

 **TARPEYO**<sup>®</sup>  
(budesonide) delayed release capsules • 4 mg



TARPEYO.com

# TAKE CHARGE WITH TARPEYO

**The first FDA-approved  
treatment for patients  
with IgA Nephropathy  
(IgAN) who are at  
high risk of disease  
progression**



Not an actual patient.

**ASK YOUR DOCTOR IF  
TARPEYO IS RIGHT FOR YOU.**

## Indication

### What is TARPEYO?

- TARPEYO<sup>®</sup> is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with a kidney disease called primary immunoglobulin A nephropathy (IgAN) who are at high risk of disease progression. It is not known if TARPEYO is safe and effective in children
- This approval is based on reduction in proteinuria. Confirmatory clinical trial results are needed to verify the clinical benefit of slowing kidney function decline

## Important Safety Information

### Who should not take TARPEYO?

Do not take TARPEYO if you are allergic to budesonide or any of the ingredients in TARPEYO. See the end of the Patient Information for a complete list of ingredients in TARPEYO.

**Please see Important Safety Information throughout  
and accompanying Patient Prescribing Information.**



Not an actual patient.

## Understanding the gut-kidney connection in IgA Nephropathy (IgAN)

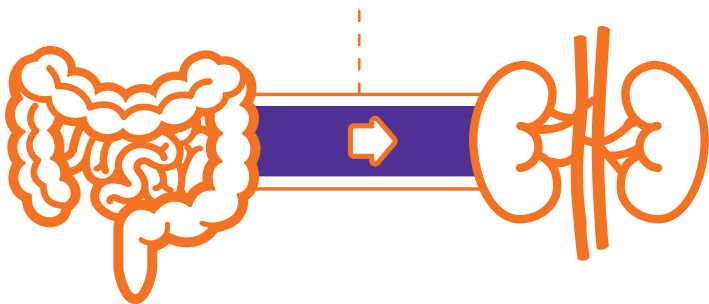
### What is IgAN?

IgAN is a **progressive autoimmune disease** affecting the kidneys. In patients with IgAN, too much of an antibody known as IgA1 builds up in your kidneys, leading to inflammation and damage.

### What may cause IgAN?

One of the main underlying causes of IgAN is thought to be an IgA1 antibody, which is most often produced in the gut.

In patients with IgAN, more IgA1 gets into the blood stream than normal, and travels to the kidneys



This type of IgA1 is usually formed in a specific area of the gut

This IgA1 can accumulate in the kidneys, which can lead to kidney inflammation and damage

## What are the potential signs and symptoms of IgAN?

Patients with IgAN may report the following:



Lower back pain



Blood in the urine



Foamy urine due to excess protein



Swelling in feet, ankles, or legs

These symptoms may be subtle, and you may not experience any of them. Excess protein in the urine, also known as proteinuria, or even blood in your urine may not be discovered until a routine urine test. A kidney biopsy by your doctor is needed to confirm a diagnosis.

### How is IgAN monitored?

Two important measures for people with IgAN are UPCR and eGFR.

- **UPCR** stands for urine protein to creatinine ratio. It is a measure of the amount of protein in the urine
- **eGFR** stands for estimated glomerular filtration rate. It is a measure of kidney function. The higher the number (the range is 0 to 120), the better your kidney function

Your doctor may monitor UPCR and eGFR closely to track if your IgAN is progressing.

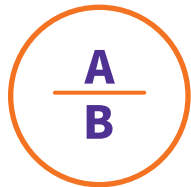
**Did you know?** By the time IgA Nephropathy is diagnosed, some kidney damage may have already occurred



Not an actual patient.

## Discover TARPEYO—the first FDA-approved treatment to reduce proteinuria in adults with IgAN at risk of rapid disease progression

### How was TARPEYO studied?



The clinical study of TARPEYO has 2 parts. In **Part A**, 97 patients received TARPEYO plus blood pressure medication, and 102 patients received placebo plus blood pressure medication.

The primary objective of the study looked at how TARPEYO reduced high levels of protein in the urine (proteinuria) after 9 months of treatment, as measured by UPCR.

The impact of TARPEYO on eGFR, a measure of kidney function, is the focus of **Part B** of the study. At this time, it has not been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.

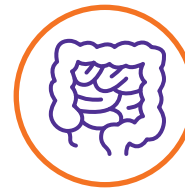
### Important Safety Information (cont'd)

**Before taking TARPEYO, tell your healthcare provider about all of your medical conditions, including if you:**

- have liver problems
- have chicken pox or measles or have recently been near anyone with chicken pox or measles
- have an infection
- have high blood sugar levels (prediabetes or diabetes)
- have glaucoma or cataracts
- have a family history of diabetes or glaucoma
- have or have had tuberculosis
- have high blood pressure (hypertension)

**Please see Important Safety Information throughout and accompanying Patient Prescribing Information.**

### How is TARPEYO thought to work?

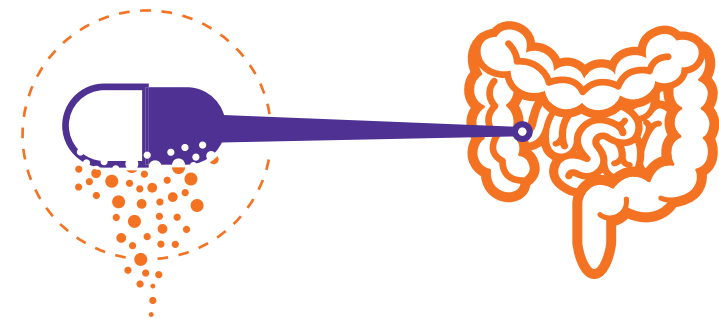


TARPEYO is designed to deliver treatment to an area of the gut thought to play a role in IgAN. Types of cells in the gut are responsible for the production of an antibody called IgA1, which can build up in the kidneys, causing IgAN. TARPEYO can reduce the amount of this antibody.\*

\*It has not been established to what extent the efficacy of TARPEYO is from local effects (in the gut) vs systemic effects (in circulation).

