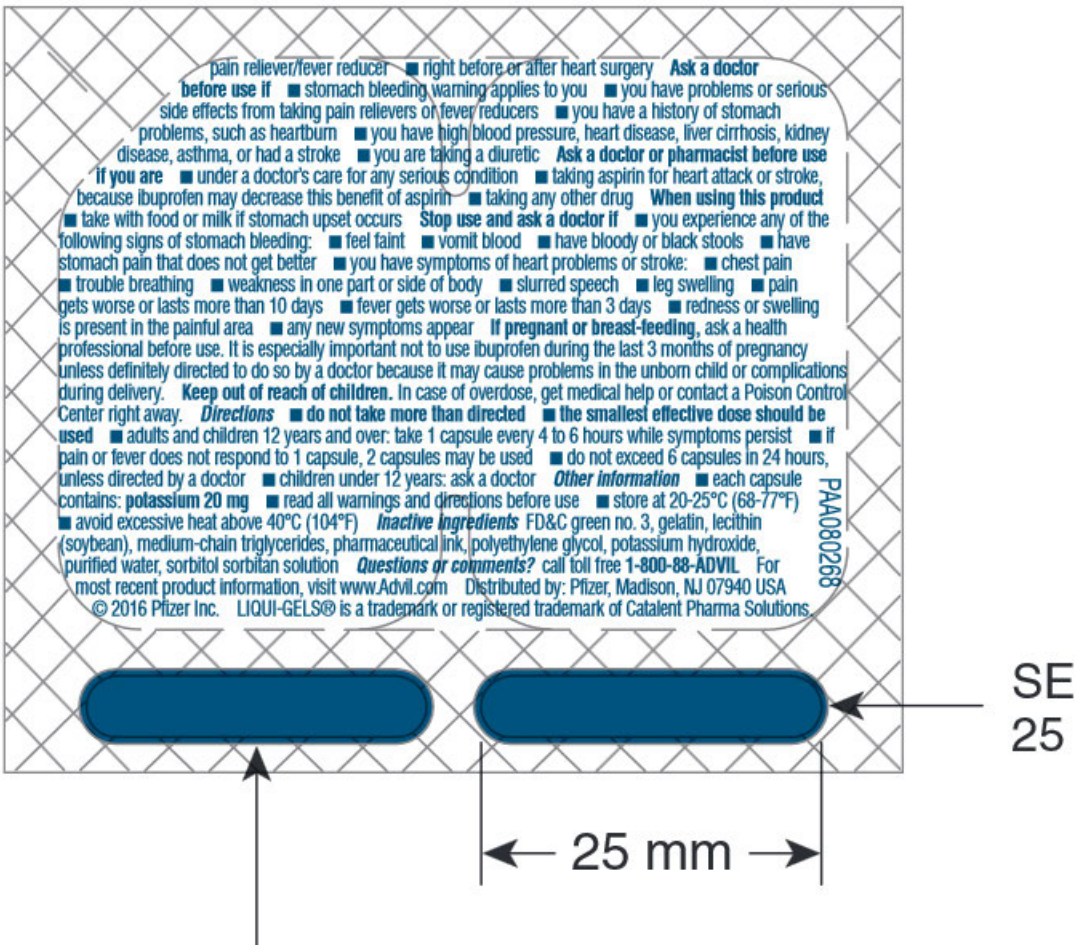




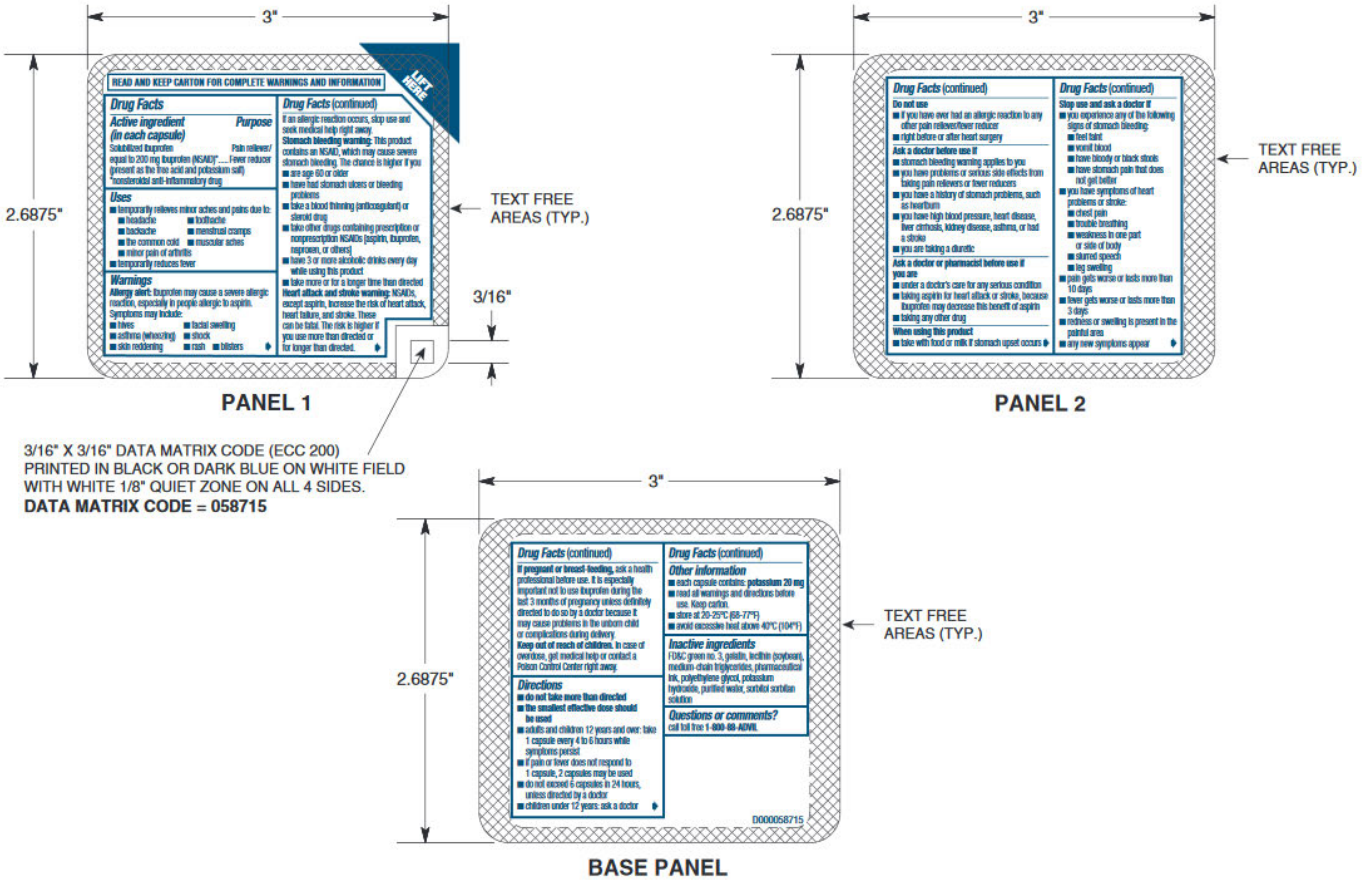
NDA 020402/S-043 approved on 08/08/2017

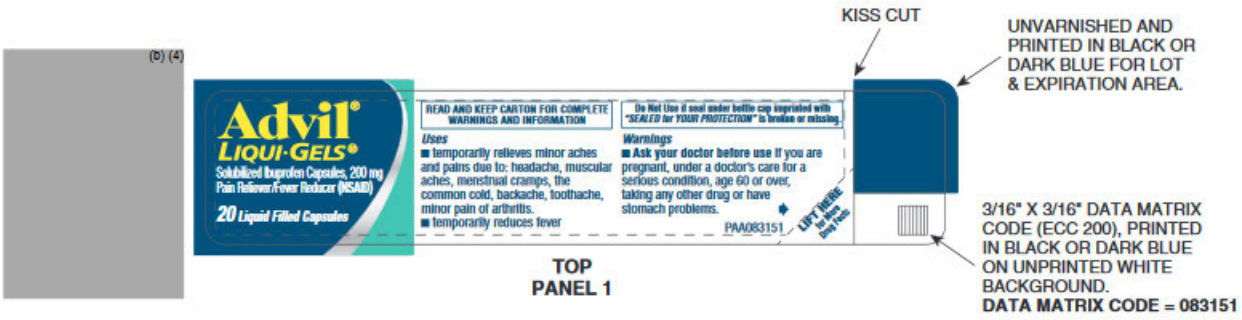

Advil®
LIQUI-GELS®
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
2 Liquid Filled Capsules
Active Ingredient (in each capsule)
Purpose
Solubilized ibuprofen equal to 200 mg (present as the free acid and potassium salt)
Pain reliever/ ibuprofen (NSAID)* .....Fever reducer
*nonsteroidal anti-inflammatory drug
Uses
■ temporarily relieves minor aches and pains due to: ■ headache ■ toothache ■ backache ■ menstrual cramps ■ the common cold ■ muscular aches ■ minor pain of arthritis
■ temporarily reduces fever
Warnings
Allergy alert: Ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin. Symptoms may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock ■ skin reddening ■ rash ■ blisters If an allergic reaction occurs, stop use and seek medical help right away. Stomach bleeding warning: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if you ■ are age 60 or older ■ have had stomach ulcers or bleeding problems ■ take a blood thinning (anticoagulant) or steroid drug ■ take other drugs containing prescription or nonprescription NSAIDs [aspirin, ibuprofen, naproxen, or others] ■ have 3 or more alcoholic drinks every day while using this product ■ take more or for a longer time than directed Heart attack and stroke warning: NSAIDs, except aspirin, increase the risk of heart attack, heart failure, and stroke. These can be fatal. The risk is higher if you use more than directed or for longer than directed. Do not use ■ if you have ever had an allergic reaction to any other
