Evrysdi™
risdiplam
60 mg
powder for oral solution

FOR TREATMENT OF SPINAL MUSCULAR ATROPHY IN ADULTS AND CHILDREN 2 MONTHS OF AGE AND OLDER

INTERACTIVE FACT SHEET

Genentech
A Member of the Roche Group

MEDIA INQUIRIES:
(650) 467-6800

INDICATIONS AND USAGE

Evrysdi is a survival of motor neuron 2 (SMN2) splicing modifier indicated for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older.

IMPORTANT SAFETY INFORMATION

Before taking Evrysdi, patients should tell their doctor if they have liver problems, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed. Evrysdi may harm an unborn or breastfed baby. Evrysdi may affect a man's ability to have children (fertility). Patients should tell their doctor about all the medicines they take.

These are not all the possible side effects of Evrysdi.

ABOUT EVRYSDI | ABOUT SMA | HOW EVRYSDI MAY WORK | CLINICAL TRIAL PROGRAM | FIREFISH | SUNFISH | SAFETY DATA

Please see additional Important Safety Information throughout this document and the full **Prescribing Information**.

M-US-00004830(v1.0)

EVRYSDI™ (RISDIPLAM) IS APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION (FDA) FOR TREATMENT OF SPINAL MUSCULAR ATROPHY (SMA) IN ADULTS AND CHILDREN 2 MONTHS OF AGE AND OLDER:

Evrysdi

DEMONSTRATED CLINICALLY-MEANINGFUL IMPROVEMENTS IN MOTOR FUNCTION

in people with **varying ages and levels of disease severity,** including Types 1, 2, and 3 SMA, as seen across two clinical trials

Evrysdi helped infants **survive without permanent ventilation*** and **achieve a key motor milestone not normally seen** in the natural course of the disease

- 90% were alive without permanent ventilation at 12 months of treatment and reached 15 months of age or older
- 81% were alive without permanent ventilation at 23 months of treatment and reached 28 months of age or older
- 41% achieved the ability to sit without support for at least 5 seconds (as measured by Item 22 on the BSID-III gross motor scale**)
- As described in the natural history of untreated infantile-onset SMA, infants would not be expected to be able to sit independently, and only 25% would be expected to survive without permanent ventilation beyond 14 months of age

Evrysdi demonstrated a favorable efficacy and safety profile in clinical trials

In children and adults with later-onset SMA, those treated with Evrysdi had a **significantly greater change in motor function** (n=115) from baseline at 12 months vs placebo (n=60)***, as measured by MFM-32**** (1.55-point difference between the means)*****

- Evrysdi demonstrated a 1.36-point mean change from baseline vs a −0.19-point mean change from baseline for placebo at month 12

Evrysdi is being studied in more than 450 people as part of a large and robust clinical trial program designed to represent a **broad spectrum of people living with SMA**

The 1st and only **at-home administered treatment for SMA**

** Permanent ventilation defined as requiring a tracheostomy or more than 21 consecutive days of either non-invasive ventilation (≥ 16 hours per day) or intubation, in the absence of an acute reversible event*

*** BSID-III is an assessment used to evaluate development in infants and toddlers 1 to 42 months of age. The gross motor subscale was adapted for use in symptomatic infants with Type 1 SMA. Sitting was one of the motor functions measured.*

**** Based on the missing data rule for MFM-32, 6 patients were excluded from the analysis (Evrysdi n=115; placebo control n=59)*

*****The MFM-32 scale has the ability to assess a wide range of motor function across a broad range of SMA patients; total MFM-32 score is expressed as a percentage of the maximum possible score, with higher scores indicating greater motor function. MFM-32 measures motor function abilities which relate to important daily functions*

****** Evrysdi™ (risdiplam) Prescribing Information. Genentech, Inc. July 2020*

What is Evrysdi?

Evrysdi is a prescription medicine used to treat spinal muscular atrophy (SMA) in adults and children 2 months of age and older.

It is not known if Evrysdi is safe and effective in children under 2 months of age.

