Warhaftig Associates

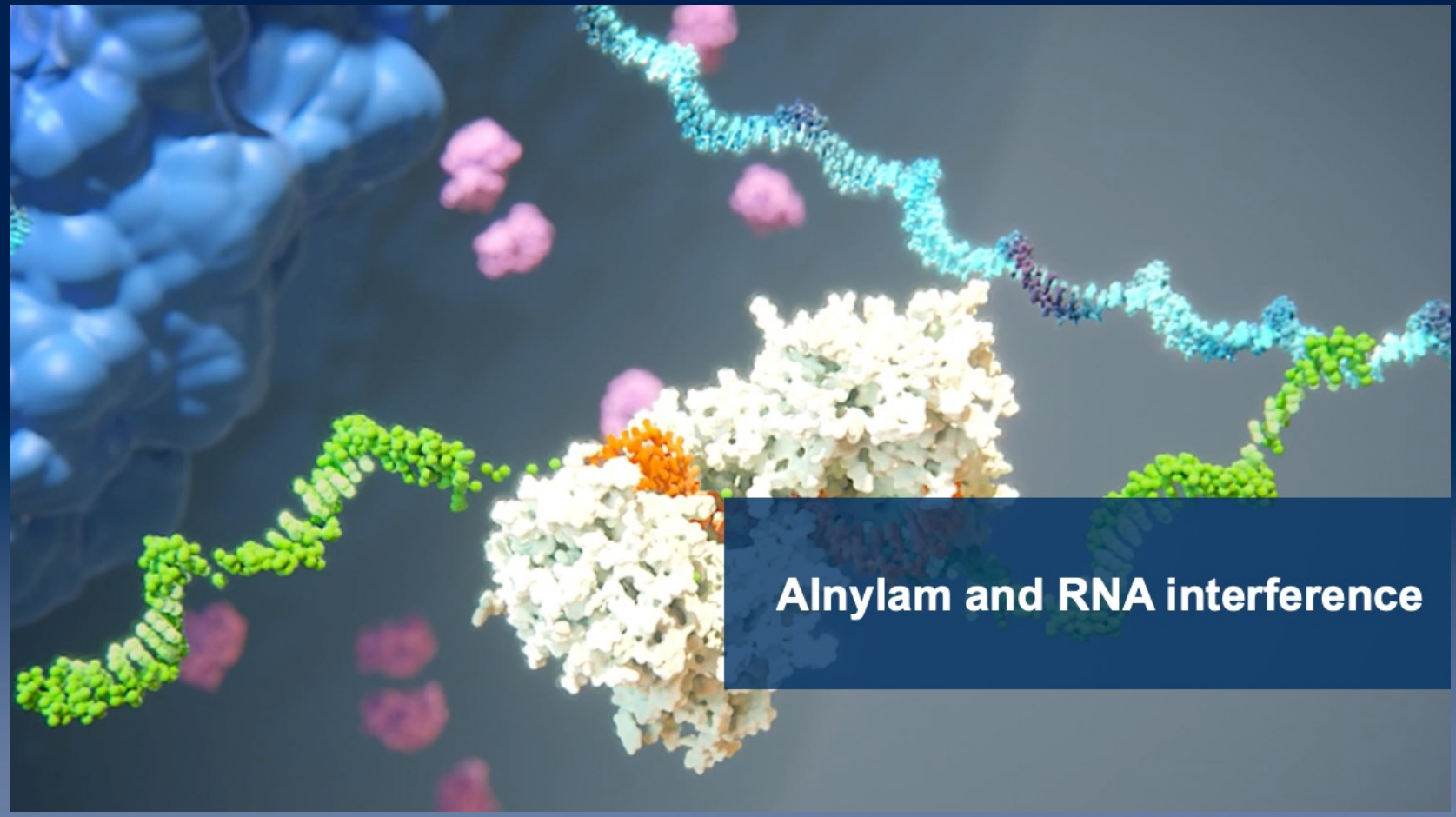
Rare disease —
an important opportunity for account managers to communicate complex concepts in compelling ways

Rare disease – not so rare!
6800 rare diseases. 25-30 million Americans who suffer from a rare condition.

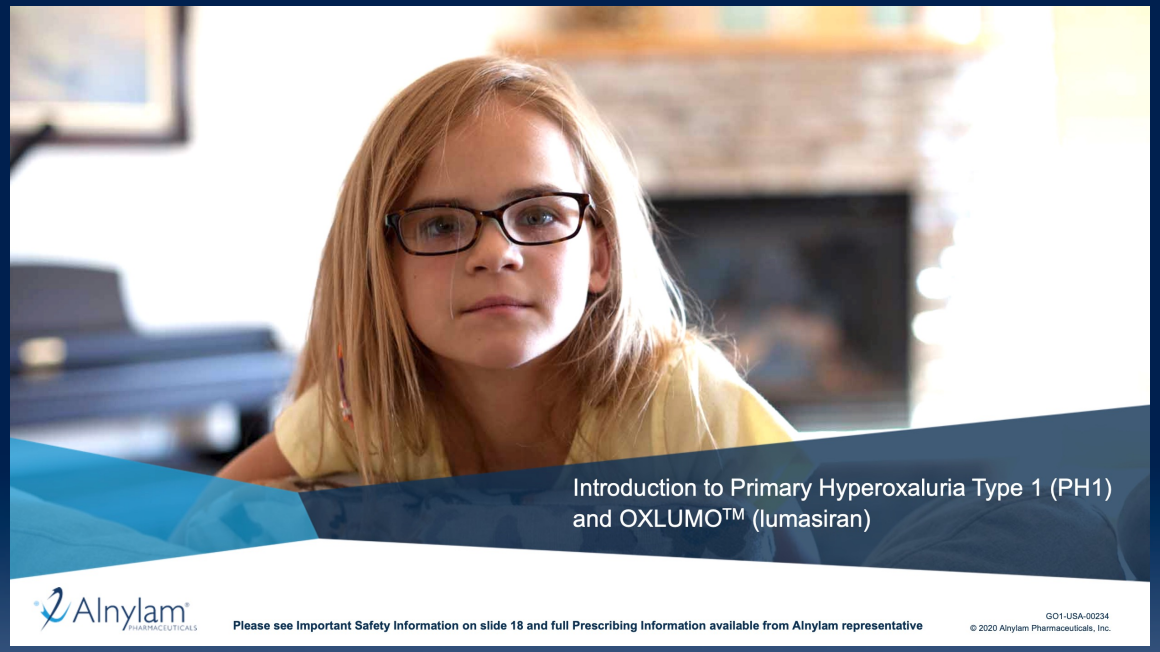
An important opportunity for account managers to broaden understanding. These conditions often require:

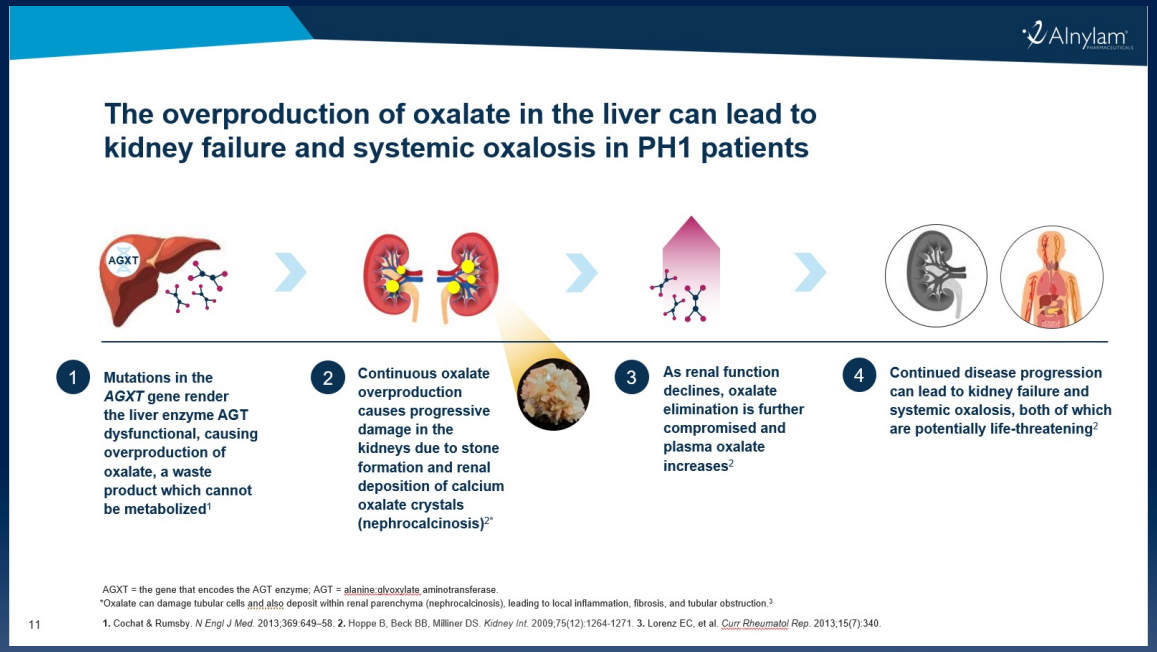
- Innovations in diagnosis
- An understanding of the disease burden
- Access
- Innovations in payment
- Broad education on the value and potential of different therapeutic platforms, eg, mRNA, RNAi, antisense, and gene therapy

Explaining the value of RNAi technology

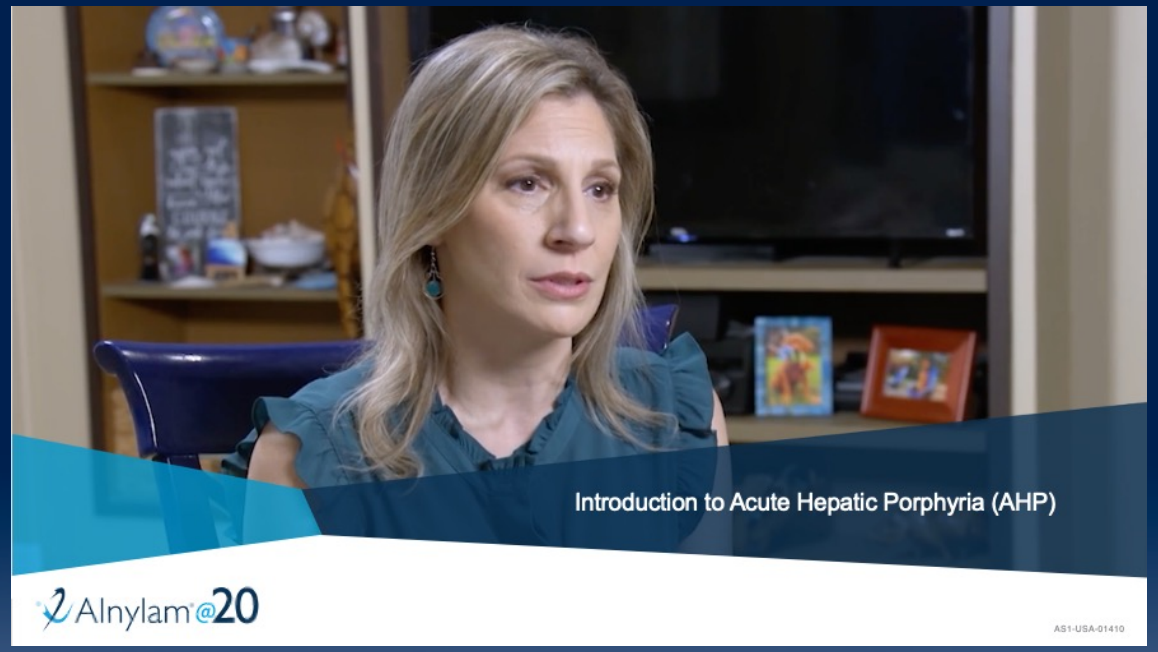


Helping payers understand the value of Oxlumo for the treatment of Primary Hyperoxayluria Type 1