TO OPEN: FOLD BACK ON DOTTED LINE.
TEAR ON ARROW OR USE SCISSORS.
Do Not Use if pouch is broken or torn.
PAA080267

BACK

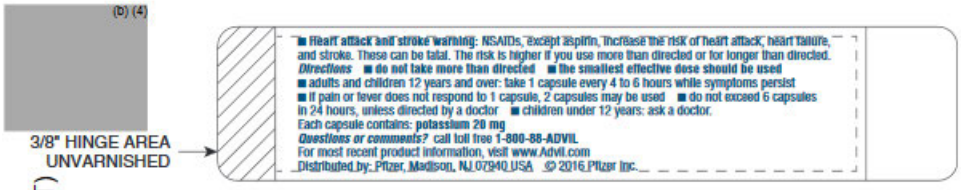

pain reliever/fever reducer ■ right before or after heart surgery **Ask a doctor before use if** ■ stomach bleeding warning applies to you ■ you have problems or serious side effects from taking pain relievers or fever reducers ■ you have a history of stomach problems, such as heartburn ■ you have high blood pressure, heart disease, liver cirrhosis, kidney disease, asthma, or had a stroke ■ you are taking a diuretic **Ask a doctor or pharmacist before use if you are** ■ under a doctor's care for any serious condition ■ taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin ■ taking any other drug **When using this product** ■ take with food or milk if stomach upset occurs **Stop use and ask a doctor if** ■ you experience any of the following signs of stomach bleeding: ■ feel faint ■ vomit blood ■ have bloody or black stools ■ have stomach pain that does not get better ■ you have symptoms of heart problems or stroke: ■ chest pain ■ trouble breathing ■ weakness in one part or side of body ■ slurred speech ■ leg swelling ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ redness or swelling is present in the painful area ■ any new symptoms appear **If