### What is unique about TARPEYO?

The TARPEYO capsule was designed with targeted-release technology to dissolve once it reaches a specific area of the gut thought to play a role in IgAN



Visit [TARPEYO.com](https://www.tarpeyo.com) to see a video on how TARPEYO works

### Important Safety Information (cont'd)

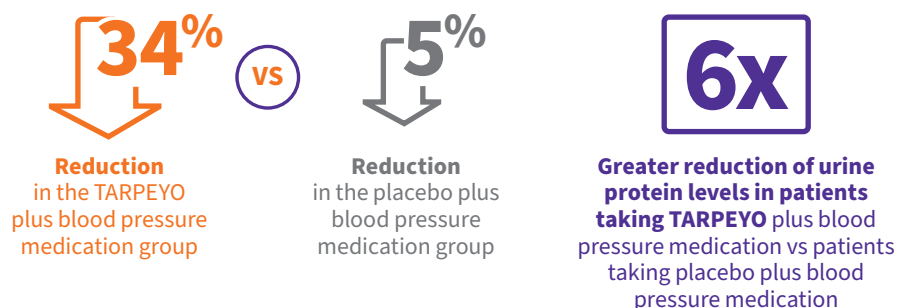
**Before taking TARPEYO, tell your healthcare provider about all of your medical conditions, including if you: (cont'd)**

- have decreased bone mineral density (osteoporosis)
- have stomach ulcers
- are pregnant or plan to become pregnant. TARPEYO may harm your unborn baby. Talk to your healthcare provider about the possible risk to your unborn baby if you take TARPEYO when you are pregnant
- are breastfeeding or plan to breastfeed. It is not known if TARPEYO passes into your breast milk or if it will affect your baby. Talk to your healthcare provider about the best way to feed your baby during treatment with TARPEYO



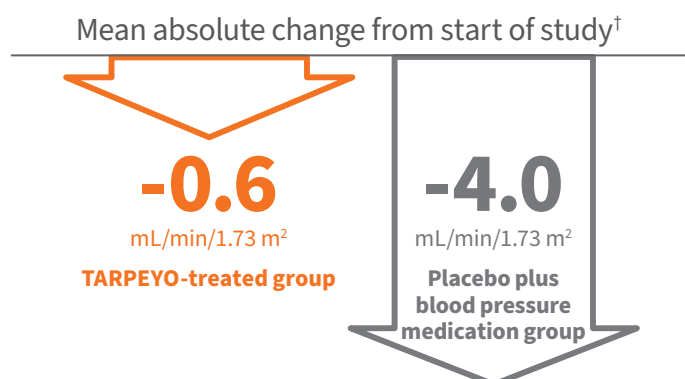
## TARPEYO study results

Proven to lower urine protein levels at 9 months (primary objective of study)\*



\*At 9 months, 97 patients received treatment with TARPEYO plus blood pressure medication and 102 patients received placebo plus blood pressure medication.

### Change in eGFR at 9 months (secondary objective of the study)



As kidney function worsens, the eGFR number goes down.

It has not yet been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.

<sup>†</sup>At the start of study, the average eGFR was 54.9 mL/min/1.73 m<sup>2</sup> in the TARPEYO group and 55.5 mL/min/1.73 m<sup>2</sup> in the placebo group.

**The overall impact on slowing kidney function decline as measured by eGFR is the focus of Part B of the study**

### Important Safety Information (cont'd)

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. TARPEYO and other medicines may affect each other, causing side effects.

**Please see Important Safety Information throughout and accompanying Patient Prescribing Information.**

## The most common side effects reported by patients in the clinical study of TARPEYO

Most common side effects	TARPEYO + blood pressure medication group (n=97)	Placebo + blood pressure medication group (n=100)
High blood pressure	16%	2%
Swelling of the lower legs, ankles, and feet	14%	4%
Muscle cramp	13%	4%
Acne	11%	2%
Irritation or inflammation of the skin	7%	1%
Weight increase	7%	3%
Shortness of breath	6%	0%
Swelling of the face	6%	1%
Indigestion	5%	2%
Tiredness	5%	2%
Thicker or more hair on your body and face	5%	0%

### TARPEYO may cause serious side effects, including:

Effects of having too much corticosteroid medicine in your blood (hypercorticism), adrenal suppression, and risk of immunosuppression.

- **Blood pressure:** Increases in blood pressure were small and resolved to baseline levels by the end of the 9-month treatment period
- **Weight gain:** Increases in body weight were minor and did not exceed 2.2 lbs. Patients returned to pre-treatment weight within 3 months of ending treatment
- Approximately 90% of patients in the clinical study stayed on TARPEYO during the 9-month treatment period
- Unlike with other products, there are no FDA-mandated tests for TARPEYO. But your doctor will likely order lab tests to determine how well you are responding to treatment



Not an actual patient.

## Start your day with TARPEYO



**4 capsules** of TARPEYO should be taken once a day and swallowed whole



Take **TARPEYO in the morning, at least 1 hour before your morning meal**



**Don't crush, chew, or open TARPEYO**  
Don't eat grapefruit, or drink grapefruit juice, while on TARPEYO treatment

## Important Safety Information (cont'd)

### How should I take TARPEYO?

- Take TARPEYO exactly as your healthcare provider tells you
- Your healthcare provider will decide how long you should take TARPEYO. Do not stop taking TARPEYO without first talking with your healthcare provider
- Take your prescribed dose of TARPEYO 1 time each day in the morning, at least 1 hour before a meal
- Take TARPEYO capsules whole. **Do not** open, chew, crush, or break TARPEYO capsules before swallowing

**Please see Important Safety Information throughout and accompanying Patient Prescribing Information.**

## When facing IgA Nephropathy (IgAN), take charge with TARPEYO



- **Learn more** about IgAN and TARPEYO at [TARPEYO.com](https://www.tarpeyo.com)
- **Download resources**
- **Sign up for updates**

Stay connected with **TARPEYO** on Facebook

## Important Safety Information (cont'd)

### How should I take TARPEYO? (cont'd)

- If you miss a dose of TARPEYO, take your prescribed dose at your next scheduled time. Do not take two doses of TARPEYO at the same time
- If you take too much TARPEYO, call your healthcare provider right away or go to the nearest hospital emergency room

### What should I avoid while taking TARPEYO?

**Do not** eat grapefruit or drink grapefruit juice during your treatment with TARPEYO. Eating grapefruit or drinking grapefruit juice can increase the level of TARPEYO in your blood.

### What are the possible side effects of TARPEYO?

#### TARPEYO may cause serious side effects, including:

- **Effects of having too much corticosteroid medicine in your blood (hypercorticism):** Long-time use of TARPEYO can cause you to have signs and symptoms of too much cortisol, a stress hormone in your blood. Tell your healthcare provider if you have any of the following signs and symptoms of hypercorticism: acne, bruise easily, rounding of your face (moon face), ankle swelling, thicker or more hair on your body and face, a fatty pad or hump between your shoulders (buffalo hump), or pink or purple stretch marks on the skin of your abdomen, thighs, breasts, or arms

## Common questions you may have

### What is TARPEYO?

TARPEYO is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with IgA Nephropathy who are at high risk of disease progression. TARPEYO was the first FDA-approved therapy that was specifically designed for IgA Nephropathy.

### How is TARPEYO thought to work?

TARPEYO is designed to deliver treatment to an area of the gut thought to play a role in IgAN. Types of cells in the gut are thought to be responsible for the production of IgA1. These types of IgA1 can build up in the kidneys and cause IgAN. TARPEYO can reduce the amount of this antibody.\*

### How is TARPEYO different from other steroids I've been prescribed for IgAN?

TARPEYO is the first FDA-approved treatment to reduce proteinuria in patients with IgAN that was designed for delivery to the area of the gut where the disease is thought to originate. Other steroids have not established efficacy and safety and are not FDA approved for IgAN.