The value of Givlaari for the treatment of Acute Hepatic Porphyria



And the value of Amvuttra for the treatment of polyneuropathy due to hATTR amyloidosis

Introduction to Hereditary Transthyretin-Mediated (hATTR) Amyloidosis and AMVUTTRA™ (vutrisiran)

A Treatment for the Polyneuropathy (PN) of hATTR Amyloidosis in Adults

[For in-venue program use: Please see Important Safety Information on slide 5 and full Prescribing Information available at this presentation and at www.amvuttrahcp.com

For virtual program use: Please see Important Safety Information on slide 5 and full Prescribing Information available by scanning the QR code and at www.amvuttrahcp.com

For hybrid program use: Please see Important Safety Information on slide 5 and full Prescribing Information available at this presentation or by scanning the QR code and at www.amvuttrahcp.com]

amvuttra (vutrisiran) injection 25 mg/0.5 mL

AMVUTTRA™ (vutrisiran) is an RNAi therapeutic that reduces TTR protein production[1,2]

hATTR amyloidosis is caused by a variant in the transthyretin (TTR) gene, resulting in misfolded TTR proteins accumulating as amyloid deposits in tissues at multiple sites of the body[3-5]

FDA-approved in June 2022, AMVUTTRA is an RNAi therapeutic that causes degradation of variant and wild-type TTR mRNA, reducing TTR protein production[1,6]

Indication
AMVUTTRA is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

1. AMVUTTRA Prescribing Information. Cambridge, MA: Alnylam Pharmaceuticals, Inc. 2. Adams D, Tournev I, Taylor M, et al. Slides presented at la Société Francophone du Nerf Périphérique (SFNP); January 21-22, 2022. 3. Hanna M. *Curr Heart Fail Rep.* 2014;11(1):50–57. 4. Castaño A, et al. *Heart Fail Rev.* 2015;20(2):163–178. 5. Damy T, et al. *J Cardiovasc Transl Res.* 2015;8(2):117–127. 6. Habtemariam BA, et al. *Clin Pharmacol Ther.* 2021;109(2):372-382.

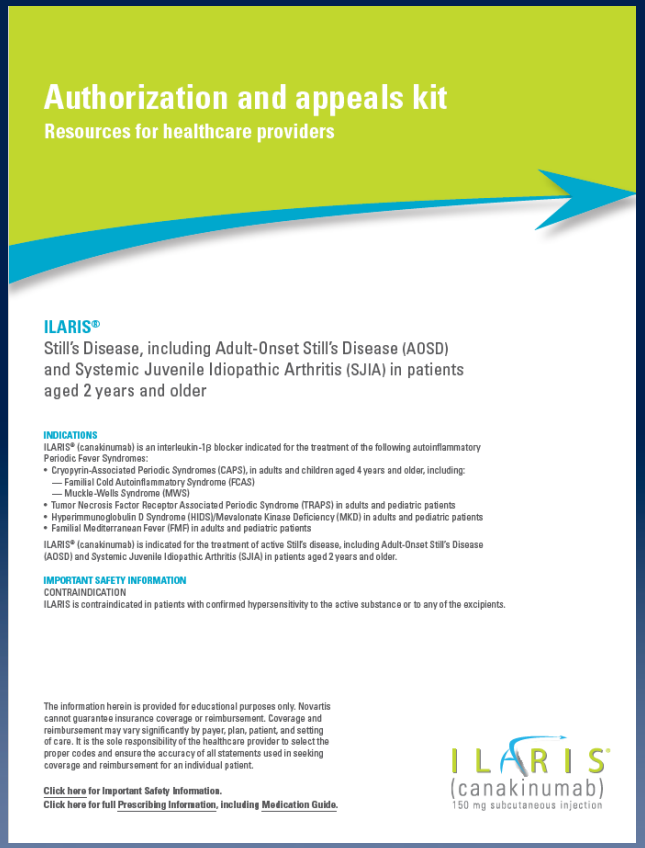
[Please insert appropriate Please See language from slide 1]

6

amvuttra (vutrisiran) injection 25 mg/0.5 mL

For Novartis' Ilaris: Kits of templated letters were developed to facilitate different types of appeals specific to each indication

Still's Disease



Authorization and appeals kit

Resources for healthcare providers

ILARIS®

Still's Disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older

INDICATIONS

ILARIS® (canakinumab) is an interleukin-1β blocker indicated for the treatment of the following autoinflammatory Periodic Fever Syndromes:

- Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children aged 4 years and older, including:
  - Familial Cold Autoinflammatory Syndrome (FCAS)
  - Muckle-Wells Syndrome (MWS)
- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adults and pediatric patients
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adults and pediatric patients
- Familial Mediterranean Fever (FMF) in adults and pediatric patients

ILARIS® (canakinumab) is indicated for the treatment of active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

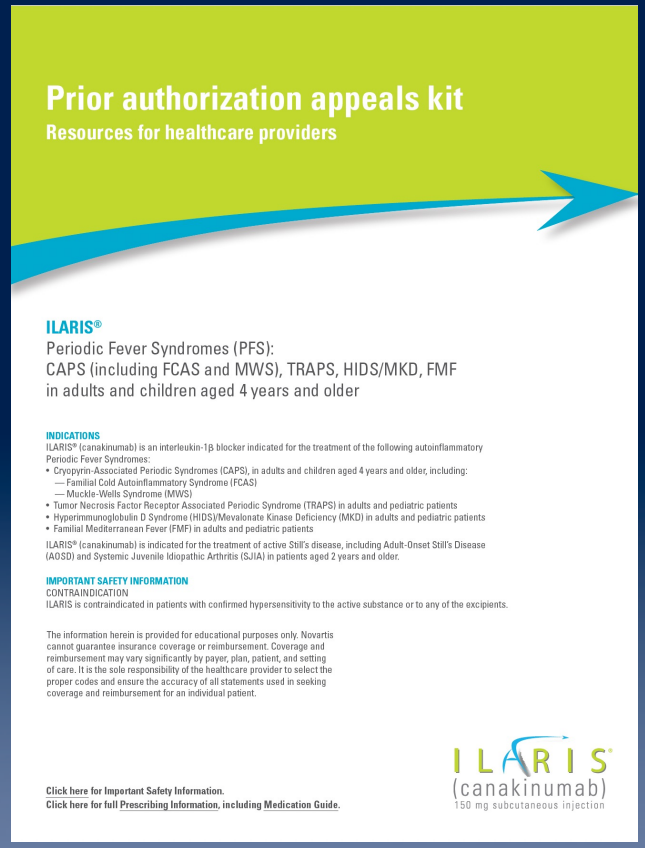
ILARIS is contraindicated in patients with confirmed hypersensitivity to the active substance or to any of the excipients.

