PANRETIN - alitretinoin gel
Advanz Pharma (US) Corp.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PANRETIN GEL safely and effectively. See full prescribing information for PANRETIN GEL.
PANRETIN GEL (alitretinoin) 0.1%, for topical use
Initial U.S. Approval: 1999

INDICATIONS AND USAGE

PANRETIN GEL is a retinoid indicated for the topical treatment of cutaneous lesions in adults with AIDS-related Kaposi's sarcoma (KS). (1)

Limitations of Use: PANRETIN GEL is not indicated when systemic anti-Kaposi's sarcoma therapy is required. (1)

DOSAGE AND ADMINISTRATION

- Apply to the affected lesions twice daily; increase to 4 times daily as tolerated. (2)
- For topical use only. (2)

DOSAGE FORMS AND STRENGTHS

Gel, 0.1% (3)

CONTRAINDICATIONS

Hypersensitivity to retinoids or any component of PANRETIN GEL (4)

WARNINGS AND PRECAUTIONS

- Embryo-Fetal Toxicity: Can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use an effective method of contraception. (5.1. 8.1,8.3)
- Photosensitivity: Minimize exposure to sunlight and sunlamps. (5.2)
- DEET toxicity: Do not use DEET-containing products (5.3)

ADVERSE REACTIONS

Most common adverse reactions (> 5%) at the application site are rash, pain, paresthesia, pruritis, exfoliative dermatitis, edema, and skin disorders. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Advanz Pharma (US) Corp. at 1-877-370-1142 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Can cause fetal harm (8.1)
- Lactation: Advise not to breastfeed (8.2)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Kaposi's Sarcoma

PANRETIN GEL is indicated for topical treatment of cutaneous lesions in adults with AIDS related Kaposi's sarcoma (KS).

Limitations of Use: PANRETIN GEL is not indicated when systemic anti-KS therapy is required (including more than 10 new KS lesions in the prior month, symptomatic lymphedema, symptomatic pulmonary KS, or symptomatic visceral involvement) *[see Clinical Studies (14.1)]*.

2 DOSAGE AND ADMINISTRATION

PANRETIN GEL is for topical use only.

Do not use occlusive dressings with PANRETIN GEL.

- Apply PANRETIN GEL twice daily to coat the entire cutaneous Kaposi sarcoma lesions.
- Gradually increase the application frequency up to four (4) times a day as tolerated.
- Continue PANRETIN GEL as long as patient is deriving benefit.
- Reduce application frequency for application site toxicity. Interrupt treatment for severe irritation; may resume at a reduced application frequency once symptoms improve.
- Avoid application of gel to normal skin and do not apply on or near mucosal surfaces.
- Wash hands after application unless gel is applied to Kaposi sarcoma lesions on the hands.
- Allow gel to dry for three to five minutes before covering with clothing.

3 DOSAGE FORMS AND STRENGTHS

Topical Gel: 0.1% alitretinoin (clear yellow gel) in a 60-gram tube.

4 CONTRAINDICATIONS

PANRETIN GEL is contraindicated in patients with a known hypersensitivity to retinoids or to any of the ingredients of the product.

5 WARNINGS AND PRECAUTIONS

5.1 Embryo-Fetal Toxicity

Based on data from animal studies and its mechanism of action, PANRETIN GEL can cause fetal harm when administered to a pregnant woman. Oral administration of alitretinoin to pregnant animals during the period of organogenesis was teratogenic and embryo-lethal at exposures 5 times the estimated daily human topical dose. Advise women of the potential risk to a fetus. Advise women of reproductive potential to use effective contraception during treatment with PANRETIN GEL and for 1 week after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

5.2 Photosensitivity

Retinoids as a class have been associated with photosensitivity. Advise patients to minimize exposure of treated areas to sunlight and sunlamps during the use of PANRETIN GEL.

5.3 Toxicity with DEET-Containing Products

Animal toxicology studies showed increased DEET toxicity when DEET was included as part of the formulation. Advise patients to not use PANRETIN GEL concurrently with products that contain DEET (N,N-diethyl-m-toluamide), a common component of insect repellent products.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:
• Photosensitivity *[see Warnings and Precautions (5.2)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of PANRETIN GEL was assessed in two multicenter, prospective, randomized, double-blind, vehicle-controlled trials (Trial 1 and Trial 2) in patients with cutaneous lesions of AIDS-related KS *[see Clinical Studies (14.1)]*. In a pooled analysis of both trials,

the most common adverse reactions in ≥ 5% of patients were rash, pain, paresthesia, pruritis, exfoliative dermatitis, edema, and skin disorder.