pregnant or breast-feeding,** ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away. ***Directions*** ■ **do not take more than directed** ■ **the smallest effective dose should be used** ■ adults and children 12 years and over: take 1 capsule every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 capsule, 2 capsules may be used ■ do not exceed 6 capsules in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor ***Other information*** ■ each capsule contains: **potassium 20 mg** ■ read all warnings and directions before use ■ store at 20-25°C (68-77°F) ■ avoid excessive heat above 40°C (104°F) ***Inactive ingredients*** FD&C green no. 3, gelatin, lecithin (soybean), medium-chain triglycerides, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitol sorbitan solution ***Questions or comments?*** call toll free **1-800-88-ADVIL** For most recent product information, visit www.Advil.com Distributed by: Pfizer, Madison, NJ 07940 USA
© 2016 Pfizer Inc. LIQUI-GELS® is a trademark or registered trademark of Catalent Pharma Solutions.
PAA080268
SE
25
25 mm


(2) 2 ct PACKETS
Advil
LIQUI-GELS
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
4
Liquid Filled
Capsules
FPO
3 0573 1769 04 3
Do Not Use if the sealed child resistant
pouch is broken or torn.
For most recent product information, visit www.Advil.com
Pfizer, Madison, NJ 07940 USA © 2017 Pfizer Inc.
D000057830
128 CODE = 057830
FPO 128 CODE
AREA
AREA FOR LOT AND
EXPIRATION DATE
128 CODE = 057830
HIGH DENSITY CODE 128.