The information herein is provided for educational purposes only. Novartis cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the healthcare provider to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Click here for Important Safety Information.
Click here for full Prescribing Information, including Medication Guide.

ILARIS® (canakinumab) 150 mg subcutaneous injection

Periodic Fever Syndromes



Prior authorization appeals kit

Resources for healthcare providers

ILARIS®

Periodic Fever Syndromes (PFS): CAPS (including FCAS and MWS), TRAPS, HIDS/MKD, FMF in adults and children aged 4 years and older

INDICATIONS

ILARIS® (canakinumab) is an interleukin-1β blocker indicated for the treatment of the following autoinflammatory Periodic Fever Syndromes:

- Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and children aged 4 years and older, including:
  - Familial Cold Autoinflammatory Syndrome (FCAS)
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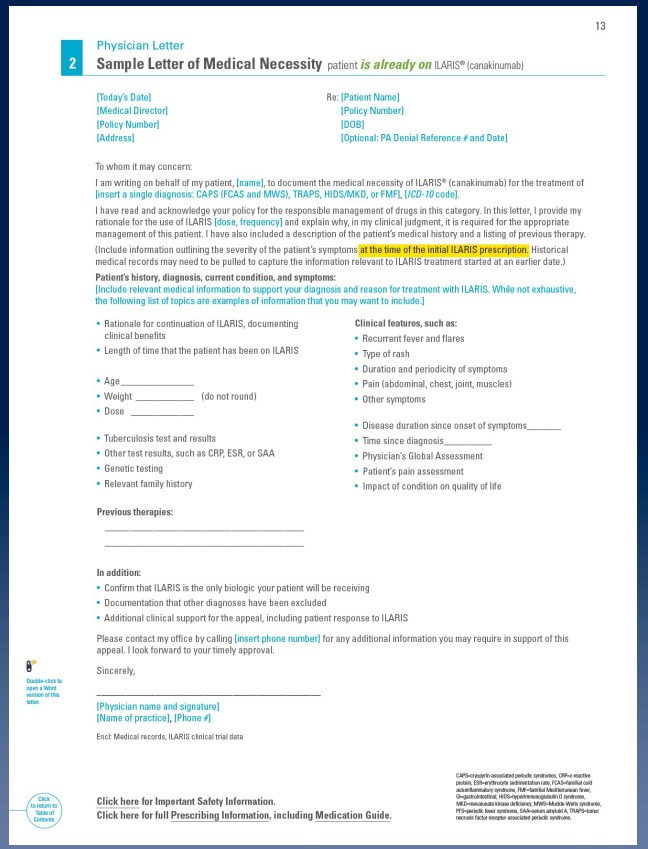
Click here for Important Safety Information.
Click here for full Prescribing Information, including Medication Guide.

ILARIS® (canakinumab) 150 mg subcutaneous injection



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Physician Letter

2 Sample Letter of Medical Necessity patient *is already on* ILARIS® (canakinumab)

[Today's Date]
[Medical Director]
[Policy Number]
[Address]

Re: [Patient Name]
[Policy Number]
[DOB]
[Optional: PA Denial Reference # and Date]

To whom it may concern:

I am writing on behalf of my patient, [name], to document the medical necessity of ILARIS® (canakinumab) for the treatment of [insert a single diagnosis: CAPS (FCAS and MWS), TRAPS, HIDS/MKD, or FMF], (*ICD-10* code).

I have read and acknowledge your policy for the responsible management of drugs in this category. In this letter, I provide my rationale for the use of ILARIS [dose, frequency] and explain why, in my clinical judgment, it is required for the appropriate management of this patient. I have also included a description of the patient's medical history and a listing of previous therapy.

(Include information outlining the severity of the patient's symptoms at the time of the initial ILARIS prescription. Historical medical records may need to be pulled to capture the information relevant to ILARIS treatment started at an earlier date.)

Patient's history, diagnosis, current condition, and symptoms:
[Include relevant medical information to support your diagnosis and reason for treatment with ILARIS. While not exhaustive, the following list of topics are examples of information that you may want to include.]

- Rationale for continuation of ILARIS, documenting clinical benefits
- Length of time that the patient has been on ILARIS
- Age_____
- Weight _____ (do not round)
- Dose _____
- Tuberculosis test and results
- Other test results, such as CRP, ESR, or SAA
- Genetic testing
- Relevant family history

Clinical features, such as:

- Recurrent fever and flares
- Type of rash
- Duration and periodicity of symptoms
- Pain (abdominal, chest, joint, muscles)
- Other symptoms
- Disease duration since onset of symptoms_____
- Time since diagnosis_____
- Physician's Global Assessment
- Patient's pain assessment
- Impact of condition on quality of life

Previous therapies:

_____
_____

In addition:

- Confirm that ILARIS is the only biologic your patient will be receiving
- Documentation that other diagnoses have been excluded
- Additional clinical support for the appeal, including patient response to ILARIS

Please contact my office by calling [insert phone number] for any additional information you may require in support of this appeal. I look forward to your timely approval.