In Trial 1, severe local skin adverse reactions (erythema and edema with or without vesiculation) occurred in 10% of patients during the first 12 weeks of treatment (versus 0% in the vehicle control). Adverse reactions led to withdrawal from the study in 7% of patients.

In Trial 2, severe local skin adverse reactions (erythema and edema with or without vesiculation) occurred in 6% of patients during the first 12 weeks of treatment (versus 0% in the vehicle control) and 1 patient withdrew due to severe skin irritation.

Table 1 lists the most common application site adverse reactions that occurred in a least 5% of patients during the double-blind phase who received PANRETIN GEL in either of the two controlled studies.

TABLE 1: Adverse Reactions at Application Site in Trial 1 and 2 in ≥ 5% of Patients Treated with PANRETIN GEL

A**dverse Event Term**	**Trial 1**		**Trial 2**	
	PANRETIN GEL N=134 %	**Vehicle Gel N=134 %**	**PANRETIN GEL N=36 %**	**Vehicle Gel N=46 %**
Rash[1]	77	11	25	4
Pain[2]	34	7	0	4
Pruritus[3]	11	4	8	4
Exfoliative dermatitis[4]	9	2	3	0

Skin disorder[5]	8	1	0	0
Edema[6]	8	3	3	0
Parethesia[7]	3	0	22	7

Includes Investigator terms:
[1] Erythema, scaling, irritation, redness, rash, dermatitis
[2] Burning, pain
[3] Itching, pruritus
[4] Flaking, peeling, desquamation, exfoliation
[5] Excoriation, cracking, scab, crusting, drainage, eschar, fissure or oozing
[6] Edema, swelling, inflammation
[7] Stinging, tingling

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animal studies and its mechanism of action, PANRETIN GEL can cause fetal harm when administered to a pregnant woman. Oral administration of alitretinoin to pregnant animals during the period of organogenesis was teratogenic and embryo lethal at exposures at least 5 times the estimated daily human topical dose (*see Data*). There are no data on the use of PANRETIN GEL in pregnant women. Advise pregnant women of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Oral administration of alitretinoin to pregnant rabbits during the period of organogenesis resulted in early resorptions, post-implantation loss, and fetal defects (limb, craniofacial, fused sternebrae) at doses ≥ 0.5 mg/kg/day (approximately 5 times the estimated daily human topical dose based on body surface area, assuming complete systemic absorption of alitretinoin, when PANRETIN GEL is administered as a 60 g tube over 1 month in a 60 kg human). Early resorptions and post-implantation loss also occurred in rats administered oral alitretinoin at doses ≥5 mg/kg/day (approximately 25 times the estimated daily human topical dose based on body surface area). Limb and craniofacial defects also occurred in mice administered oral alitretinoin on day 11 of gestation at single doses ≥50 mg/kg (approximately 127 times the estimated daily human topical

dose based on body surface area).

8.2 Lactation

Risk Summary

It is not known whether alitretinoin or its metabolites are excreted in human milk. Because many drugs are excreted in human milk and because of the potential for adverse reactions from PANRETIN GEL in the nursing child, advise patients that breastfeeding is not recommended during treatment with PANRETIN GEL and for 1 week after the last dose.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating PANRETIN GEL.

Contraception

Females

PANRETIN GEL can cause embryo-fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*. Advise females of reproductive potential to use effective contraception during treatment with PANRETIN GEL and for 1 week after the last dose.

Males

Advise males with female partners of reproductive potential to use effective contraception during treatment with PANRETIN GEL and for 1 week after the last dose.

8.4 Pediatric Use

The safety and effectiveness of PANRETIN GEL have not been established in pediatric patients.

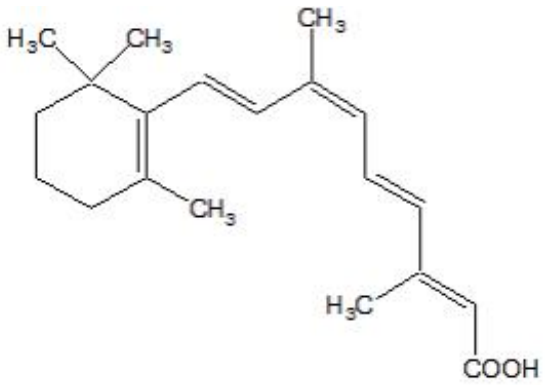
8.5 Geriatric Use

Clinical studies of PANRETIN GEL did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger adult patients.