\*It has not been established to what extent the efficacy of TARPEYO is from local effects (in the gut) vs systemic effects (in circulation).

## Indication

### What is TARPEYO?

- TARPEYO<sup>®</sup> is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with a kidney disease called primary immunoglobulin A nephropathy (IgAN) who are at high risk of disease progression. It is not known if TARPEYO is safe and effective in children
- This approval is based on reduction in proteinuria. Confirmatory clinical trial results are needed to verify the clinical benefit of slowing kidney function decline

## Important Safety Information (cont'd)

### What are the possible side effects of TARPEYO? (cont'd)

#### TARPEYO may cause serious side effects, including: (cont'd)

- **Adrenal suppression:** When TARPEYO is taken for a long period of time (chronic use), adrenal suppression can happen. This is a condition in which the adrenal glands do not make enough steroid hormones. Symptoms of adrenal suppression include tiredness,

**Please see Important Safety Information throughout and accompanying Patient Prescribing Information.**

## Common questions you may have (cont'd)

### What did TARPEYO clinical studies show?

**In a clinical study at 9 months, TARPEYO was shown to help lower the level of protein in urine (proteinuria).<sup>†</sup>** The overall impact on slowing kidney function decline as measured by eGFR is the focus of Part B of the study. The most common side effects (occurring in  $\geq 10\%$  of patients treated with TARPEYO at a higher incidence than blood pressure medication alone) were: high blood pressure; swelling of the lower legs, ankles, and feet; muscle cramp; and acne.

### How often will I need to monitor my lab values while taking TARPEYO?

You will need to have your labs measured to determine how well you are responding to treatment. Your doctor will decide which lab values and how often they will monitor them. With TARPEYO, there is no FDA-required monthly lab monitoring, as seen with other products.

### Is there a program that can help provide financial assistance for TARPEYO?

Yes, TARPEYO Touchpoints is a program that was developed to help support your treatment journey. A Care Navigator can help with financial support options you may be eligible for. They can also connect you with nurses and resources, and help track your prescription shipment each month.

<sup>†</sup>In Part A of the TARPEYO clinical study, 97 patients received TARPEYO plus blood pressure medication, and 102 patients received placebo plus blood pressure medication.

## Important Safety Information (cont'd)

weakness, nausea and vomiting, and low blood pressure. Tell your healthcare provider if you are under stress or have any symptoms of adrenal suppression during treatment with TARPEYO

### What are the possible side effects of TARPEYO? (cont'd)

- **Risk of immunosuppression:** TARPEYO weakens your immune system. Taking medicines that weaken your immune system makes you more likely to get infections. Avoid contact with people who have contagious diseases, such as chicken pox or measles, during treatment with TARPEYO. Tell your healthcare provider right away if you come in contact with anyone who has chicken pox or measles. Consult with your healthcare provider regarding appropriate vaccination scheduling
- Tell your healthcare provider if you develop any symptoms of infection during treatment with TARPEYO, including fever, feeling tired, chills, aches, pain, and nausea and vomiting



## Access made easy

TARPEYO Touchpoints<sup>™</sup> is your one-stop resource for personalized services and assistance to support your treatment journey.



### A team of support

- A TARPEYO Touchpoints Care Navigator is your primary point of contact
- The Care Navigator can help with financial support options, connect you with nurses and resources, and help track your prescription shipment each month



### Financial assistance programs

- Financial assistance programs may reduce or eliminate your out-of-pocket costs



### Help with insurance paperwork

- TARPEYO Touchpoints can help with things like insurance benefits, appeals, and prior authorizations



### Home delivery of your medicine

- TARPEYO will be shipped directly to your doorstep by a specialty pharmacy

**TARPEYO** is shipped from an exclusive specialty pharmacy directly to your doorstep



Not an actual patient.

## TARPEYO Touchpoints helps you explore financial programs

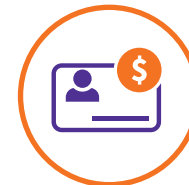
Your doctor will fill out an enrollment form to connect you to TARPEYO Touchpoints services.



### IF YOU HAVE COMMERCIAL INSURANCE

#### TARPEYO Touchpoints Copay Assistance Program\*†

You may be eligible to pay as little as **\$0 per prescription**



### IF YOU ARE UNINSURED/UNDERINSURED

#### TARPEYO Touchpoints Patient Assistance Program (PAP)\*\*‡

You may be eligible to receive TARPEYO at no cost

**Start on TARPEYO as quickly as possible—TARPEYO Touchpoints offers a program to provide medicine at no cost to commercially insured patients while insurance coverage is pursued.<sup>§</sup>**

**TARPEYO Touchpoints is available Monday through Friday, 8 AM to 8 PM ET, at 1-833-444-8277**

\*Please view the full terms and conditions on [TARPEYOTouchpoints.com](https://www.TARPEYOTouchpoints.com).

†To qualify for the TARPEYO Touchpoints Copay Assistance Program, you must: (a) be a resident of the United States or a US territory, (b) have a valid prescription for TARPEYO, (c) be commercially insured and approved, (d) be enrolled by your doctor through TARPEYO Touchpoints.

‡To qualify for the TARPEYO Touchpoints Patient Assistance Program, you must: (a) be a resident of the United States or a US territory, (b) have a valid prescription for TARPEYO, (c) have no coverage/not enough coverage or insurance that doesn't cover TARPEYO, (d) meet annual household income threshold based on household size, (e) agree to and provide income verification (soft credit check, tax returns, 3 months of pay stubs, unemployment checks, or bank statements), (f) be enrolled by your doctor through TARPEYO Touchpoints. (g) Not valid for prescriptions reimbursed in whole or in part by any government-funded program including but not limited to Medicare, Medicare Part D, Medicaid, Medigap, VA, CHAMPUS, DOD, TRICARE, or any state, patient foundation, or other pharmaceutical program.

§Your doctor will need to complete section 6 of the enrollment form which is an additional prescription to receive a limited supply of TARPEYO at no cost for eligible patients who experience a delay in insurance coverage.

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## Indication

### What is TARPEYO?

- TARPEYO<sup>®</sup> is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with a kidney disease called primary immunoglobulin A nephropathy (IgAN) who are at high risk of disease progression. It is not known if TARPEYO is safe and effective in children
- This approval is based on reduction in proteinuria. Confirmatory clinical trial results are needed to verify the clinical benefit of slowing kidney function decline

## Important Safety Information

### Who should not take TARPEYO?

**Do not take TARPEYO if** you are allergic to budesonide or any of the ingredients in TARPEYO. See the end of the Patient Information for a complete list of ingredients in TARPEYO.