Sincerely,

_____

[Physician name and signature]
[Name of practice], [Phone #]

Encl: Medical records, ILARIS clinical trial data

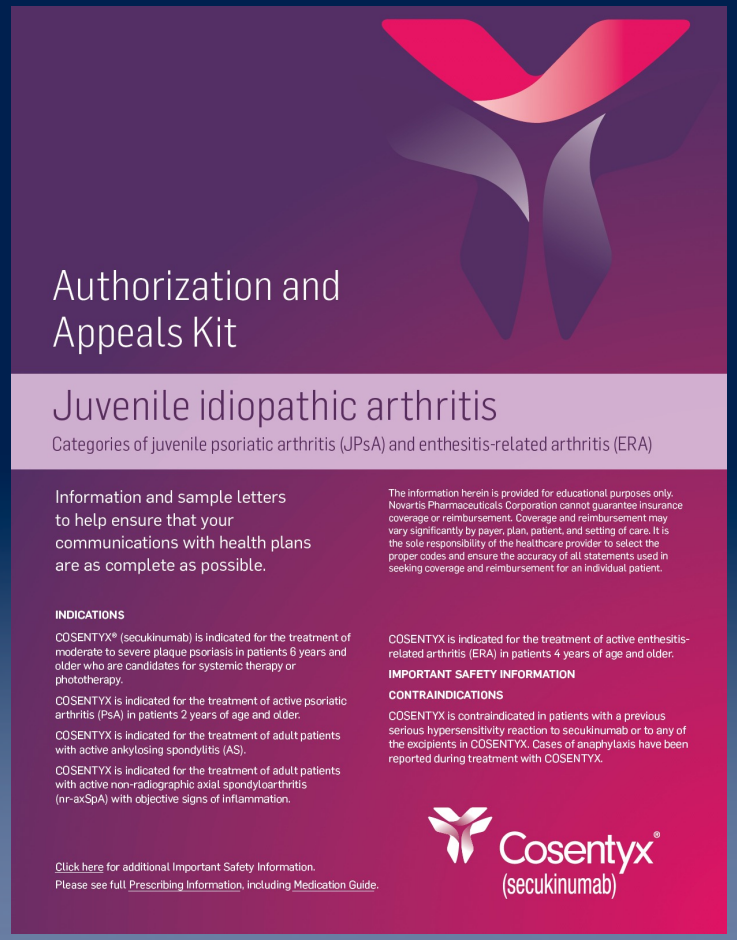
Double-click to open a Word version of this letter.

Click to return to Table of Contents

Click here for Important Safety Information.
Click here for full Prescribing Information, including Medication Guide.

CAPS=cryopyrin-associated periodic syndromes, CRP=c-reactive protein, ESR=erythrocyte sedimentation rate, FCAS=familial cold autoinflammatory syndrome, FMF=familial Mediterranean fever, GI=gastrointestinal, HIDS=hyperimmunoglobulin D syndrome, MKD=mevalonate kinase deficiency, MWS=Muckle-Wells syndrome, PFS=periodic fever syndrome, SAA=serum amyloid A, TRAPS=tumor necrosis factor receptor-associated periodic syndrome.

For Cosentyx: Kits of templated letters were developed to facilitate different types of appeals specific to each indication, including Juvenile Idiopathic Arthritis



Authorization and Appeals Kit

Juvenile idiopathic arthritis

Categories of juvenile psoriatic arthritis (JPsA) and enthesitis-related arthritis (ERA)

Information and sample letters to help ensure that your communications with health plans are as complete as possible.

The information herein is provided for educational purposes only. Novartis Pharmaceuticals Corporation cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the healthcare provider to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

INDICATIONS

COSENTYX® (secukinumab) is indicated for the treatment of moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy.

COSENTYX is indicated for the treatment of active psoriatic arthritis (PsA) in patients 2 years of age and older.

COSENTYX is indicated for the treatment of adult patients with active ankylosing spondylitis (AS).

COSENTYX is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.

COSENTYX is indicated for the treatment of active enthesitis-related arthritis (ERA) in patients 4 years of age and older.

IMPORTANT SAFETY INFORMATION

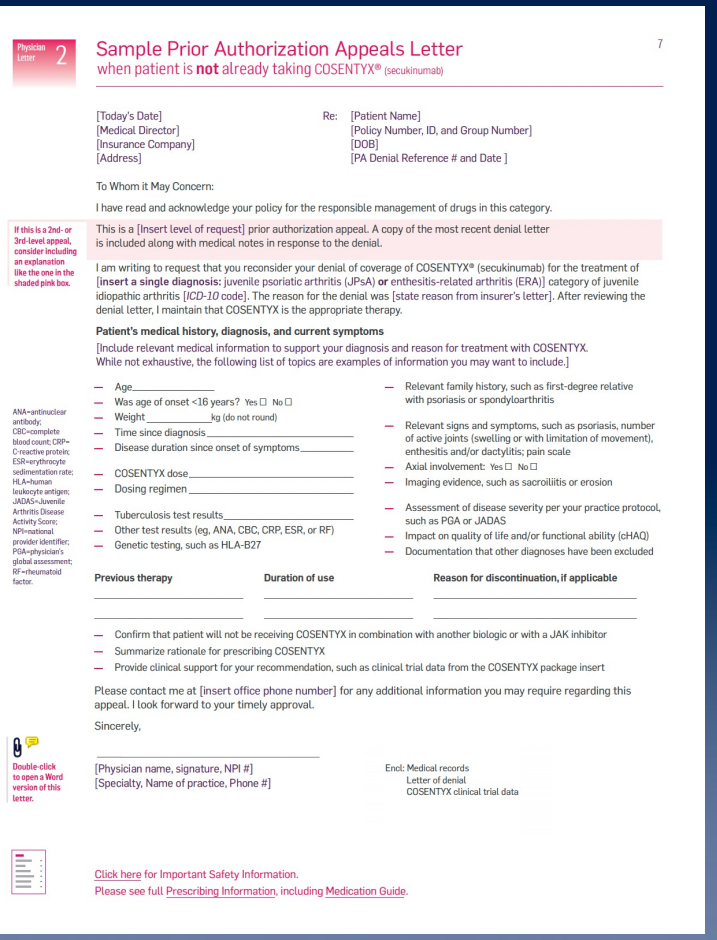
CONTRAINDICATIONS

COSENTYX is contraindicated in patients with a previous serious hypersensitivity reaction to secukinumab or to any of the excipients in COSENTYX. Cases of anaphylaxis have been reported during treatment with COSENTYX.