11 DESCRIPTION

PANRETIN GEL is a retinoid. PANRETIN GEL 0.1% contains alitretinoin and is intended for topical application only. The chemical name is (2E,4E,6Z,8E)-3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid, also known as 9-cis-retinoic acid. Chemically, alitretinoin is related to vitamin A. It is a yellow powder with a molecular weight of 300.44 and a molecular formula of $C_{20}H_{28}O_2$. It is slightly soluble in ethanol (7.01 mg/g at 25°C) and insoluble in water. The structural formula of alitretinoin is as

follows:



PANRETIN GEL is a clear, yellow gel containing 0.1% (w/w) alitretinoin. Each gram of PANRETIN GEL contains 1 mg alitretinoin. PANRETIN GEL contains the following inactive ingredients: butylated hydroxytoluene NF, dehydrated alcohol USP 92%, hydroxypropyl cellulose NF, and polyethylene glycol 400 NF.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Alitretinoin (9-cis-retinoic acid) is a naturally occurring endogenous retinoid that binds to and activates all known intracellular retinoid receptor subtypes (RARα, RARβ, RARγ, RXRα, RXRβ and RXRγ). Once activated these receptors function as transcription factors that regulate the expression of genes that control the process of cellular differentiation and proliferation in both normal and neoplastic cells. Alitretinoin inhibits the growth of Kaposi's sarcoma (KS) cells in vitro.

12.2 Pharmacodynamics

Alitretinoin exposure-response relationships and the time course of pharmacodynamic response are unknown.

12.3 Pharmacokinetics

The range of 9-cis-retinoic acid plasma concentrations in patients with cutaneous lesions of AIDS-related KS after multiple daily applications of PANRETIN GEL for up to 60 weeks was similar to the range of circulating, naturally occurring 9-cis-retinoic acid plasma concentrations in untreated healthy participants.

Elimination

Metabolism

9-cis-retinoic acid is metabolized to 4-hydroxy-9-cis-retinoic acid and 4-oxo-9-cis-retinoic acid by CYP2C9, 3A4, 1A1, and 1A2. 4-oxo-9-cis-retinoic acid is the major circulating metabolite following oral administration of 9-cis-retinoic acid.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment Of Fertility

Carcinogenicity studies with alitretinoin have not been conducted. Alitretinoin was not mutagenic in vitro (bacterial assay, Chinese hamster ovary cell HGPRT mutation assay) and was not clastogenic in vitro (chromosome aberration test in human lymphocytes) or in vivo (mouse micronucleus test).

14 CLINICAL STUDIES

14.1 Kaposi's Sarcoma

PANRETIN GEL was evaluated in two multicenter, randomized, double-blind, vehicle-controlled studies in adult patients with cutaneous lesions of AIDS-related KS. In both studies the primary efficacy objective was the patients' cutaneous KS tumor response rate through 12 weeks of study drug treatment which was assessed by evaluating from 3 to 8 KS index lesions according to the modified AIDS Clinical Trials Group (ACTG) response criteria as applied to topical therapy (i.e., evaluation of height and area reductions of the index lesions only; progressive disease in non-index lesions and new lesions were not considered progressive disease; progressive disease was scored only in the treated index lesions). A global evaluation by physicians was also carried out. It considered all the patient's treated lesions (index and other) compared to baseline. In this evaluation, patients with at least a 50% improvement in the KS lesions were considered responders. In addition, photographs of lesions in patients considered responders by the modified ACTG criteria were examined by the FDA for a cosmetically beneficial response, defined as at least a 50% improvement in appearance compared to baseline, considering both the KS lesions and dermal toxicity at the lesion site, in at least 50% of the index lesions and maintained for at least 3 weeks. Visceral disease was not monitored in these trials and the appearance of new KS lesions was not considered part of the response assessment.