### Before taking TARPEYO, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- plan to have surgery
- have chicken pox or measles or have recently been near anyone with chicken pox or measles
- have an infection
- have high blood sugar levels (prediabetes or diabetes)
- have glaucoma or cataracts
- have a family history of diabetes or glaucoma
- have or have had tuberculosis
- have high blood pressure (hypertension)
- have decreased bone mineral density (osteoporosis)
- have stomach ulcers
- are pregnant or plan to become pregnant. TARPEYO may harm your unborn baby. Talk to your healthcare provider about the possible risk to your unborn baby if you take TARPEYO when you are pregnant
- are breastfeeding or plan to breastfeed. It is not known if TARPEYO passes into your breast milk or if it will affect your baby. Talk to your healthcare provider about the best way to feed your baby during treatment with TARPEYO

### Tell your healthcare provider about all the medicines you take,

including prescription and over-the-counter medicines, vitamins, and herbal supplements. TARPEYO and other medicines may affect each other, causing side effects.

### How should I take TARPEYO?

- Take TARPEYO exactly as your healthcare provider tells you
- Your healthcare provider will decide how long you should take TARPEYO. Do not stop taking TARPEYO without first talking with your healthcare provider
- Take your prescribed dose of TARPEYO 1 time each day in the morning, at least 1 hour before a meal
- Take TARPEYO capsules whole. Do not open, chew, crush, or break TARPEYO capsules before swallowing
- If you miss a dose of TARPEYO, take your prescribed dose at your next scheduled time. Do not take two doses of TARPEYO at the same time
- If you take too much TARPEYO, call your healthcare provider right away or go to the nearest hospital emergency room

### What should I avoid while taking TARPEYO?

**Do not** eat grapefruit or drink grapefruit juice during your treatment with TARPEYO. Eating grapefruit or drinking grapefruit juice can increase the level of TARPEYO in your blood.

### What are the possible side effects of TARPEYO?

#### TARPEYO may cause serious side effects, including:

- **Effects of having too much corticosteroid medicine in your blood (hypercorticism):** Long-time use of TARPEYO can cause you to have signs and symptoms of too much cortisol, a stress hormone in your blood. Tell your healthcare provider if you have any of the following signs and symptoms of hypercorticism: acne, bruise easily, rounding of your face (moon face), ankle swelling, thicker or more hair on your body and face, a fatty pad or hump between your shoulders (buffalo hump), or pink or purple stretch marks on the skin of your abdomen, thighs, breasts, or arms
- **Adrenal suppression:** When TARPEYO is taken for a long period of time (chronic use), adrenal suppression can happen. This is a condition in which the adrenal glands do not make enough steroid hormones. Symptoms of adrenal suppression include tiredness, weakness, nausea and vomiting, and low blood pressure. Tell your healthcare provider if you are under stress or have any symptoms of adrenal suppression during treatment with TARPEYO
- **Risk of immunosuppression:** TARPEYO weakens your immune system. Taking medicines that weaken your immune system makes you more likely to get infections. Avoid contact with people who have contagious diseases, such as chicken pox or measles, during treatment with TARPEYO. Tell your healthcare provider right away if you come in contact with anyone who has chicken pox or measles. Consult with your healthcare provider regarding appropriate vaccination scheduling
- Tell your healthcare provider if you develop any symptoms of infection during treatment with TARPEYO, including fever, feeling tired, chills, aches, pain, and nausea and vomiting

#### The most common side effects of TARPEYO include:

- high blood pressure
- swelling of the lower legs, ankles, and feet
- muscle cramp
- acne
- irritation or inflammation of the skin
- weight increase
- shortness of breath
- swelling of the face
- indigestion
- tiredness
- thicker or more hair on your body and face

These are not all the possible side effects of TARPEYO. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**Please see accompanying Patient Prescribing Information.**



# TAKE CHARGE WITH TARPEYO



## Specifically designed for and studied in IgA Nephropathy

TARPEYO is the first FDA-approved therapy that was specifically designed for IgAN



## Targets a source of IgAN in the gut

Designed to deliver treatment to an area of the gut thought to play a role in IgAN\*



## Significantly reduced protein in urine

34% reduction seen in the TARPEYO-treated group vs 5% reduction in the placebo plus blood pressure medication group at 9 months<sup>†</sup>



## Once-daily oral medicine

4 capsules of TARPEYO should be taken once a day and swallowed whole

\*It has not been established to what extent the efficacy of TARPEYO is from local effects (in the gut) vs systemic effects (in circulation).

<sup>†</sup>At 9 months, 97 patients received treatment with TARPEYO plus blood pressure medication and 102 patients received placebo plus blood pressure medication.

Learn more at [TARPEYO.com](https://www.tarpeyo.com) and  
talk to your doctor today

## Indication

### What is TARPEYO?

- TARPEYO<sup>®</sup> is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with a kidney disease called primary immunoglobulin A nephropathy (IgAN) who are at high risk of disease progression. It is not known if TARPEYO is safe and effective in children
- This approval is based on reduction in proteinuria. Confirmatory clinical trial results are needed to verify the clinical benefit of slowing kidney function decline

**Please see Important Safety Information throughout and  
accompanying Patient Prescribing Information.**

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TARPEYO safely and effectively. See full prescribing information for TARPEYO.

**TARPEYO (budesonide) delayed release capsules, for oral use**  
**Initial U.S. Approval: 1997**

### INDICATIONS AND USAGE

TARPEYO is a corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR)  $\geq$  1.5 g/g. (1)

This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial. (1)

### DOSAGE AND ADMINISTRATION

- The recommended dosage is 16 mg administered orally once daily, in the morning at least 1 hour before a meal. (2)
- Swallow whole. Do not open, crush or chew. (2)  
When discontinuing, reduce dosage to 8 mg once daily for the last two weeks. (2, 5.1)

### DOSAGE FORMS AND STRENGTHS

Delayed release capsules: 4 mg (3)

### CONTRAINDICATIONS

- Hypersensitivity to budesonide or any of the ingredients in TARPEYO. (4)

### WARNINGS AND PRECAUTIONS

- Hypercorticism and Adrenal Axis Suppression:** Follow general warnings concerning corticosteroids, patients with hepatic impairment may be at increased risk. Taper upon discontinuation. (2, 5.1, 8.6, 12.3)
- Risks of immunosuppression:** Avoid use in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. May affect vaccine efficacy. (5.2)
- Other Corticosteroid Effects:** Monitor patients with concomitant conditions where corticosteroids may have unwanted effects (e.g., hypertension, diabetes mellitus). (5.3)

### ADVERSE REACTIONS

Most common adverse reactions ( $\geq$ 5%) are hypertension, peripheral edema, muscle spasms, acne, dermatitis, weight increase, dyspnea, face edema, dyspepsia, fatigue, hirsutism. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Calliditas Therapeutics at 1-844-IGA-0011 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

Potent CYP3A4 Inhibitors (e.g. ketoconazole, grapefruit juice): Can increase systemic budesonide concentrations: avoid concomitant use. (7.1)

### USE IN SPECIFIC POPULATIONS

Lactation: Routine monitoring of linear growth in infants is recommended with chronic use of budesonide in the nursing mother. (8.2).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2021

## FULL PRESCRIBING INFORMATION: CONTENTS\*

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

TARPEYO is indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR)  $\geq$  1.5 g/g.

