HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use WELGEMDA safely and effectively. See full prescribing information for WELGEMDA.

WELGEMDA™ (ribitol) for oral solution
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------
WELGEMDA is indicated for the treatment of limb-girdle muscular dystrophy type 2I/R9 (LGMD2I/R9) in adult and pediatric patients weighing at least 30 kg. (1)

----------DOSAGE AND ADMINISTRATION----------
Recommended dosage:
- Patients weighing 30 kg to 50 kg: 9 g orally twice daily. (2.1)
- Patients weighing more than 50 kg: 12 g orally twice daily. (2.1)
- Take with or without food at approximately the same times each day. (2.1)
- WELGEMDA must be reconstituted prior to administration. See Full Prescribing Information for reconstitution instructions. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
For oral solution: 9 g or 12 g per packet (3)

----------CONTRAINDICATIONS----------
None. (4)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥10%) were diarrhea, abdominal pain, nausea, arthralgia, dyspepsia, influenza, and flatulence. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact BridgeBio Pharma, Inc. at 1-844-550-2246 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Issued: 11/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

WELGEMDA is indicated for the treatment of limb-girdle muscular dystrophy type 2I/R9 (LGMD2I/R9) in adult and pediatric patients weighing at least 30 kg.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage of WELGEMDA is based on body weight as follows:

- 30 kg to 50 kg: 9 g orally twice daily
- greater than 50 kg: 12 g orally twice daily

Take WELGEMDA with or without food at approximately the same times each day.

WELGEMDA must be reconstituted prior to administration. Prepare WELGEMDA as instructed below *[see Dosage and Administration (2.3)]*.

2.2 Missed Dose

If a dose of WELGEMDA is missed, administer the missed dose as soon as possible within a 4-hour window of the missed dose and administer the next dose at the regularly scheduled time. Otherwise, skip the missed dose, and administer the next dose at the regularly scheduled time.

If a dose is not fully swallowed or vomiting occurs after taking a dose of WELGEMDA, do not administer another dose to make up for the missed dose. Wait and administer the next dose at the regularly scheduled time.

2.3 Preparation of Oral Solution

Reconstitute WELGEMDA with room temperature water immediately prior to oral administration. Do not open a packet until ready to prepare and administer a dose.

It is recommended that a healthcare provider discuss with the patient or caregiver how to prepare WELGEMDA prior to administration of the first dose.

Preparation of WELGEMDA

- Empty the entire contents of one packet of WELGEMDA into an empty cup.
- Add approximately 120 mL of room temperature water into the cup and stir until dissolved. This may take 2 minutes or more. The solution may appear slightly hazy but should be free of undissolved solids.
- Take the dose immediately following reconstitution. Do not store for future use.

3 DOSAGE FORMS AND STRENGTHS

For oral solution: 9 g or 12 g of ribitol as white to off-white granules in single-dose packets.

4 CONTRAINDICATIONS

None.

6 ADVERSE REACTIONS

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.

In Study 1, a randomized, placebo-controlled, double-blind study in patients with LGMD2I/R9 *[see Clinical Studies (14)]*, a total of 74 patients received WELGEMDA. All 74 patients were exposed to WELGEMDA for at least 12 months (median 21 months, range 17-31 months).

In Study 1, patients were randomized to either WELGEMDA (a polyol) or mannitol (a polyol active placebo) to maintain blinding for gastrointestinal adverse reactions that are known to be caused by polyols.

Common adverse reactions (incidence at least 5% in patients treated with WELGEMDA) are presented in Table 1. The most common adverse reactions (incidence at least 10% in patients treated with WELGEMDA) in Study 1 were diarrhea, abdominal pain, nausea, arthralgia, dyspepsia, influenza, and flatulence.

In Study 1, there were no severe or serious adverse reactions of diarrhea.

No discontinuation occurred due to adverse reactions associated with WELGEMDA.