IMPORTANT SAFETY INFORMATION

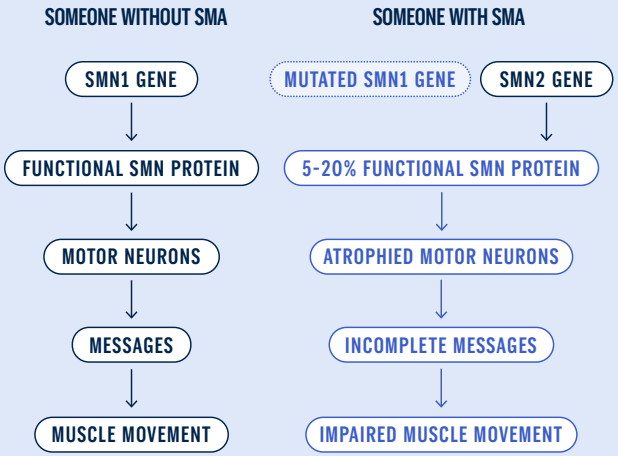
- Before taking Evrysdi, patients should tell their healthcare provider about all of their medical conditions, including if they:
  - have liver problems

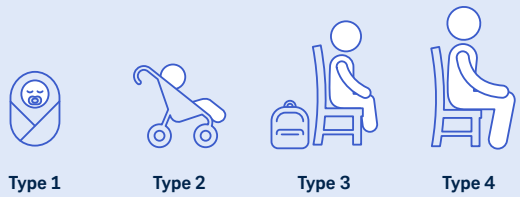
ABOUT SMA:

SMA is a severe, progressive neuromuscular disease that can be fatal. It affects approximately one in 10,000 babies and is the leading genetic cause of infant mortality.

SMA is caused by a mutation in the survival motor neuron 1 (SMN1) gene that results in a **deficiency of SMN protein**, leading to the progressive loss of nerve cells (motor neurons) in the spinal cord that control muscle movement.

SMA affects people differently. There are **four primary types of SMA** (1, 2, 3 and 4) based on the age symptoms begin and the highest physical milestones reached. Disease severity is also correlated to the number of SMN2 gene copies a person has.





Depending on severity, SMA causes muscle weakness over time and can impact a person's ability to perform daily tasks such as

WALKING, EATING, BREATHING

AND MANY OTHERS.

IMPORTANT SAFETY INFORMATION

- Before taking Evrysdi, patients should tell their healthcare provider about all of their medical conditions, including if they:
  - are pregnant or plan to become pregnant. If patients are pregnant, or are planning to become pregnant, they should ask their healthcare provider for advice before taking this medicine. Evrysdi may harm one's unborn baby.
  - are a woman who can become pregnant:
    - Before patients start their treatment with Evrysdi, their healthcare provider may test them for pregnancy. Because Evrysdi may harm one's unborn baby, one's healthcare provider will decide if taking Evrysdi is right for them during this time

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HOW EVRYSDI IS DESIGNED TO WORK:

Evrysdi is designed to treat SMA by

INCREASING PRODUCTION OF SMN PROTEIN

A survival of motor neuron 2 (SMN2) splicing modifier, Evrysdi is designed to treat patients with spinal muscular atrophy (SMA) caused by mutations in chromosome 5q that lead to SMN protein deficiency. More specifically, Evrysdi **was shown to increase the inclusion of exon 7,** a key building block for making full-length SMN protein, in SMN2 messenger RNA (mRNA). In preclinical studies, Evrysdi was shown to cross the blood-brain barrier to increase SMN protein throughout the body.*

**Evrysdi may cause alternative splicing of additional genes*

An increase in production of full-length SMN protein is essential to the health and functioning of motor neurons and their ability to send signals to the muscles in the body to move. In clinical trials, on average, treatment with Evrysdi led to an increase in SMN protein with a greater than two-fold median change from baseline within four weeks of treatment initiation. The increase was sustained across all SMA types for at least 12 months of treatment.