In Trial 1, a total of 268 patients were entered from centers in the U.S. and Canada. Patients were treated topically three to four times a day with either PANRETIN GEL or a matching vehicle gel for a minimum of 12 weeks, followed by an open-label phase in patients who had not yet progressed on PANRETIN GEL. Median age of patients was 39 years, 99% were men, 75% were White, 16% Hispanic, and 7% Black. Fifty-seven percent of patients had a CD4+ lymphocyte count <200/mm3 and 36% had CD4+ lymphocyte count less than 100/mm3; 12% had visceral KS. Responses during the double-blind phase are shown in **Table 2**. New lesions in untreated areas were seen in about 50% of patients.

Trial 2 was an international study with a planned enrollment of 270 patients. Patients were treated topically twice a day with PANRETIN GEL or a matching vehicle for 12 weeks. The study was stopped early because of positive-interim results in the initial 82 patients. Median age of patients was 36 years for PANRETIN-GEL and 39 years for matching vehicle; all patients were men; 89% White; 5% Hispanic, and 4% Black; 67% had a CD4+ lymphocyte count ≤200/mm3 and 39% had CD4+ lymphocyte count ≤100/mm3; and 16% had visceral KS.

Results of the study are shown in **Table 2**. Responses to PANRETIN GEL were seen both in previously untreated patients and in patients with prior systemic and/or topical KS treatment.

Table 2: Response Rates

	Trial 1		Trial 2	
	PANRETIN GEL N=134	**Vehicle Gel N=134**	**PANRETIN GEL N=36**	**Vehicle Gel N=45**
Modified ACTG Response	35%*	16%	36%	7%
	P = 0.0012			
Physician's Global Subjective Assessment (all treated lesions)	19%	4%	47%	11%
	P = 0.00014			
Photograph Response	15%	4%	19%	2%
	P = 0.0026			

*All responses were partial responses except 1% complete response for modified ACTG response in Trial 1.

In the clinical trials, the cumulative percentage of patients who experienced a response was less than 1% at 2 weeks, 10% at 4 weeks, and 28% at 8 weeks. Photographs of some patients revealed an erythematous and edematous response, leading to a cosmetically mixed outcome.

16 HOW SUPPLIED/STORAGE AND HANDLING

PANRETIN GEL is a clear yellow gel and is supplied in a 60-gram tubes containing 0.1% alitretinoin.
Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].
PANRETIN GEL is flammable; keep away from heat or flame.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Embryo-Fetal Toxicity

Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform females of the risk to a fetus and potential loss of pregnancy *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)].*

Advise females of reproductive potential to use effective contraception during treatment and for 1 week after the last dose of PANRETIN GEL *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)].*

Advise males with female partners of reproductive potential to use effective contraception during treatment and for 1 week following the last dose of PANRETIN GEL *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.3)]*.

Lactation

Advise patients not to breastfeed during treatment with PANRETIN GEL and for 1 week after the last dose of PANRETIN GEL *[see Use in Specific Populations (8.2)].*

Photosensitivity

Advice patients that PANRETIN GEL can cause photosensitivity and to avoid sunlight and sunlamps and use measures such as protective clothing in PANRETIN-applied areas *[see Warnings and Precautions (5.2)].*

Toxicity with DEET-Containing Products

Advise patients to avoid DEET-containing products such as insect repellant while using PANRETIN GEL *[see Warnings and Precautions (5.3)].*

Manufactured for:
Advanz Pharma (US) Corp.
Bannockburn IL, 60015
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Revised: 11/2025

PATIENT INFORMATION
PANRETIN GEL (PAN-reh-tin)
(alitretinoin)

Important information: PANRETIN GEL is for use on skin (topical use) only. Do not use PANRETIN GEL in or near your eyes, inside your nose, mouth, lips, vagina, tip of the penis, rectum, or anus.

What is PANRETIN GEL?

PANRETIN GEL is a prescription medicine used to treat skin lesions in adults with AIDS-related Kaposi's sarcoma (KS).

PANRETIN GEL is not used to treat KS when a medicine taken by mouth or injection (systemic treatment) is needed.
It is not known if PANRETIN GEL is safe and effective in children.

Do not use PANRETIN GEL if you are allergic to retinoids or any of the ingredients in PANRETIN GEL. See the end of this Patient Information leaflet for a complete list of ingredients in PANRETIN GEL.

Before using PANRETIN GEL, tell your healthcare provider about all of your medical conditions, including if you:

• are pregnant or plan to become pregnant. PANRETIN GEL can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with PANRETIN GEL.

Females who are able to become pregnant:

o Your healthcare provider should check to see if you are pregnant before you start treatment with PANRETIN GEL.

o You should use effective birth control (contraception) during treatment and for 1 week after the last dose of PANRETIN GEL.