Table 1: Adverse Reactions with a Frequency of ≥5% in Patients Treated with WELGEMDA in Study 1

Adverse Reaction	**WELGEMDA (N=74) %**	**Placebo (Mannitol)[1] (N=38) %**
Diarrhea	39	53
Abdominal Pain[2]	24	37
Nausea	16	8
Arthralgia	15	11
Dyspepsia[3]	11	3
Influenza	11	8
Flatulence	10	26
Contusion	8	3
Altered Sensation/Sensory Disturbance[4]	8	3

Constipation	7	0
Ligament Sprain	7	5
Oropharyngeal Pain	5	3
Pain in Extremity	5	0

[1] The known osmotic laxative effect of oral mannitol may have contributed to the increased frequency of diarrhea, flatulence, and abdominal pain in the placebo group.
[2] Includes similar terms.
[3] Includes gastroesophageal reflux disease and dyspepsia.
[4] Includes hypoesthesia and paresthesia.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on the use of WELGEMDA in pregnant women to inform a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal developmental studies, there were no malformations or embryofetal toxicities noted in rats or rabbits exposed to ribitol at exposures comparable to the maximum recommended human dose (MRHD) during organogenesis; oral administration of ribitol during pregnancy and lactation in rats did not result in any statistically significant findings *(see Data)*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, 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.

There is a pregnancy safety study for WELGEMDA. If a patient becomes pregnant while receiving WELGEMDA, the patient or healthcare provider should report WELGEMDA exposure by contacting BridgeBio Pharma, Inc. at 1-844-550-2246.

Data

Animal Data

No evidence of malformations or embryofetal toxicity was noted in a study in which pregnant rats were administered daily oral doses of 0, 1000, 2000, and 3000 mg/kg/day ribitol during the period of organogenesis. Exposure (AUC) at the highest dose of 3000 mg/kg/day was comparable to that in humans at the MRHD.

No evidence of malformations or embryofetal toxicity was noted in a study in which pregnant rabbits were administered daily oral doses of 0, 200, 600, and 2000 mg/kg/day ribitol during the period of organogenesis. Exposure (AUC) at the highest dose of 2000 mg/kg/day was comparable to that in humans at the MRHD.

Oral administration of 0, 1000, 2000, and 3000 mg/kg/day ribitol during pregnancy and lactation in rats (i.e., gestational day 6 to postnatal day 20) did not result in any statistically significant findings in

the offspring. Exposure (AUC) at the highest dose of 3000 mg/kg/day was comparable to that in humans at the MRHD.

8.2 Lactation

Risk Summary

There are no data to assess the presence of exogenous ribitol or its metabolite in human milk, the effects on the breastfed infant, or the effects on milk production. However, endogenous ribitol is present in human milk. Following oral administration, increased levels of ribitol were detected in rat milk *(see Data).* The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for WELGEMDA and any potential adverse effects on the breastfed infant from WELGEMDA or from the underlying maternal condition.

Data

Endogenous ribitol is naturally present at low levels in rat milk. Oral administration of up to 3000 mg/kg/day ribitol during pregnancy and lactation in rats resulted in approximately 70- to 125-fold increases in ribitol concentration in milk, as well as detection of ribitol in the plasma from nursing pups. There were no statistically significant effects of ribitol on the developing offspring *[see Use in Specific Populations (8.1)].*

8.4 Pediatric Use

The safety and effectiveness of WELGEMDA for the treatment of limb-girdle muscular dystrophy type 2I/R9 have been established in pediatric patients weighing 30 kg or more *[see Clinical Studies (14)]*. The safety and efficacy in pediatric patients were consistent with what was observed in adults in Study 1.

The safety and effectiveness in pediatric patients weighing less than 30 kg have not been established.

Juvenile Animal Data

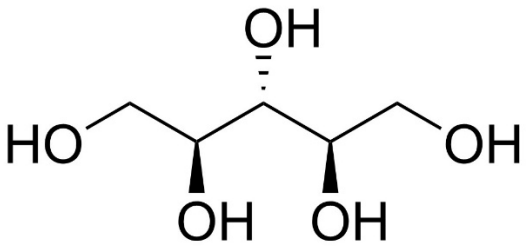
Juvenile male and female rats were administered daily oral doses of 0, 1000, 2000, and 3000 mg/kg/day ribitol from postnatal day (PND) 7 to PND 97. There was decreased sperm density at the mid and high doses. Exposure (AUC) at the no observed adverse effect level of 1000 mg/kg/day was lower than that at the MRHD.

8.5 Geriatric Use

Clinical studies of WELGEMDA did not include patients aged 65 years and older to determine whether they respond differently from younger adult patients.