This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

### 2 DOSAGE AND ADMINISTRATION

The recommended duration of therapy is 9 months, with a dosage of 16 mg administered orally once daily [see *Clinical Studies* (14.1)]. When discontinuing therapy, reduce the dosage to 8 mg once daily for the last 2 weeks of therapy [see *Warnings and Precautions* (5.1)].

The delayed release capsules should be swallowed whole in the morning, at least 1 hour before a meal. Do not open, crush or chew.

If a dose is missed, take the prescribed dose at the next scheduled time. Do not double the next dose.

Safety and efficacy of treatment with subsequent courses of TARPEYO have not been established.

### 3 DOSAGE FORMS AND STRENGTHS

Delayed release capsule containing 4 mg budesonide. White coated opaque capsules printed with "CAL10 4MG" in black ink.

### 4 CONTRAINDICATIONS

TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis have occurred with other budesonide formulations.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Hypercorticism and Adrenal Axis Suppression

When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy [see *Dosing and Administration* (2)] or switching between corticosteroids, monitor for signs of adrenal axis suppression.

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure of oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B) [see *Use in Specific Populations* (8.6), *Clinical Pharmacology* (12.3)].

#### 5.2 Risks of Immunosuppression

Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressant doses of corticosteroids.

Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. Avoid exposure to active, easily-transmitted infections (e.g., chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.

How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, consider therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG). If exposed to measles, consider prophylaxis with pooled intramuscular immunoglobulin (IG). If chickenpox develops, consider treatment with antiviral agents.

### 5.3 Other Corticosteroid Effects

TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where corticosteroids may have unwanted effects.

## 6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypercorticism and adrenal suppression [see Warnings and Precautions (5.1)]
- Risks of immunosuppression [see Warnings and Precautions (5.2)]
- Other corticosteroid effects [see Warnings and Precautions (5.3)]

### 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 TARPEYO has been evaluated in a randomized controlled study in 197 patients.

The most common adverse reactions reported in greater than or equal to 5% of TARPEYO-treated patients are listed in Table 1.

The majority of adverse reactions were mild or moderate in severity.

**Table 1: Reported adverse reactions occurring in greater than or equal to 5% of TARPEYO treated patients, and greater than or equal to 2% higher than Placebo**

Adverse Reaction	TARPEYO 16 mg (N=97)	Placebo (N=100)
	n (%)	n (%)
Patients with any Adverse Reaction	84 (87)	73 (73)
Hypertension	15 (16)	2 (2)
Peripheral edema	14 (14)	4 (4)
Muscle spasms	13 (13)	4 (4)
Acne	11 (11)	2 (2)
Dermatitis	7 (7)	1 (1)
Weight increased	7 (7)	3 (3)
Dyspnea	6 (6)	0 (0)
Face edema	6 (6)	1 (1)
Dyspepsia	5 (5)	2 (2)
Fatigue	5 (5)	2 (2)
Hirsutism	5 (5)	0 (0)

Most adverse reactions that occurred at a greater incidence for TARPEYO compared to placebo were consistent with hypercortisolism.

## 7 DRUG INTERACTIONS

### 7.1 Interaction with CYP3A4 Inhibitors

Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors; e.g. ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine [see Clinical Pharmacology (12.3)].

Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide [see Clinical Pharmacology (12.3)].

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

The available data from published case series, epidemiological studies and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgA Nephropathy. Infants exposed to in-utero corticosteroids, including budesonide, are at risk for hypoadrenalism (see Clinical Considerations). In animal reproduction studies with pregnant rats and rabbits, administration of subcutaneous budesonide during organogenesis at doses approximately 0.3 times or 0.03 times, respectively, the maximum recommended human dose (MRHD), resulted in increased fetal loss, decreased pup weights, and skeletal abnormalities. Maternal toxicity was observed in both rats and rabbits at these dose levels (see Data).

The estimated background risk of major birth defects and miscarriage of the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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.

## Clinical Considerations

### Disease-Associated Maternal and/or Embryo/Fetal Risk

IgA nephropathy in pregnancy is associated with adverse maternal outcomes, including increased rates of cesarean section, pregnancy-induced hypertension, pre-eclampsia and preterm delivery, and adverse fetal/neonatal outcomes, including stillbirth and low birth weight.

### Fetal/Neonatal Adverse Reactions

Hypoadrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy. Infants should be carefully observed for signs of hypoadrenalism, such as poor feeding, irritability, weakness, and vomiting, and managed accordingly [see Warnings and Precautions (5.1)].

### Data

#### Animal Data

Budesonide was teratogenic and embryo-lethal in rabbits and rats.

In an embryo-fetal development study in pregnant rats dosed subcutaneously with budesonide during the period of organogenesis on gestation days 6 to 15 there were effects on fetal development and survival at subcutaneous doses up to approximately 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose (MRHD) on a body surface area basis).

In an embryo-fetal development study in pregnant rabbits dosed during the period of organogenesis on gestation days 6 to 18, there was an increase in maternal abortion, and effects on fetal development and reduction in litter weights at subcutaneous doses from approximately 25 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis).

Maternal toxicity, including reduction in body weight gain, was observed at subcutaneous doses of 5 mcg/kg in rabbits (approximately 0.006 times the maximum recommended human dose on a body surface area basis) and 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose on a body surface area basis).

In a peri- and post-natal development study, subcutaneous treatment of pregnant rats with budesonide during the period from Day 15 post coitum to Day 21 post partum, budesonide had no effects on delivery, but did have an effect on growth and development of offspring. In addition, offspring survival was reduced and surviving offspring had decreased mean body weights at birth and during lactation at exposures  $\geq 0.012$  times the MRHD (on a mg/m<sup>2</sup> basis at maternal subcutaneous doses of 20 mcg/kg/day and higher). These findings occurred in the presence of maternal toxicity.

### 8.2 Lactation

#### Risk Summary

Breastfeeding is not expected to result in significant exposure of the infant to TARPEYO. Lactation studies have not been conducted with oral budesonide, including TARPEYO, and no information is available on the effects of the drug on the breastfed infant or the effects on the drug on milk production. One published study reports that budesonide is present in human milk following maternal inhalation of budesonide (see Data). Routine monitoring of linear growth in infants is recommended with chronic use of budesonide in the nursing mother. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TARPEYO and any potential adverse effects on the breastfed infant from TARPEYO, or from the underlying maternal condition.

### Data

One published study reports that budesonide is present in human milk following maternal inhalation of budesonide, which resulted in infant doses approximately 0.3% to 1% of the maternal weight-adjusted dosage and a milk to plasma ratio was approximately 0.5. Budesonide was not detected in plasma, and no adverse events were noted in the breastfed infants following maternal use of inhaled budesonide.