Click here for additional Important Safety Information.

Please see full Prescribing Information, including Medication Guide.

Cosentyx® (secukinumab)



Physician Letter 2

Sample Prior Authorization Appeals Letter

when patient is **not** already taking COSENTYX® (secukinumab)

7

[Today's Date]
[Medical Director]
[Insurance Company]
[Address]

Re: [Patient Name]
[Policy Number, ID, and Group Number]
[DOB]
[PA Denial Reference # and Date]

To Whom it May Concern:

I have read and acknowledge your policy for the responsible management of drugs in this category.

If this is a 2nd- or 3rd-level appeal, consider including an explanation like the one in the shaded pink box.

This is a [Insert level of request] prior authorization appeal. A copy of the most recent denial letter is included along with medical notes in response to the denial.

I am writing to request that you reconsider your denial of coverage of COSENTYX® (secukinumab) for the treatment of [**insert a single diagnosis:** juvenile psoriatic arthritis (JPsA) **or** enthesitis-related arthritis (ERA)] category of juvenile idiopathic arthritis [*ICD-10* code]. The reason for the denial was [state reason from insurer's letter]. After reviewing the denial letter, I maintain that COSENTYX is the appropriate therapy.

Patient's medical history, diagnosis, and current symptoms

[Include relevant medical information to support your diagnosis and reason for treatment with COSENTYX. While not exhaustive, the following list of topics are examples of information you may want to include.]

- Age_____
- Was age of onset <16 years? Yes ☐ No ☐
- Weight _____kg (do not round)
- Time since diagnosis_____
- Disease duration since onset of symptoms_____
- COSENTYX dose_____
- Dosing regimen_____
- Tuberculosis test results_____
- Other test results (eg, ANA, CBC, CRP, ESR, or RF)
- Genetic testing, such as HLA-B27
- Relevant family history, such as first-degree relative with psoriasis or spondyloarthritis
- Relevant signs and symptoms, such as psoriasis, number of active joints (swelling or with limitation of movement), enthesitis and/or dactylitis; pain scale
- Axial involvement: Yes ☐ No ☐
- Imaging evidence, such as sacroiliitis or erosion
- Assessment of disease severity per your practice protocol, such as PGA or JADAS
- Impact on quality of life and/or functional ability (cHAQ)
- Documentation that other diagnoses have been excluded

ANA=antinuclear antibody; CBC=complete blood count; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; HLA=human leukocyte antigen; JADAS=Juvenile Arthritis Disease Activity Score; NPI=national provider identifier; PGA=physician's global assessment; RF=rheumatoid factor.

Previous therapy	Duration of use	Reason for discontinuation, if applicable

- Confirm that patient will not be receiving COSENTYX in combination with another biologic or with a JAK inhibitor
- Summarize rationale for prescribing COSENTYX
- Provide clinical support for your recommendation, such as clinical trial data from the COSENTYX package insert

Please contact me at [insert office phone number] for any additional information you may require regarding this appeal. I look forward to your timely approval.

Sincerely,

Double-click to open a Word version of this letter.

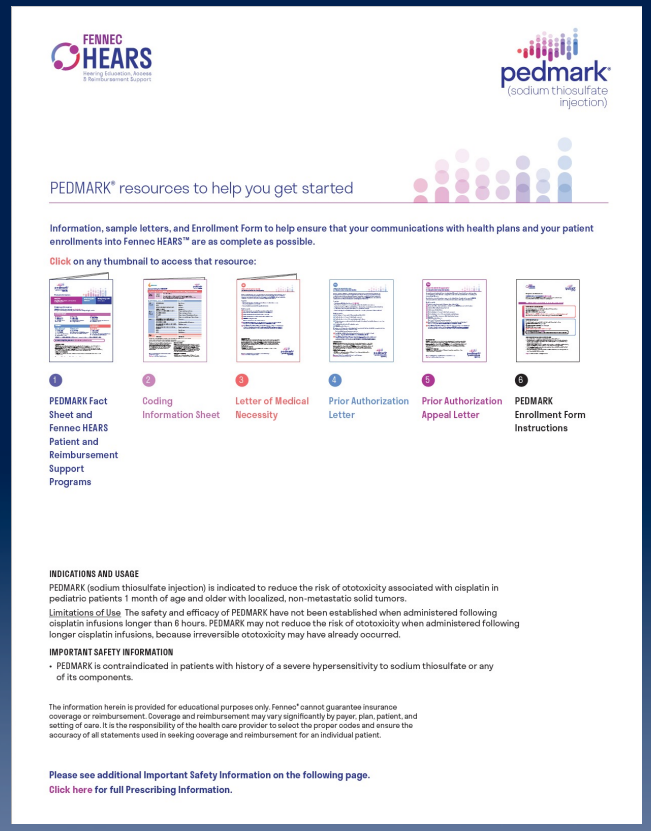
[Physician name, signature, NPI #]
[Specialty, Name of practice, Phone #]

Encl: Medical records
Letter of denial
COSENTYX clinical trial data

Click here for Important Safety Information.

Please see full Prescribing Information, including Medication Guide.

Patient support resources for Pedmark, a new treatment for the prevention of ototoxicity due to treatment with cisplatin in rare pediatric cancers



FENNEC HEARS
Hearing Education, Access & Reimbursement Support

pedmark® (sodium thiosulfate injection)

PEDMARK® resources to help you get started

Information, sample letters, and Enrollment Form to help ensure that your communications with health plans and your patient enrollments into Fennec HEARS™ are as complete as possible.