11 DESCRIPTION

WELGEMDA (ribitol), also known as adonitol, is a pentose alcohol. The chemical name for ribitol is (2*R*,3s,4*S*)-pentane-1,2,3,4,5-pentol. Its molecular formula is $C_5H_{12}O_5$ and its molecular weight is 152.15 g/mol. The molecular structure of ribitol is depicted below:



Ribitol is a white to off-white solid. It is freely soluble in water.

WELGEMDA (ribitol) for oral solution contains 9 g or 12 g of ribitol as white to off-white granules in each packet. The inactive ingredient is colloidal silicon dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ribitol is an endogenous pentose alcohol. The precise mechanism of ribitol in the treatment of limb-girdle muscular dystrophy type 2I/R9 (LGMD2I/R9) is not fully known but may involve increases in plasma ribitol, CDP-ribitol, and ribitol-5-phosphate levels as well as increased expression of matriglycan in muscle tissue.

12.2 Pharmacodynamics

In Study 1 *[see Clinical Studies (14)]*, the least squares (LS) mean change from baseline in glycosylated alpha-dystroglycan (αDG) (% of control) assessed by Western blot at Month 3 was 17.12 in patients treated with WELGEMDA compared to -0.04 in the placebo group ($p<0.0001$). The increase was maintained through Month 12 with the LS mean change from baseline of 23.60 in the WELGEMDA group compared to 0.82 in the placebo group ($p<0.0001$). Glycosylated αDG levels assessed by Western blot can be meaningfully influenced by differences in sample processing, analytical technique, reference materials, and quantitation methodologies. Therefore, comparing glycosylated αDG results from different assay protocols will require a standardized reference material and additional bridging studies.

In Study 1, the baseline mean of serum creatine kinase (CK) was 2449.5 U/L in patients treated with WELGEMDA and 2099.5 U/L in patients who received placebo. At Month 12, the LS mean change from baseline in serum CK was -1869.2 U/L in patients treated with WELGEMDA compared to +186.3 U/L in patients who received placebo ($p<0.0001$) *[see Clinical Studies (14)]*.

Cardiac Electrophysiology

At 1.76 times the mean maximum concentration provided by the maximum recommended dose of 12 g, clinically significant QTc interval prolongation was not observed.

12.3 Pharmacokinetics

Pharmacokinetics of ribitol have been characterized in healthy adult volunteers and patients with LGMD2I/R9. Pharmacokinetics of ribitol are approximately dose-proportional between 3 g and 9 g twice daily after multiple doses. At steady-state, the mean (CV%) C_{max} is 141 (30.8) mcg/mL and $AUC_{0\text{-}24h}$ is 788 (23.2) mcg*h/mL, following the recommended dosage of 9 g or 12 g twice daily (based on body weight).

Absorption

Following oral administration under fasted conditions, the median time to maximum plasma concentration (T_{max}) of ribitol is 1 hour.

Effect of Food

Administration of WELGEMDA with a high-fat, high-calorie meal (approximately 800 to 1000 calories, with approximately 500 to 600 calories from fat, 200 calories from carbohydrate, and 150 calories from protein) decreased C_{max} by 52% with no significant effect on overall exposure (AUC) *[see Dosage and Administration (2.1)].*

Distribution

The mean apparent volume of distribution following 9 g or 12 g twice daily at steady-state is 96.8 L. The plasma protein binding of ribitol is approximately 35%.

Elimination

The apparent oral clearance (CL/F) of ribitol is 30.6 L/h. The mean elimination half-life of ribitol following 9 g or 12 g twice daily at steady-state is approximately 2.30 hours.

Metabolism

In vitro studies indicate that hepatic metabolism of ribitol is limited. Ribulose was a minor metabolite with plasma AUC approximately 3.2% that of ribitol.

Excretion

Ribitol is primarily excreted via glomerular filtration. In healthy subjects following a single dose of 9 g, approximately 18% of the dose is excreted unchanged into the urine.

Specific Populations

No clinically significant effects on the pharmacokinetics of ribitol were observed based on age, sex, race, fukutin-related protein (*FKRP*) mutation status, or mild renal impairment. The pharmacokinetics of ribitol have not been studied in patients with moderate to severe renal impairment or in patients with hepatic impairment.