Males with female partners who are able to become pregnant:

o You should use effective birth control (contraception) during treatment and for 1 week after the last dose of PANRETIN GEL.

• are breastfeeding or plan to breastfeed. It is not known if PANRETIN GEL passes into your breast milk. Do not breastfeed during treatment and for 1 week after your last dose of PANRETIN GEL.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially tell your healthcare provider about skin products that you use. You should not use products that contain DEET (N, N-diethyl-m-toluamide), during treatment with PANRETIN Gel. DEET is an ingredient commonly found in insect repellent.

How should I use PANRETIN GEL?

- Use PANRETIN GEL exactly as your healthcare provider tells you to use it.
- To open the PANRETIN GEL, remove the cap and use the point of the cap to puncture the metal safety seal.
- Apply PANRETIN GEL to affected areas 2 times a day.
- Slowly increase the number of times you apply PANRETIN GEL up to 4 times a day as tolerated.
- Cover the entire KS lesions with PANRETIN GEL.
- Avoid applying PANRETIN GEL to healthy skin around the KS lesions. **Do not** use PANRETIN GEL in or near the eyes, inside your nose, mouth, lips, vagina, tip of the penis, rectum or anus.
- Allow PANRETIN GEL to dry for 3 to 5 minutes before covering with clothing.
- **Do not** cover the treated area with bandages or dressings.
- Wash your hands with soap and water after applying PANRETIN GEL, unless PANRETIN Gel is applied to KS lesions on your hands.

What should I avoid while using PANRETIN GEL?

- Avoid sunlight and the use of sunlamps during treatment with PANRETIN GEL. PANRETIN GEL can make your skin sensitive to the sun and the light from sunlamps. Wear protective clothing that cover the treated areas if you have to be in sunlight during treatment with PANRETIN GEL.
- PANRETIN Gel is flammable. Avoid fire, flame, and smoking during and right after applying PANRETIN Gel to your skin.

- You should avoid scratching skin areas treated with PANRETIN GEL.

What are the possible side effects of PANRETIN GEL?
The most common side effects of PANRETIN GEL at the treatment site, include:

- rash
- pain
- stinging or tingling of the skin
- itching
- skin peeling or shedding
- redness or swelling
- skin cracking, scabbing, crusting, or drainage

Your healthcare provider may decrease how often you apply PANRETIN Gel or temporarily stop your treatment with PANRETIN GEL if you develop severe skin reactions.
Tell your healthcare provider about any side effect that bothers you or that does not go away.
These are not all of the possible side effects of PANRETIN GEL.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store PANRETIN GEL?

- Store PANRETIN GEL at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep the cap on the tube tightly closed after each use.
- Keep away from heat.

Keep PANRETIN GEL and all medicines out of the reach of children.

General information about the safe and effective use of PANRETIN GEL.
Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use PANRETIN GEL for a condition for which it was not prescribed. Do not give PANRETIN GEL to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about PANRETIN GEL that is written for health professionals.

What are the ingredients in PANRETIN GEL?
Active ingredient: alitretinoin
Inactive ingredients: butylated hydroxytoluene NF, dehydrated alcohol USP, hydroxypropyl cellulose NF, and polyethylene glycol 400 NF.

Manufactured for:
Advanz Pharma (US) Corp.
Bannockburn IL, 60015

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This patient information has been approved by the U.S. Food and Drug Administration
Revise 11/2025

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

NDC 59212-601-22
Panretin® gel
(alitretinoin) 0.1%

PANRETIN
alitretinoin gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:59212-601
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ALITRETINOIN (UNII: 1UA8E65KDZ) (ALITRETINOIN - UNII:1UA8E65KDZ)	ALITRETINOIN	60 mg in 60 g

Inactive Ingredients	
Ingredient Name	**Strength**

POLYETHYLENE GLYCOL 400 (UNII: B697894SGQ)	
HYDROXYPROPYL CELLULOSE (UNII: RFW2ET671P)	
ALCOHOL (UNII: 3K9958V90M)	
BUTYLATED HYDROXYTOLUENE (UNII: 1P9D0Z171K)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:59212-601-22	60 g in 1 TUBE; Type 0: Not a Combination Product	09/10/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA020886	09/10/2019	

Labeler - Advanz Pharma (US) Corp. (118997081)

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