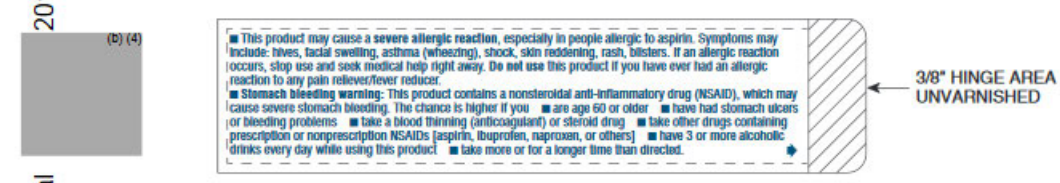

3"
2.6875"
READ AND KEEP CARTON FOR COMPLETE WARNINGS AND INFORMATION
LIFT HERE
Drug Facts
Active ingredient (in each capsule)
Purpose
Solubilized ibuprofen
Pain reliever/ equal to 200 mg ibuprofen (NSAID)* ..... Fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug
Uses
■ temporarily relieves minor aches and pains due to:
■ headache ■ toothache
■ backache ■ menstrual cramps
■ the common cold ■ muscular aches
■ minor pain of arthritis
■ temporarily reduces fever
Warnings
Allergy alert: ibuprofen may cause a severe allergic reaction, especially in people allergic to aspirin.
Symptoms may include:
■ hives ■ facial swelling
■ asthma (wheezing) ■ shock
■ skin reddening ■ rash ■ blisters
Drug Facts (continued)
If an allergic reaction occurs, stop use and seek medical help right away.
Stomach bleeding warnings: This product contains an NSAID, which may cause severe stomach bleeding. The chance is higher if you
■ are age 60 or older
■ have had stomach ulcers or bleeding problems
■ take a blood thinning (anticoagulant) or steroid drug
■ take other drugs containing prescription or nonprescription NSAIDs (aspirin, ibuprofen, naproxen, or others)
■ have 3 or more alcoholic drinks every day while using this product
■ take more or for a longer time than directed
Heart attack and stroke warning: NSAIDs, except aspirin, increase the risk of heart attack, heart failure, and stroke. These can be fatal. The risk is higher if you use more than directed or for longer than directed.
TEXT FREE AREAS (TYP.)
3/16"
PANEL 1
3/16" X 3/16" DATA MATRIX CODE (ECC 200)
PRINTED IN BLACK OR DARK BLUE ON WHITE FIELD
WITH WHITE 1/8" QUIET ZONE ON ALL 4 SIDES.
DATA MATRIX CODE = 058715
3"
2.6875"
Drug Facts (continued)
Do not use
■ if you have ever had an allergic reaction to any other pain reliever/fever reducer
■ right before or after heart surgery
Ask a doctor before use if
■ stomach bleeding warning applies to you
■ you have problems or serious side effects from taking pain relievers or fever reducers
■ you have a history of stomach problems, such as heartburn
■ you have high blood pressure, heart disease, liver cirrhosis, kidney disease, asthma, or had a stroke
■ you are taking a diuretic
Ask a doctor or pharmacist before use if you are
■ under a doctor's care for any serious condition
■ taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin
■ taking any other drug
When using this product
■ take with food or milk if stomach upset occurs
Drug Facts (continued)
Stop use and ask a doctor if
■ you experience any of the following signs of stomach bleeding:
■ feel faint
■ vomit blood
■ have bloody or black stools
■ have stomach pain that does not get better
■ you have symptoms of heart problems or stroke:
■ chest pain
■ trouble breathing
■ weakness in one part or side of body
■ slurred speech
■ leg swelling
■ pain gets worse or lasts more than 10 days
■ fever gets worse or lasts more than 3 days
■ redness or swelling is present in the painful area
■ any new symptoms appear
TEXT FREE AREAS (TYP.)
PANEL 2
3"
2.6875"
Drug Facts (continued)
If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions
■ do not take more than directed
■ the smallest effective dose should be used
■ adults and children 12 years and over: take 1 capsule every 4 to 6 hours while symptoms persist
■ if pain or fever does not respond to 1 capsule, 2 capsules may be used
■ do not exceed 6 capsules in 24 hours, unless directed by a doctor
■ children under 12 years: ask a doctor
Drug Facts (continued)
Other information
■ each capsule contains: potassium 20 mg
■ read all warnings and directions before use. Keep carton
■ store at 20-25°C (68-77°F)
■ avoid excessive heat above 40°C (104°F)
Inactive ingredients
FD&C green no. 3, gelatin, lecithin (soybean), medium-chain triglycerides, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitol sorbitan solution
Questions or comments?
call toll free 1-800-88-ADVIL
D000058715
TEXT FREE AREAS (TYP.)
BASE PANEL