Drug Interaction Studies

CYP450 Enzymes

Ribitol is not a substrate of CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, or 3A4. Ribitol does not inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6, or 3A4. It does not induce CYP1A2, 2B6, or 3A4.

Transporter Systems

Ribitol is not a substrate or inhibitor of OAT1, OAT3, OCT2, OATP1B1, OATP1B3, MATE1, MATE2-K, BCRP, P-gp, or BSEP. It is not an inhibitor of OCT1.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Long-term animal studies to evaluate the carcinogenic potential of ribitol have not been conducted.

Mutagenesis

Ribitol was negative in the bacterial mutagenicity (Ames) assay, in vitro mammalian cell micronucleus assay in human peripheral blood lymphocytes, and in vivo micronucleus assay in mice.

Impairment of Fertility

Oral administration of 0, 1000, 2000, and 3000 mg/kg/day ribitol prior to and throughout mating in male and female rats resulted in no adverse effects on fertility. Exposure (AUC) at the high dose of 3000 mg/kg/day was comparable to that in humans at the MRHD.

14 CLINICAL STUDIES

The efficacy of WELGEMDA for the treatment of limb-girdle muscular dystrophy type 2I/R9 (LGMD2I/R9) in adult and pediatric patients weighing 30 kg or more was evaluated in a randomized, placebo-controlled, double-blind study in which 112 patients were randomized (2:1) to twice daily oral administration of WELGEMDA (n=74) or placebo (n=38) for 36 months (Study 1; NCT05775848). Randomization was stratified by *FKRP* mutation status (L276I homozygous or other genotypes), age (12 to less than 18 years or 18 to 60 years), and functional qualification status based on performance on clinical endpoints at screening. Patients were required to have a genetically confirmed diagnosis of LGMD2I/R9.

In Study 1, 53 (47%) patients were male, and the age at first treatment ranged from 12 to 60 years (median 37 years). The majority (96%) of patients were White, 0.9% were Black, and 3% were multiple races. Eighty-three (74%) patients were homozygous for the L276I mutation and 29 (26%) patients had other *FKRP* genotypes. Baseline characteristics were largely similar in WELGEMDA and placebo groups, except for sex (53% were male in the WELGEMDA group compared to 37% male in the placebo group).

A preplanned interim analysis was conducted on 73 of 112 patients who were treated for 12 months (WELGEMDA, n=50; placebo, n=23). Multiplicity-protected key functional efficacy outcomes that were assessed at the time of the interim analysis included change from baseline in 100-meter timed test (100MTT) velocity and the change from baseline in the seated forced vital capacity percent predicted (FVC%) following 12 months of treatment with WELGEMDA or placebo.

100MTT velocity, a performance outcome (PerfO), is a fixed-distance (100 meters) ambulatory assessment used to quantify maximal ambulatory ability (time in seconds or speed in meters/second).

FVC, another PerfO, is the total amount of air that can forcibly be exhaled following a deep breath, provided as a percentage of predicted value, with reference baseline based on age, sex, height, and ethnicity.

Among 73 patients contributing to these efficacy analyses, statistically significant improvements in the 100MTT and FVC were seen in the patients treated with WELGEMDA compared to the placebo group after 12 months of treatment (see Table 2).

Table 2: Change From Baseline to Month 12 in the 100MTT velocity and FVC%, Interim Analysis, Study 1

Efficacy Endpoints **Change from Baseline at Month 12***	**WELGEMDA** **(n=74)**	**Placebo** **(n=38)**
100MTT velocity, m/sec		
Number of patients with observed or multiply imputed value	n=40	n=21
Baseline, mean	1.33 m/sec	1.37 m/sec
Change from baseline LS Mean (99% CI)	0.14 (0.08, 0.21)	-0.12 (-0.22, -0.03)
Treatment difference LS Mean (99% CI)	0.27 (0.15, 0.38)	
p-value	<0.0001	
FVC% (seated)		
Number of patients with observed or multiply imputed value	n=35	n=22
Baseline, mean	78.0%	77.2%
Change from baseline LS Mean (99% CI)	2.97 (0.13, 5.81)	-1.92 (-5.64, 1.80)
Treatment difference LS Mean (99% CI)	4.89 (0.21, 9.57)	
p-value	0.0071	

*Based on a mixed model for repeated measures including fixed effects for treatment, visit, treatment-by-visit interaction, stratification factors (mutation status, age group), and baseline value as covariates; unstructured covariance matrix.
Abbreviations: 100MTT, 100-meter timed test; FVC%, forced vital capacity percent predicted; LS, least squares.