Delivery and Administration:

Delivered directly to patients via a specialty pharmacy

Strawberry-flavored liquid that can be taken by mouth once daily after a meal or breastfeeding, or given by feeding tube

Either self-administered or administered with the help of a caregiver

Recommended dose based on age and weight

IMPORTANT SAFETY INFORMATION

- Before taking Evrysdi, patients should tell their healthcare provider about all of their medical conditions, including if they:
  - Patients should talk to their healthcare provider about birth control methods that may be right for them. Patients should use birth control while on treatment and for at least 1 month after stopping Evrysdi
  - are an adult male planning to have children: Evrysdi may affect a man's ability to have children (fertility). If this is of concern to patients, they should make sure to ask a healthcare provider for advice
  - are breastfeeding or plan to breastfeed. It is not known if Evrysdi passes into breast milk and may harm one's baby. If patients plan to breastfeed, they should discuss with their healthcare provider about the best way to feed one's baby while on treatment with Evrysdi

COMPREHENSIVE CLINICAL TRIAL PROGRAM:

Evrysdi is being studied in a large and robust clinical trial program, including

MORE THAN 450 PEOPLE

ranging in age from 2 months to 60 years

This approval is based on data from two pivotal clinical studies designed to represent a broad spectrum of people living with SMA: FIREFISH in symptomatic infants aged 2 to 7 months; and SUNFISH in children and adults aged 2 to 25 years, including:

- Older infants (2-7 months)
- Those over age 18
- People with scoliosis or joint contractures

For more information on the clinical studies:

FIREFISH SUNFISH

IMPORTANT SAFETY INFORMATION

- **Patients should tell their healthcare provider about all the medicines they take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Patients should keep a list of them to show their healthcare provider and pharmacist when they get a new medicine
- Patients should receive Evrysdi from the pharmacy as a liquid that can be given by mouth or through a feeding tube. The liquid solution is prepared by the patient's pharmacist. If the medicine in the bottle is a powder, **do not use it**. The patient should contact their pharmacist for a replacement

FIREFISH

Two-part open-label pivotal study designed to assess Evrysdi safety, tolerability and efficacy as well as the drug's movement in the body (pharmacokinetics or PK) and the body's reaction to the drug (pharmacodynamics or PD)

- Part 1 (n=21) determined the dose for Part 2
  - Included **infants aged 2 to 7 months with Type 1 SMA**
  - Efficacy was established on survival without permanent ventilation and the ability to sit, specifically the proportion of **infants sitting without support for at least 5 seconds** at 12 months of treatment assessed by the Gross Motor Scale of the Bayley Scales of Infant and Toddler Development Third Edition (BSID-III)*

Data from FIREFISH Part 1 showed:

After 12 months of treatment with Evrysdi, **90% (19/21) of infants were alive without permanent ventilation**** and reached 15 months of age or older.

- In the natural history of infantile-onset SMA, only 25% of infants would be expected to survive without permanent ventilation beyond 14 months of age

After a minimum of 23 months of treatment with Evrysdi, **81% (17/21) of infants were alive without permanent ventilation**** and reached an age of 28 months or older; median 32 months; range 28 to 45 months.

After 12 months of treatment with the recommended dose of Evrysdi, **41% (7/17) of infants were able to sit without support for at least 5 seconds** as measured by the BSID-III gross motor scale.*

- In the natural history of infantile-onset SMA, infants would not be expected to be able to sit independently

** BSID-III is an assessment used to evaluate development in infants and toddlers 1 to 42 months of age. The gross motor subscale was adapted for use in symptomatic infants with Type 1 SMA. Sitting was one of the motor functions measured.*

*** Permanent ventilation defined as requiring a tracheostomy or more than 21 consecutive days of either non-invasive ventilation (≥ 16 hours per day) or intubation, in the absence of an acute reversible event*

**** 1 patient could not swallow at baseline and 1 infant died in recommended dose cohort (determined by the investigator not to be related to Evrysdi)*

IMPORTANT SAFETY INFORMATION

- Avoid getting Evrysdi on one's skin or in one's eyes. If Evrysdi gets on one's skin, wash the area with soap and water. If Evrysdi gets in one's eyes, rinse one's eyes with water
- The most common side effects of Evrysdi include:
  - For infantile-onset SMA:
    - fever
    - diarrhea
    - rash
    - runny nose, sneezing, sore throat, and cough (upper respiratory infection)
    - lung infection
    - constipation
    - vomiting