TOP
PANEL 1



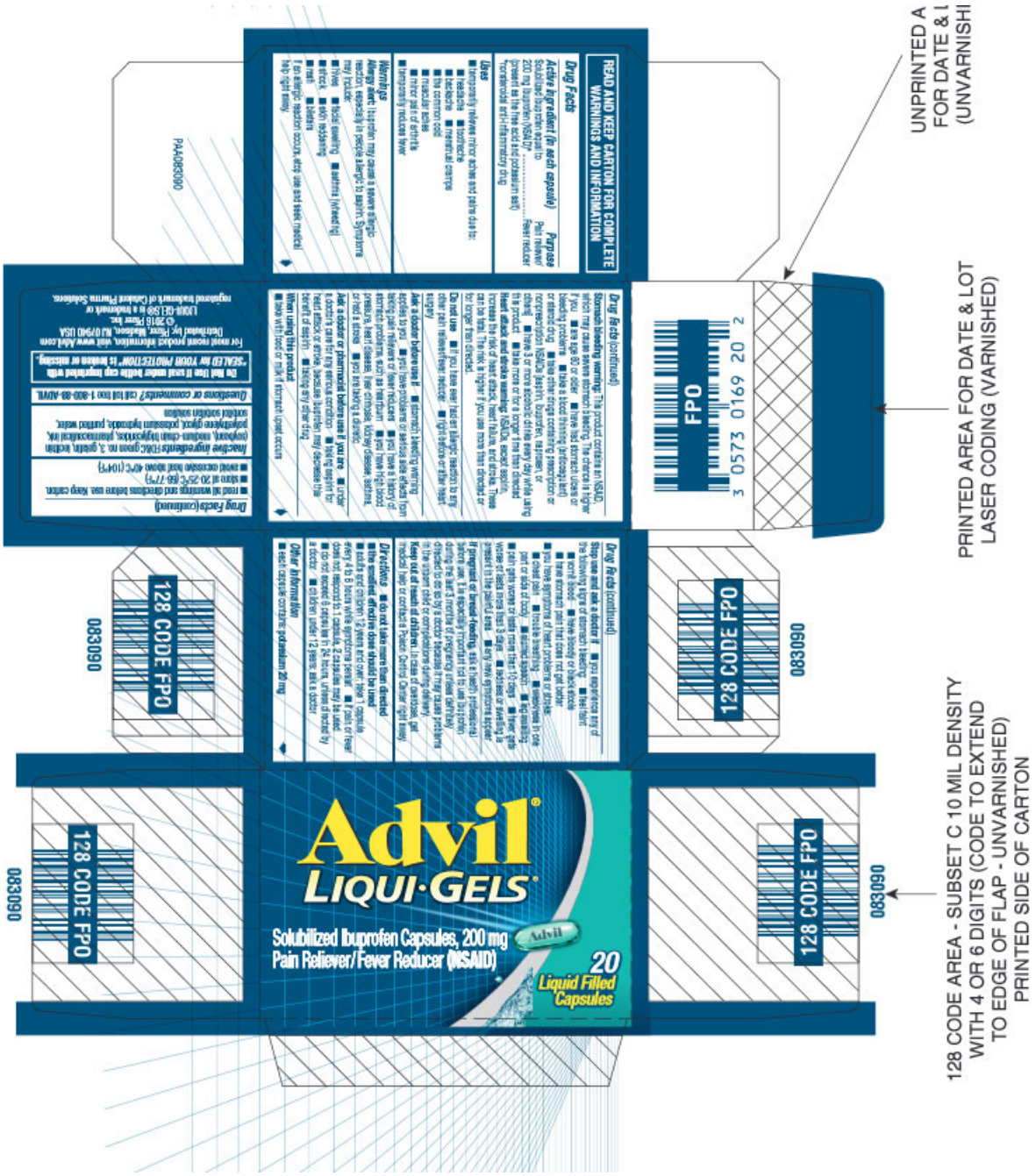
BASE
PANEL 3

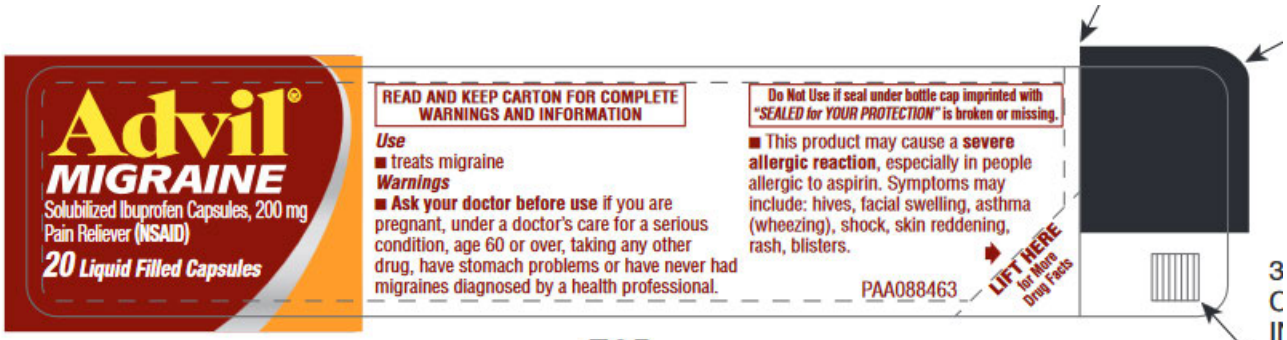