Assuming a daily average milk intake of about 150 mL/kg/day and a milk to plasma ratio of 0.5, the estimated oral dose of budesonide for a 5 kg infant is expected to be less than 2 mcg/day for a maternal dose of 16 mg TARPEYO. Assuming 100% bio-availability in the infant this is about 0.1% of the maternal dose and about 3% of the highest inhaled dose used clinically for asthma in infants.

### 8.4 Pediatric Use

The safety and efficacy of TARPEYO in pediatric patients have not been established.

### 8.5 Geriatric Use

Clinical studies of TARPEYO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

### 8.6 Hepatic Impairment

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to budesonide [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]. Avoid use in patients with severe hepatic impairments (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

## 10 OVERDOSAGE

Reports of acute toxicity and/or death following overdose of corticoids are rare.

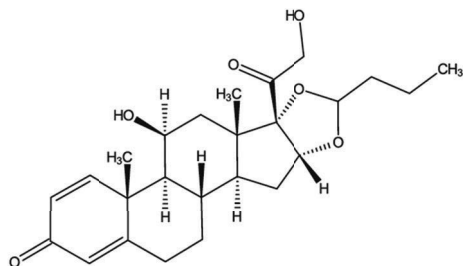
In the event of acute overdose, no specific antidote is available. Treatment consists of supportive and symptomatic therapy.



## 11 DESCRIPTION

TARPEYO (budesonide) delayed release capsules, for oral administration, contain budesonide, a synthetic corticosteroid, as the active ingredient. Budesonide is designated chemically as 16 $\alpha$ , 17 $\alpha$ -[(1R*S*)-Butylidenebis(oxy)]-11 $\beta$ , 21-dihydroxypregna-1,4-diene-3,20-dione.

Budesonide is provided as a mixture of two epimers (22R and 22S). The empirical formula of budesonide is C<sub>25</sub>H<sub>34</sub>O<sub>6</sub> and its molecular weight is 430.5. Its structural formula is:



Budesonide is a white to off-white, tasteless, odorless powder that is practically insoluble in water, sparingly soluble in alcohol, and freely soluble in chloroform.

The beads in each capsule contain the following inactive ingredients: sugar spheres (sucrose and starch), hypromellose, polyethylene glycol, citric acid monohydrate, ethyl cellulose, medium chain triglycerides and oleic acid. The capsule shells contain hypromellose and titanium oxide (E171); and the printing ink on the capsules contain shellac, propylene glycol and black iron oxide (E172). The enteric coating on the capsules contain: methacrylic acid and methacrylate copolymer, talc and dibutyl sebacate.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Budesonide is a corticosteroid with potent glucocorticoid activity and weak mineralocorticoid activity that undergoes substantial first pass metabolism. Mucosal B-cells present in the ileum, including the Peyer's patches, express glucocorticoid receptors and are responsible for the production of galactose-deficient IgA1 antibodies (Gd-Ag1) causing IgA nephropathy. Through their anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, corticosteroids can modulate B-cell numbers and activity. It has not been established to what extent TARPEYO's efficacy is mediated via local effects in the ileum vs systemic effects.

### 12.2 Pharmacodynamics

Treatment with corticosteroids, including TARPEYO, is associated with a suppression of endogenous cortisol concentrations and an impairment of the hypothalamus-pituitary-adrenal (HPA) axis function.

### 12.3 Pharmacokinetics

#### Absorption

Following single oral administration of TARPEYO 16 mg to healthy subjects, the average geometric mean C<sub>max</sub> (CV%) was 4.4 ng/mL (58.3), and AUC<sub>0-24</sub> was 24.1 h\*ng/mL (49.7). Median T<sub>lag</sub> (min, max) was 3.1 h (0, 6) while median T<sub>max</sub> (min, max) was 5.1 h (4.5, 10).

#### Food Effect

There was no clinically relevant food effect observed on the overall systemic exposure of budesonide when either a moderate or high fat meal was consumed 1 hour after administration of TARPEYO.

#### Distribution

Approximately 85 to 90% of budesonide binds to plasma proteins in blood over the concentration range of 0.43 to 99 ng/mL. The volume of distribution at steady state reported in the literature is 3 to 4 L/kg.

#### Metabolism

Budesonide is metabolized by the liver (and to lesser extent the gut), primarily by oxidative pathways via CYP3A4 to two main metabolites, 16 $\alpha$ -hydroxyprednisolone and 6 $\beta$ -hydroxybudesonide, which have less than 1% of the corticosteroid activity of budesonide.

#### Elimination

Budesonide had a high plasma clearance, 0.9 to 1.8 L/min in healthy adults, which is close to the estimated liver blood flow, and, accordingly, suggests that budesonide is a high hepatic clearance drug.

Following single oral administration of TARPEYO 16 mg to healthy subjects, the elimination half-life (t<sub>1/2</sub>) for TARPEYO ranged from 5.0 to 6.8 hours.

#### Excretion

Budesonide was excreted in urine and feces in the form of metabolites. After oral as well as intravenous administration of micronized [<sup>3</sup>H]-budesonide, approximately 60% of the recovered radioactivity was found in urine. The major metabolites, including 16 $\alpha$ -hydroxyprednisolone and 6 $\beta$ -hydroxybudesonide, are mainly renally excreted, intact or in conjugated forms. No unchanged budesonide was detected in urine.

#### Specific Populations

##### Age, race, and body weight

The effect of age, race, and body weight on the pharmacokinetics of TARPEYO has not been established.

##### Sex

Of the 143 healthy volunteers included in the Phase 1 studies, 29% were female. Pharmacokinetics of budesonide was similar between males and females.

#### Hepatic Impairment

Subjects with moderate hepatic impairment (Child-Pugh class B) had 3.5 times the budesonide AUC compared with healthy volunteers while subjects with mild hepatic impairment (Child-Pugh class A) had approximately 40% higher budesonide AUC compared with healthy volunteers.

Patients with severe hepatic impairment (Child-Pugh Class C) have not been studied.

#### Renal Impairment

Intact budesonide is not excreted renally. The main metabolites of budesonide, which have negligible corticosteroid activity, are largely (60%) excreted in urine.

#### Drug Interaction Studies

Budesonide is metabolized via CYP3A4. Potent inhibitors of CYP3A4 can increase plasma levels of budesonide.

Thus, clinically relevant drug interactions with potent CYP3A inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, cyclosporine, and grapefruit juice, are to be expected. Conversely, induction of CYP3A4 potentially could result in the lowering of budesonide plasma concentrations.

#### Effects of Other Drugs on Budesonide

##### Ketoconazole

In an open, non-randomized, cross-over study, 6 healthy subjects were given budesonide 10 mg as a single dose, either alone or concomitantly with the last ketoconazole dose of 3 days treatment with ketoconazole 100 mg twice daily. Co-administration of ketoconazole resulted in 8-fold the AUC of budesonide, compared to budesonide alone.