Click on any thumbnail to access that resource:

1. PEDMARK Fact Sheet and Fennec HEARS Patient and Reimbursement Support Programs
2. Coding Information Sheet
3. Letter of Medical Necessity
4. Prior Authorization Letter
5. Prior Authorization Appeal Letter
6. PEDMARK Enrollment Form Instructions

INDICATIONS AND USAGE

PEDMARK (sodium thiosulfate injection) is indicated to reduce the risk of ototoxicity associated with cisplatin in pediatric patients 1 month of age and older with localized, non-metastatic solid tumors.

Limitations of Use The safety and efficacy of PEDMARK have not been established when administered following cisplatin infusions longer than 8 hours. PEDMARK may not reduce the risk of ototoxicity when administered following longer cisplatin infusions, because irreversible ototoxicity may have already occurred.

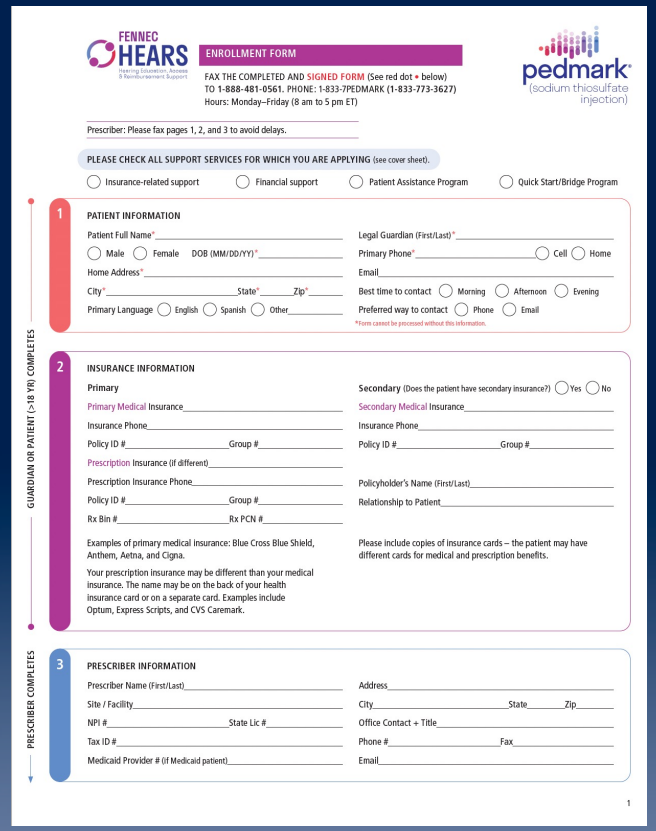
IMPORTANT SAFETY INFORMATION

- PEDMARK is contraindicated in patients with history of a severe hypersensitivity to sodium thiosulfate or any of its components.

The information herein is provided for educational purposes only. Fennec® cannot guarantee insurance coverage or reimbursement. Coverage and reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the responsibility of the health care provider to select the proper codes and ensure the accuracy of all statements used in seeking coverage and reimbursement for an individual patient.

Please see additional Important Safety Information on the following page.

Click here for full Prescribing Information.



FENNEC HEARS
Hearing Education, Access & Reimbursement Support

ENROLLMENT FORM

FAX THE COMPLETED AND SIGNED FORM (See red dot • below)
TO 1-888-481-0561. PHONE: 1-833-7PEDMARK (1-833-773-3627)
Hours: Monday–Friday (8 am to 5 pm ET)

pedmark® (sodium thiosulfate injection)

Prescriber: Please fax pages 1, 2, and 3 to avoid delays.

PLEASE CHECK ALL SUPPORT SERVICES FOR WHICH YOU ARE APPLYING (see cover sheet).

◯ Insurance-related support ◯ Financial support ◯ Patient Assistance Program ◯ Quick Start/Bridge Program

GUARDIAN OR PATIENT (>18 YR) COMPLETES

1 PATIENT INFORMATION

Patient Full Name*_____ Legal Guardian (First/Last)*_____

◯ Male ◯ Female DOB (MM/DD/YY)*_____ Primary Phone*_____ ◯ Cell ◯ Home

Home Address*_____ Email_____

City*_____ State*_____ Zip*_____ Best time to contact ◯ Morning ◯ Afternoon ◯ Evening

Primary Language ◯ English ◯ Spanish ◯ Other_____ Preferred way to contact ◯ Phone ◯ Email

*Form cannot be processed without this information.

2 INSURANCE INFORMATION

Primary

Primary Medical Insurance_____

Insurance Phone_____

Policy ID #_____ Group #_____

Prescription Insurance (if different)_____

Prescription Insurance Phone_____

Policy ID #_____ Group #_____

Rx Bin #_____ Rx PCN #_____

Examples of primary medical insurance: Blue Cross Blue Shield, Anthem, Aetna, and Cigna.

Your prescription insurance may be different than your medical insurance. The name may be on the back of your health insurance card or on a separate card. Examples include Optum, Express Scripts, and CVS Caremark.

Secondary (Does the patient have secondary insurance?) ◯ Yes ◯ No

Secondary Medical Insurance_____

Insurance Phone_____

Policy ID #_____ Group #_____

Policyholder's Name (First/Last)_____

Relationship to Patient_____

Please include copies of insurance cards – the patient may have different cards for medical and prescription benefits.

PRESCRIBER COMPLETES

3 PRESCRIBER INFORMATION

Prescriber Name (First/Last)_____ Address_____

Site / Facility_____ City_____ State_____ Zip_____

NPI #_____ State Lic #_____ Office Contact + Title_____

Tax ID #_____ Phone #_____ Fax_____

Medicaid Provider # (if Medicaid patient)_____ Email_____

1

PAA

Sample Prior Authorization Appeals Letter
for PEDMARK® (sodium thiosulfate injection)

An appeal letter can be submitted when a prior authorization (PA) request has been denied. You can submit more than one appeal. Plans generally publish their appeal guidelines on their website. An appeal should be submitted along with a Letter of Medical Necessity.

Use of the information in this letter does not guarantee that the health plan will provide reimbursement for PEDMARK, and is not intended to be a substitute for or to influence the independent medical judgment of the physician.