RELEASED BACK
PANEL 2

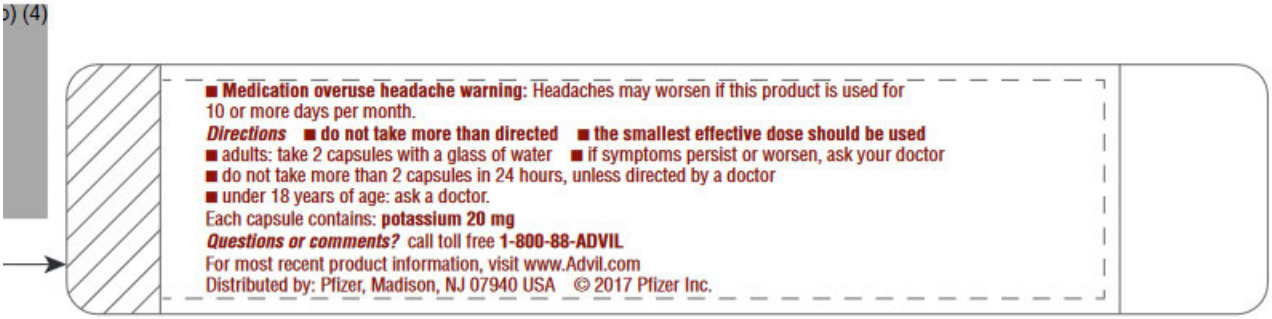
2017 16:06 (GMT)