In an open, randomized, cross-over study 8 healthy subjects were given Entocort EC 3 mg as a single dose, either alone or concomitantly with the last ketoconazole dose of 4 days treatment with ketoconazole 200 mg once daily. Co-administration of ketoconazole resulted in 6.5-fold the AUC of budesonide, compared to budesonide alone.

##### Grapefruit Juice

In an open, randomized, cross-over study, 8 healthy subjects were given Entocort EC 3 mg, either alone, or concomitantly with 600 mL concentrated grapefruit juice (which inhibits CYP3A4 activity predominantly in the intestinal mucosa), on the last of 4 daily administrations. Concomitant administration of grapefruit juice resulted in doubling the bioavailability of budesonide compared to budesonide alone.

##### Proton Pump Inhibitors

The pharmacokinetics of TARPEYO have not been evaluated in combination with proton pump inhibitors (PPIs). Since the disintegration of TARPEYO is pH dependent, the release properties and uptake of budesonide may be altered when TARPEYO is taken after treatment with PPIs. In a study assessing intragastric and intraduodenal pH in healthy volunteers after repeated dosing with the PPI omeprazole 40 mg once daily, intragastric and intraduodenal pH did not exceed that required for disintegration of TARPEYO. Beyond the duodenum, PPIs such as omeprazole are unlikely to affect pH.

##### Oral Contraceptives (CYP3A4 Substrates)

In a parallel study, the pharmacokinetics of budesonide were not significantly different between healthy female subjects who received oral contraceptives containing desogestrel 0.15 mg and ethinyl estradiol 30  $\mu$ g and healthy female subjects who did not receive oral contraceptives. Budesonide 4.5 mg once daily for one week did not affect the plasma concentrations of ethinyl estradiol, a CYP3A4 substrate. The effect of budesonide 16 mg once daily on the plasma concentrations of desogestrel and ethinyl estradiol was not studied.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies with budesonide were conducted in rats and mice. In a two-year study in Sprague-Dawley rats, budesonide caused a statistically significant increase in the incidence of gliomas in male rats at an oral dose of 50 mcg/kg (approximately 0.03 times the maximum recommended human dose (MRHD) on a body surface area basis). In addition, there were increased incidences of primary hepatocellular tumors in male rats at 25 mcg/kg (approximately 0.015 times the MRHD on a body surface area basis) and above. No tumorigenicity was seen in female rats at oral doses up to 50 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis). In an additional two-year study in male Sprague-Dawley rats, budesonide caused no gliomas at an oral dose of 50 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis). However, it caused a statistically significant increase in the incidence of hepatocellular tumors at an oral dose of 50 mcg/kg (approximately 0.03 times the MRHD of a body surface area basis). The concurrent reference corticosteroids (prednisolone and triamcinolone acetonide) showed similar findings. In a 91-week study in mice, budesonide caused no treatment-related carcinogenicity at oral doses up to 200 mcg/kg (approximately 0.06 times the MRHD on a body surface area basis).

Budesonide was not genotoxic in the Ames test, the mouse lymphoma cell forward gene mutation (TK<sup>-/-</sup>) test, the human lymphocyte chromosome aberration test, the *Drosophila melanogaster* sex-linked recessive lethal test, the rat hepatocyte UDS test and the mouse micronucleus test.

In rats, budesonide had no effect on fertility at subcutaneous doses up to 80 mcg/kg (approximately 0.05 times the MRHD on a body surface area basis). However, it caused a decrease in prenatal viability and viability in pups at birth and during lactation, along with a decrease in maternal food consumption and body weight gain, at subcutaneous doses of 20 mcg/kg (approximately 0.012 times the MRHD on a body surface area basis) and above. No such effects were noted at 5 mcg/kg (approximately 0.003 times the MRHD on a body surface area basis).

## 14 CLINICAL STUDIES

### 14.1 Treatment of IgAN

The effect of TARPEYO on proteinuria was assessed in a randomized, double-blind, multicenter study (Nef-301, NCT: 03643965) in patients with biopsy-proven IgAN, eGFR  $\geq 35$  mL/min/1.73 m<sup>2</sup>, and proteinuria (defined as either  $\geq 1$  g/day or UPCR  $\geq 0.8$  g/g) who were on a stable dose of maximally-tolerated RAS inhibitor therapy. Patients with other glomerulopathies, nephrotic syndrome, or those who had been treated with systemic immunosuppressive medications were excluded. Patients were randomized 1:1 to either TARPEYO 16 mg once daily or placebo and treated for nine months followed by a 2-week taper of either TARPEYO 8 mg once daily or placebo.

Of the 199 patients who completed the Month 9 visit, 68% were male, 86% were Caucasian, 12% were Asian, and 16% were from the US. The median age was 44 years (range 23 to 73 years). At baseline, the mean eGFR was approximately 58 mL/min/1.73 m<sup>2</sup>, with 62% of patients having an eGFR  $< 60$  mL/min/1.73 m<sup>2</sup>. The mean baseline UPCR was 1.6 g/g and 25% of patients had proteinuria  $> 3.5$  g/24 hours. Approximately 73% of patients had a history of hypertension and 5% had a history of type 2 diabetes mellitus. At baseline, 98% were treated with an ACE inhibitor or ARB and  $< 1\%$  of patients were on an SGLT2 inhibitor.

The primary endpoint was the percentage reduction in UPCR at 9 months compared to baseline. The results are shown in Table 2.

**Table 2: Analysis of the primary efficacy endpoint at 9 months in Phase 3 Study Nef-301**

Primary Endpoint: UPCR g/g <sup>a</sup>	TARPEYO 16 mg (N=97)	Placebo (N=102)
Percentage reduction from baseline (Adjusted for baseline) <sup>b</sup>	34%	5%
TARPEYO 16 mg versus Placebo : Percentage reduction (95% CI) <sup>c</sup> ; 2-sided p-value	31% (16% to 42%); p=0.0001	

<sup>a</sup> All patients with a UPCR reading regardless of use of prohibited medication at 9 months.

<sup>b</sup> Adjusted geometric least squares mean ratio of UPCR relative to baseline were based on a longitudinal repeated measures model.

<sup>c</sup> The estimate of the ratio of geometric mean ratio of UPCR relative to baseline comparing TARPEYO 16 mg with placebo was reported as percentage reduction along with the respective 95% confidence interval from the longitudinal repeated measures model and p-values.

CI: confidence interval; UPCR: urine protein creatinine ratio.

The treatment effect for the UPCR endpoint at 9 months were consistent across key subgroups, including key demographic (such as age, sex, race) and baseline disease (such as baseline proteinuria) characteristics.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

TARPEYO (budesonide) delayed release capsules 4 mg, are white opaque-coated capsules marked with "CAL10 4 MG" in black ink on the body of the capsule. They are supplied as follows: NDC 81749-004-01: Bottles of 120 capsules. Child-resistant cap.