Checklist to consider

- ◯ Include the patient's name, member ID, group number, and date of birth
- ◯ Restate why the PA was denied and why, in your clinical judgment, PEDMARK is appropriate for this patient
- ◯ Include the PA denial # and the date of the denial
- ◯ Include a copy of the denial letter
- ◯ Confirm that the patient's tumor is localized and nonmetastatic
- ◯ Confirm that the patient is at risk for ototoxicity due to cisplatin therapy
- ◯ Document that all PA requirements specified by the plan have been met
- ◯ PEDMARK Prescribing Information

Reprints available from your Fennec® representative:

- ◯ Brock PR, Maibach R, Childs M, et al. Sodium thiosulfate for protection from cisplatin-induced hearing loss. *N Engl J Med.* 2018;378(25):2376-2385. doi:10.1056/NEJMoa1801109
- ◯ Freyer DR, Chen L, Krailo MD, et al. Effects of sodium thiosulfate versus observation on development of cisplatin-induced hearing loss in children with cancer (ACCL0431): a multicentre, randomised, controlled, open-label, phase 3 trial. *Lancet.* 2017;18(1):63-74. doi:10.1016/S1470-2045(16)30625-8

INDICATIONS AND USAGE

PEDMARK (sodium thiosulfate injection) is indicated to reduce the risk of ototoxicity associated with cisplatin in pediatric patients 1 month of age and older with localized, non-metastatic solid tumors.

Limitations of Use The safety and efficacy of PEDMARK have not been established when administered following cisplatin infusions longer than 8 hours. PEDMARK may not reduce the risk of ototoxicity when administered following longer cisplatin infusions, because irreversible ototoxicity may have already occurred.

IMPORTANT SAFETY INFORMATION

- PEDMARK is contraindicated in patients with history of a severe hypersensitivity to sodium thiosulfate or any of its components.

Please see additional Important Safety Information on the last page.

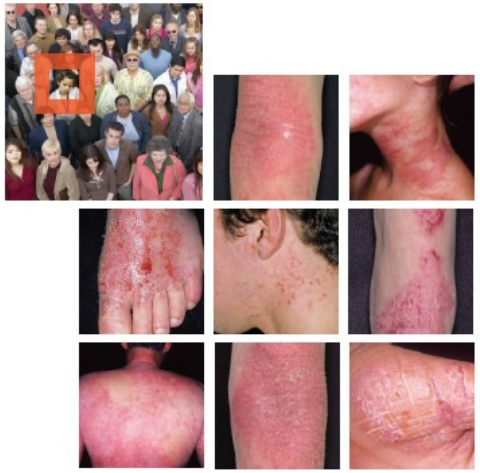
Click here for full Prescribing Information.

pedmark® (sodium thiosulfate injection)

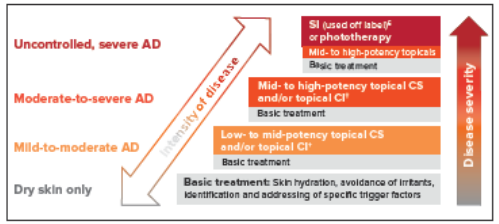
Resources developed with HEOR can provide guidance to plans for estimating the prevalence of a condition in their population

Atopic Dermatitis

Overview of Treatment Guidelines and Patterns of Medication Use



Guidelines* have historically recommended a step therapy approach to treatment of atopic dermatitis (AD)[1-6]



- Patients with AD may respond to good skin care and standard therapy with topical corticosteroids and calcineurin inhibitors[4,7]
- Moderate-to-severe patients may not be responsive to step therapies, including off-label use of systemic agents[1,7]

Patients with moderate-to-severe disease with persistent symptoms have limited options[2,4,6-8]

Topical therapies	Long-term, continued use is limited by safety risks and patient concerns[2,8]
Systemic immunosuppressants	These agents may help resolve symptoms, but patients face the risk of potentially serious adverse effects[4,6]

The chronic inflammatory nature of AD[2] and substantial burden of disease in patients with moderate-to-severe disease[9] highlight the need for new therapies.

Real world evidence shows rare use of systemic immunosuppressants to treat AD[10,11]

In a retrospective analysis of national claims data, adults with AD were treated with the following medications (N=75,860):	n	%
Systemic immunosuppressants (SI) or phototherapy (PT) (regardless of other medications)	1616	2.1%*
Any systemic corticosteroid (CS) without SI or PT	26,381	34.8%
Any topical CS† without SI, PT, or systemic CS	28,198	37.2%
Any topical calcineurin inhibitor (CI)† without SI, PT, or systemic CS	1963	2.6%
No topical corticosteroid or topical calcineurin inhibitor (ie, no prescription medication for AD)	19,013	25.1%

*Includes 1% of members who received SI and no PT (regardless of other medications); 1% who received PT and no SI (regardless of other medications); and 0.1% who received both PT and SI.

†Patients in the topical CS and topical CI categories are not mutually exclusive. A patient could be counted in both categories.

Study description: Medication use among adult patients with atopic dermatitis (AD) was estimated in a retrospective analysis of claims data from January 1, 2010, through September 30, 2015 (more than 27 million lives). AD patients were identified by ICD-9 code 6918. The first AD diagnosis in the identification period was considered the index event and its date the index date.

Exclusion criteria: During the 6-month pre-index period, patients were excluded for the following conditions because immunosuppressants and systemic steroids are commonly used for these conditions: rheumatoid arthritis, psoriatic arthritis, psoriasis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, lupus, and organ transplant.

Endpoints: In the 12-month follow-up period, the proportion of patients who used phototherapy, immunosuppressants (azathioprine, cyclosporine, methotrexate, mycophenolate mofetil), systemic steroids, topical steroids, topical calcineurin inhibitors, and no treatment.[10,11]

Warhaftig Associates: Who we are

- Access, payer communications, and patient support:
  It's all we do
- Over 30 years of collaboration with managed market, brand, patient support, field, and HEOR teams
- We create resources that communicate the impact and value of therapies for rare diseases

Let’s talk. Call Matt Warhaftig at 212 995-1700.
Warhaftig.com

Contact information:

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