al\Final

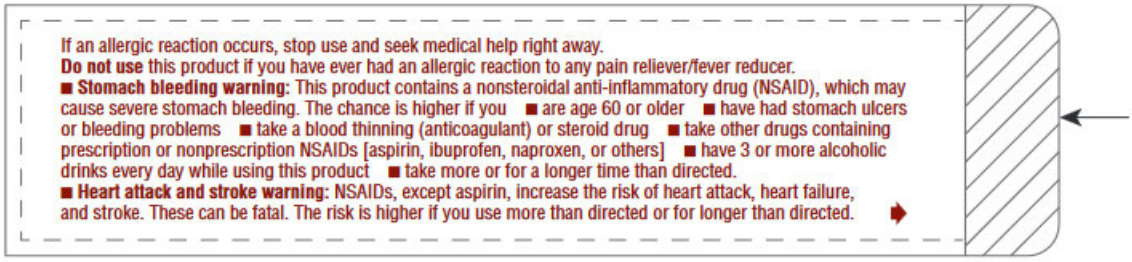

Advil
LIQUI-GELS
Solubilized Ibuprofen Capsules, 200 mg
Pain Reliever/Fever Reducer (NSAID)
20
Liquid Filled
Capsules
128 CODE FPO
083090
FPO
3 0573 0169 20 2
UNPRINTED A
FOR DATE & L
(UNVARNISH
PRINTED AREA FOR DATE & LOT
LASER CODING (VARNISHED)
128 CODE AREA - SUBSET C 10 MIL DENSITY
WITH 4 OR 6 DIGITS (CODE TO EXTEND
TO EDGE OF FLAP - UNVARNISHED)
PRINTED SIDE OF CARTON



TOP PANEL 1



BASE



RELEASED BACK PANEL 2

020402Orig1s043lbl.pdf

020402s042lbl.pdf

3.1.2 RX PRESCRIBING INFORMATION, PATIENT LABELING, & DRUG FACTS LABELING (OTC)

Reviewer Assessment:

Was labeling submitted in this supplement? **YES**
Are the Prescribing Information or Drug Facts Labeling (OTC) contained in the submission the same as the review model labeling (not including allowable differences under 21 CFR 314.94(a)(8))? **YES**
Is the Prescribing Information shared by other ANDAs? **NO** (If yes please list ANDA numbers).
Are the specific requirements for format met under 21 CFR 201.57 (new), or 201.80 (old), or 201.66 (OTC)? **YES**

Comment:

3.1.3 DESCRIPTION, HOW SUPPLIED, MANUFACTURED BY STATEMENT

[For OTC products, please include the inactives in Table 8; package sizes being marketed in Table 9; and drug product manufacturer/distributor statement in Table 10.]

Reviewer Assessment:

Are there changes to the inactives in the DESCRIPTION section or OTC labeling? **YES**
Are there changes to the dosage form description(s) or package size(s) in HOW SUPPLIED section or OTC package sizes? **YES**
Are there changes to the manufacturer/distributor/packer statements? **YES**
If yes, then comment below in Tables 8, 9, and 10.

Table 8: Comparison of DESCRIPTION Section or Inactive Ingredients Subsection (OTC)		
Previous Labeling Review	**Currently Proposed**	**Assessment**
Inactive ingredients gelatin, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol	**FD&C Blue #1, gelatin, (b) (4), pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol**	**We note that the Applicant has different colors for their respective proposed drug products; we find it acceptable.**

Table 9: Comparison of HOW SUPPLIED Section or Packaging Sizes for OTC Products		
Previous Labeling Review	**Currently Proposed**	**Assessment**

Table 9: Comparison of HOW SUPPLIED Section or Packaging Sizes for OTC Products		
Packaging sizes of 20s, 40s, 80s, 120s	S-016 (Pain Reliever/Fever Reducer) • Blue Colored Capsules 8's, 20's, 200's, 240's, 300's Bottle Label • Orange Colored Capsules 8's, 20's, 200's, 240's 300's Bottle Label • Clear Capsules 8's 20's, 200's, 240's, 300's Bottle Label ---------- S-021 (Migraine) 20's Bottle Label ---------- S-020 (Minis) 8's, 300's Bottle Label	We note that there are different additional packaging sizes for the Applicant's new proposed packaging, we find it acceptable.

Table 10: Manufacturer/Distributor/Packer Statements		
Previous Labeling Review	**Currently Proposed**	**Assessment**
Distributed by: McNeil Consumer Healthcare Division of McNEIL-PPC, Inc. Fort Washington, PA 19034 USA	Manufactured for: Bionpharma Inc. 600 Alexander Road, Princeton, NJ 08540	We note that application was transferred to Bionpharmac Inc per the 12/4/2015 Administrative Change/Applicant cover letter; we find it acceptable.

4. SPECIAL CONSIDERATIONS

Please include other information that may pertain to your drug product application.

Oluwakemi Odesina

Digitally signed by Oluwakemi Odesina
Date: 11/16/2018 10:30:33AM
GUID: 5423006c00721f6b43db6c5df1f43327

Theresa Liu

Digitally signed by Theresa Liu
Date: 11/16/2018 01:39:32PM
GUID: 508da70a00028d58911de18a598cda6f