Store at 20-25°C (68 - 77°F); excursions permitted to 15° to 30°C (59° to 86°F). [See USP Controlled Room Temperature].

Keep container tightly closed. Protect from moisture.

## 17 PATIENT COUNSELING INFORMATION

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

Advise patients that TARPEYO may cause hypercorticism and adrenal axis suppression and to follow a taper schedule, as instructed by their healthcare provider if discontinuing therapy [see *Warnings and Precautions* (5.1)].

TARPEYO causes immunosuppression. Advise patients to avoid exposure to people with chicken pox or measles and, if exposed, to consult their healthcare provider immediately. There is an increased risk of developing a variety of infections, including worsening of existing tuberculosis, fungal, bacterial, viral or parasitic infections, or ocular herpes simplex, and to contact their healthcare provider if they develop any symptoms of infection [see *Warnings and Precautions* (5.3)]. Provide advice regarding vaccination schedules for immunocompromised patients.

Advise patients that TARPEYO delayed release capsules should be swallowed whole and not chewed, crushed or broken and to take TARPEYO in the morning, at least 1 hour before a meal [See *Dosage and Administration* (2)].

Advise patients to avoid the consumption of grapefruit juice for the duration of their TARPEYO therapy [See *Drug Interactions* (7.1)].

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### Manufactured for and distributed by:

Calliditas Therapeutics AB  
Stockholm, Sweden

Patent: <http://www.calliditas.com/patents>

**Patient Information**  
**TARPEYO (tar-PAY-oh)**  
**(budesonide)**  
**delayed release capsules**

**What is TARPEYO?**

TARPEYO is a prescription medicine used to reduce levels of protein in the urine (proteinuria) in adults with a kidney disease called primary immunoglobulin A nephropathy (IgAN), who are at high risk of disease progression.

It is not known if TARPEYO is safe and effective in children.

**Do not take TARPEYO if you are allergic to budesonide or any of the ingredients in TARPEYO. See the end of this leaflet for a complete list of ingredients in TARPEYO.**

**Before taking TARPEYO, tell your healthcare provider about all of your medical conditions, including if you:**

- have liver problems.
- plan to have surgery.
- have chickenpox or measles or have recently been near anyone with chickenpox or measles.
- have an infection.
- have high blood sugar levels (prediabetes or diabetes).
- have glaucoma or cataracts.
- have a family history of diabetes or glaucoma.
- have or have had tuberculosis.
- have high blood pressure (hypertension).
- have decreased bone mineral density (osteoporosis).
- have stomach ulcers.
- are pregnant or plan to become pregnant. TARPEYO may harm your unborn baby. Talk to your healthcare provider about the possible risk to your unborn baby if you take TARPEYO when you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if TARPEYO passes into your breast milk or if it will affect your baby. Talk to your healthcare provider about the best way to feed your baby during treatment with TARPEYO.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TARPEYO and other medicines may affect each other causing side effects.

**How should I take TARPEYO?**

- Take TARPEYO exactly as your healthcare provider tells you.
- Your healthcare provider will decide how long you should take TARPEYO. Do not stop taking TARPEYO without first talking with your healthcare provider.
- Take your prescribed dose of TARPEYO 1 time each day in the morning, at least 1 hour before a meal.
- Take TARPEYO capsules whole. **Do not** open, chew, crush, or break TARPEYO capsules before swallowing.
- If you miss a dose of TARPEYO, take your prescribed dose at your next scheduled time. **Do not** take two doses of TARPEYO at the same time.
- If you take too much TARPEYO, call your healthcare provider right away or go to the nearest hospital emergency room.

**What should I avoid while taking TARPEYO?**

**Do not** eat grapefruit or drink grapefruit juice during your treatment with TARPEYO. Eating grapefruit or drinking grapefruit juice can increase the level of TARPEYO in your blood.

**What are the possible side effects of TARPEYO?**

**TARPEYO may cause serious side effects, including:**

- **Effects of having too much corticosteroid medicine in your blood (hypercorticism).** Long-time use of TARPEYO can cause you to have signs and symptoms of too much cortisol, a stress hormone in your blood. Tell your healthcare provider if you have any of the following signs and symptoms of hypercorticism:
  - acne
  - thicker or more hair on your body and face
  - bruise easily
  - a fatty pad or hump between your shoulders (buffalo hump)
  - rounding of your face (moon face)
  - pink or purple stretch marks on the skin of your abdomen, thighs, breasts, or arms
  - ankle swelling



• **Adrenal suppression.** When TARPEYO is taken for a long period of time (chronic use), adrenal suppression can happen. This is a condition in which the adrenal glands do not make enough steroid hormones. Symptoms of adrenal suppression include:

- tiredness
- weakness
- nausea and vomiting
- low blood pressure

Tell your healthcare provider if you are under stress or have any symptoms of adrenal suppression during treatment with TARPEYO.

• **Risk of immunosuppression.** TARPEYO weakens your immune system. Taking medicines that weaken your immune system makes you more likely to get infections. Avoid contact with people who have contagious diseases, such as chickenpox or measles, during treatment with TARPEYO. Tell your healthcare provider right away if you come in contact with anyone who has chickenpox or measles. Consult with your healthcare provider regarding appropriate vaccination scheduling.

• Tell your healthcare provider if you develop any symptoms of infection during treatment with TARPEYO, including:

- fever
- feeling tired
- chills
- aches
- pain
- nausea and vomiting

**The most common side effects of TARPEYO include:**

- high blood pressure
- swelling of the lower legs, ankles, and feet
- muscle cramp
- acne
- irritation or inflammation of the skin
- weight increase
- shortness of breath
- swelling of the face
- indigestion
- tiredness
- thicker or more hair on your body and face

These are not all the possible side effects of TARPEYO.

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 TARPEYO?**

- Store TARPEYO at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep TARPEYO in a tightly closed container.
- Protect from moisture.

**Keep TARPEYO and all medicines out of the reach of children.**

**General information about the safe and effective use of TARPEYO.**

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

**What are the ingredients in TARPEYO?**

**Active ingredient:** budesonide

**Inactive ingredients:** sugar spheres (sucrose and starch), hypromellose, polyethylene glycol, citric acid monohydrate, ethyl cellulose, medium chain triglycerides and oleic acid.

The capsules contain: hypromellose and titanium oxide (E171).

The printing ink on the capsules contain: shellac, propylene glycol and black iron oxide (E172).

The enteric coating on the capsules contain: methacrylic acid and methacrylate copolymer, talc and dibutyl sebacate.

Manufactured for and distributed by: Calliditas Therapeutics AB, Stockholm, Sweden

TARPEYO is a registered trademark of Calliditas Therapeutics AB, or its affiliates.

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Patent: <http://www.calliditas.com/patents>

For more information, go to [www.TARPEYOTouchpoints.com](http://www.TARPEYOTouchpoints.com) or call 1-933-444-8277.