Additional exploratory endpoints assessed in Study 1 that were not a part of the preplanned interim analysis included the North Star Assessment for Limb Girdle Muscular Dystrophies (NSAD) and the 10-meter walk test (10MWT).

NSAD, a clinician-reported outcome, is a 29-item scale of motor performance (items suitable for ambulatory and non-ambulatory patients). It uses a point-scale of 0-1 or 0-2 for each item, with a maximum score of 54 points, with higher scores indicating better motor function.

10MWT assesses the velocity at which a patient can walk 10 meters.

At month 12, improvements were seen in the changes from baseline in NSAD and 10MWT in patients treated with WELGEMDA compared to placebo.

The least squares (LS) mean [95% CI] change in the NSAD total score from baseline at month 12 was -1.3 (-2.4, -0.2) in the placebo group (n=22) and 1.3 (0.5, 2.1) in the patients treated with WELGEMDA (n=46), with a treatment difference, 2.6 points [1.3, 4.0].

The LS mean [95% CI] change in the 10MWT velocity from baseline at month 12 was -0.10 m/sec (-0.17, -0.04) in the placebo group (n=19) and 0.13 m/sec (0.09, 0.18) in the patients treated with WELGEMDA (n=36), with a treatment difference, 0.24 m/sec [0.16, 0.31].

16 HOW SUPPLIED/STORAGE AND HANDLING

WELGEMDA (ribitol) for oral solution is supplied as white to off-white granules in child-resistant foil packets in the following package configurations:

- 9 g of ribitol per packet: carton of 56 packets (NDC 82228-009-56)
- 12 g of ribitol per packet: carton of 56 packets (NDC 82228-012-56)

Store WELGEMDA at 20°C to 25°C (68°F to 77°F); excursions are permitted between 15°C to 30°C (59°F to 86°F). Store in the original, sealed packet to protect from moisture and light.

Keep WELGEMDA out of the reach of children.

17 PATIENT COUNSELING INFORMATION

Advise the patient or caregiver:

- To take WELGEMDA twice daily with or without food at approximately the same times each day *[see Dosage and Administration (2.1)]*.
- If a dose of WELGEMDA is missed, take the missed dose as soon as possible within a 4-hour window of the missed dose and take the next dose at the regularly scheduled time. Otherwise, skip the missed dose, and take the next dose at the regularly scheduled time *[see Dosage and Administration (2.2)]*.
- If a dose is not fully swallowed or vomiting occurs after taking a dose of WELGEMDA, do not take another dose to make up for the missed dose. Wait and take the next dose at the regularly scheduled time *[see Dosage and Administration (2.2)]*.
- Reconstitute WELGEMDA with room temperature water immediately prior to oral administration *[see Dosage and Administration (2.3)]*. Advise patients to not open a packet until they are ready to prepare and take a dose.
  - Empty the entire contents of one packet of WELGEMDA into an empty cup.
  - Add approximately 120 mL of room temperature water into the cup.
  - Stir until dissolved. This may take 2 minutes or more. The solution may appear slightly hazy but should be free of undissolved solids.
  - Take the dose immediately following reconstitution. Do not store for future use.
- The patient may experience diarrhea while taking WELGEMDA and should notify their healthcare provider if persistent or worsening diarrhea occurs *[see Adverse Reactions (6.1)]*.

Pregnancy

- Advise patients to inform their healthcare provider if they are pregnant or intend to become pregnant during treatment with WELGEMDA. Advise patients that there is a pregnancy safety study that monitors pregnancy outcomes in women exposed to WELGEMDA during pregnancy, and they may be enrolled by calling BridgeBio Pharma, Inc. at 1-844-550-2246 *[see Use in Specific Populations (8.1)]*.

Manufactured for ML Bio Solutions Inc.,
San Francisco, CA, 94158, USA

Distributed by BridgeBio Pharma, Inc.,
Palo Alto, CA, 94304, USA