SUNFISH

Two-part, multi-center clinical trial designed to assess Evrysdi tolerability, safety, efficacy, PK, and PD

- Part 1 was dose-finding and exploratory, pivotal Part 2 was randomized, double-blind and placebo-controlled
- Included **people aged 2 to 25 with Type 2 or 3 SMA**
  - In Part 2, at baseline, 67% of patients had scoliosis (32% of them with severe scoliosis)
  - Patients were randomized 2:1 to receive either Evrysdi at the recommended dose or placebo
- Part 2: Primary endpoint was mean **change from baseline in the Motor Function Measure (MFM-32*) total score** after one year of treatment with Evrysdi, compared to placebo

Data at month 12 from SUNFISH Part 2 showed:

Evrysdi-treated patients had a significantly greater change in motor function (n=115) from baseline vs placebo (n=60)**, as measured by MFM-32 (1.55-point difference between the means; 95% CI: 0.30, 2.81; p=0.0156)***

Evrysdi demonstrated a 1.36-point mean change from baseline (95% CI: 0.61, 2.11) vs a –0.19-point mean change from baseline for placebo (95% CI: –1.22, 0.84)

The percentage of Evrysdi-treated patients who had a change in baseline MFM-32 total score of 3 or more (95% CI) was 38.3% (28.9, 47.6), compared to 23.7% (12.0, 35.4) for placebo

Additionally, Evrysdi treatment was shown to **improve upper limb motor function in children and adults** compared to baseline, as measured by the Revised Upper Limb Module (RULM)****, a secondary endpoint of the study (1.59 point difference; p=0.0028) between the means in Evrysdi and placebo groups (1.61 points [95% CI: 1.00, 2.22]; 0.02 [95% CI: -0.83, 0.87]), respectively.

* *The MFM-32 scale has the ability to assess a wide range of motor function across a broad range of SMA patients; total MFM-32 score is expressed as a percentage of the maximum possible score, with higher scores indicating greater motor function. MFM-32 measures motor function abilities which relate to important daily functions*

** *Based on the missing data rule for MFM-32, 6 patients were excluded from the analysis (Evrysdi n=115; placebo control n=59)*

*** *Evrysdi™ (risdiplam) Prescribing Information. Genentech, Inc. July 2020*

**** *RULM assesses the ability to push, pull, place, tear, open, raise, and lift objects, as well as hand, arm, and reaching movements in children and adults with SMA. It can capture progressive muscle weakness across the spectrum of SMA, reflective of the SUNFISH Part 2 study population*

IMPORTANT SAFETY INFORMATION

The most common side effects of Evrysdi include:

- For later-onset SMA:
  - fever
  - diarrhea
  - rash

These are not all of the possible side effects of Evrysdi. For more information on the risk and benefits profile of Evrysdi, patients should ask their healthcare provider or pharmacist. Patients may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. Patients may also report side effects to Genentech at 1-888-835-2555.

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SAFETY DATA:

The adverse reaction profile of Evrysdi was **evaluated in pediatric and adult SMA patients** across the FIREFISH and SUNFISH clinical trials:

Most common adverse reactions in later-onset SMA (incidence at least 10% of Evrysdi patients and more frequently than control) were fever*, diarrhea, and rash**

Most common adverse reactions in infantile-onset SMA were similar to those observed in later-onset SMA patients. Additionally, adverse reactions with an incidence of at least 10% were upper respiratory tract infection***, pneumonia, constipation, and vomiting

There were no treatment-related safety findings leading to withdrawal from either study. These are not all the possible side effects of Evrysdi. For more information, patients should speak with their healthcare professional.

** Includes pyrexia and hyperpyrexia*

*** Includes rash, erythema, rash maculo-papular, rash erythematous, rash papular, dermatitis allergic, and folliculitis*

**** Includes nasopharyngitis, rhinitis, respiratory tract infection*

The Evrysdi clinical development program was led by Genentech as part of a collaboration with the SMA Foundation and PTC Therapeutics

IMPORTANT SAFETY INFORMATION

Please see full Prescribing Information for additional Important Safety Information.

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For more information, go to www.Evrysdi.com or call 1-833-387-9734.