Chiesi TOTAL care℠

Lesa, Chiesi Total Care Pharmacist

Revcovi® (elapegademase-lvlr) Starter Kit

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see accompanying Prescribing Information.

Revcovi®
elapegademase-lvlr
injection

Chiesi TOTAL care℠

Getting Started Guide

To get a patient started on Revcovi® (elapegademase-lvlr) follow **2 steps** outlined in this guide.

Visit chiesitotalcare.com or call 1-866-272-7078 – we're ready to help!

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see accompanying Prescribing Information.

Revcovi®
elapegademase-lvlr
injection

Step 1:

Fill out the Physician Order/Prescription & Statement of Medical Necessity Form

Chiesi TOTAL care

Physician Order/Prescription & Statement of Medical Necessity

Revcovi® elapegademase-lvlr injection 1.6 mg/mL

Please fax completed form to Chiesi Total Care℠ staff at 866-272-7079

PATIENT INFORMATION

Patient Name (Last, First) _____

Social Security # _____ - _____ - _____ Sex: ☐ Male ☐ Female Date of Birth _____/_____/_____ (mm/dd/yyyy)

Address _____ City _____ State _____ Zip _____

Primary Phone (Required) _____ Cell Phone _____ Language: ☐ English ☐ Other _____

Parent/Guardian (If applicable) _____ Relationship to Patient _____

CLINICAL INFORMATION

Diagnosis: ☐ Adenosine deaminase severe combined immune deficiency (ADA-SCID) ICD-10 code D81.31 (primary)

☐ Secondary ICD-10 _____ ☐ Other ICD-10 _____

Treatment information

☐ Initial Rx for ADA-SCID ☐ Continuation on ERT ☐ Restart after Gene Therapy ☐ Restart after HSCT

☐ New patient/returning to therapy ☐ Other _____ Allergies: ☐ None ☐ Specify _____

Height _____ inches or _____ cm Weight _____ lb or _____ kg Known Drug Allergies: _____

INSURANCE INFORMATION

Primary Prescription Insurance	**Primary Medical Insurance**	**Secondary Medical Insurance**
Policy Holder	Policy Holder	Policy Holder
Policy ID #	Policy ID #	Policy ID #
Group #	Group #	Group #
Phone	Phone	Phone

☐ Eligible for Medicare ☐ Eligible for Medicaid ☐ No Insurance

Please attach copies of patient insurance and prescription cards—front and back.

REVCOVI (elapegademase-lvlr) PRESCRIPTION/ORDER

Revcovi (elapegademase-lvlr) 2.4 mg/1.5 mL single use vial NDC 10122-502-01 QTY _____ Refills _____

Instructions: Inject _____ mg intramuscularly (IM) _____ times per week.

Provide medical supplies, including syringes and needles, to safely administer prescribed medication.

☐ Skilled nursing visits _____ times for medication administration teaching

PRESCRIBER/OFFICE INFORMATION

Prescriber's Name (Print) _____ Practice/Group Name _____

Address _____ Suite _____

City _____ State _____ Zip _____

Office Contact Person _____

Office Phone _____ Office Fax _____

License # _____ NPI # _____

By signing below, I certify that I am the prescribing provider mentioned above, that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that all the medical necessity information is true, accurate, and complete. The patient's records contain supporting documentation that substantiates the utilization and medical necessity of the products marked above. I provide permission to use my personal information and the personal information of the patient provided above to facilitate this request and complete any regulatory or legal requirements associated with this request. I understand that the personal information provided herein may be shared with Chiesi, successors, and their agents and service providers as needed to support this request. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary for the Chiesi Total Care Program and/or their agents and service providers. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian. If my patient is eligible for free product, I understand that receiving free product is not contingent on any purchase obligations. I also understand that no free product may be submitted for reimbursement to any payer, including Medicare and Medicaid; nor may I bill any payer for administration of such product. I understand that any falsification, omission, or concealment of material fact may result in criminal liability.

Prescriber's Signature _____ _____ Date _____

Substitution Permitted Dispense as Written

Revcovi is available as 2.4 mg/1.5 mL (1.6 mg/mL) intramuscular injection.

Questions? Chiesi Total Care is here to help! Please contact Chiesi Total Care at 866-272-7078 if you have questions regarding this form.

Please see Important Safety Information on the reverse side.

A

B

You may also attach separate instructions.

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

A Specify appropriate ICD-10 Diagnosis code(s) for secondary diagnosis

(Other uses are at prescriber's discretion)

ICD-10 Diagnosis Codes	
Diagnosis	**Current indication**
D81.3	Adenosine deaminase deficiency, unspecified
D81.31	Severe combined immunodeficiency due to adenosine deaminase deficiency
D81.9	Combined immunodeficiency, unspecified

Intended as a reference for coding and billing for product and associated services. Not intended to be a directive, nor does the use of the recommended codes guarantee reimbursement. Providers are responsible for ensuring the accuracy and validity of all billing and claims for appropriate reimbursement.

B Recommended starting dose

0.4 mg/kg/wk based on ideal body weight or actual weight, whichever is greater

Divided into 2 weekly doses for a minimum of 12-24 weeks

Until immune reconstitution is achieved

- Once immune reconstitution is achieved, dose may be gradually adjusted down to maintain trough ADA activity >30 mmol/hr/L, trough dAXP levels <0.02 mmol/L, and/or to maintain adequate immune reconstitution based on the clinical assessment of the patient
- Improvement in the general clinical status of the patient may be gradual but should be apparent by the end of the first year of therapy

Refer to administration guide for details.

Sample dosing assuming 60 kg patient @ 0.4 mg/kg/wk

Instructions: Inject 12 mg

intramuscularly (IM) 2 times per week.

Step 2:

Once you have completed the form:

1. Attach copies of patient insurance and prescription cards – front and back.
2. First prescription for the patient:

   The first copy of the form must be faxed for each patient. Fax completed form to Chiesi Total Care℠ at 1-866-272-7079. **Please complete one form per patient.**
3. Subsequent prescriptions:

   If you wish to send additional forms via e-script please search for "Eversana Life Science Services" in your EMR/HMR's e-prescribing software.

The fillable pdf can be downloaded and saved for future use.

Scan the QR code to download a copy.

FPO

Chiesi TOTAL care℠

Visit chiesitotalcare.com or call 1-866-272-7078 – we're ready to help!

Chiesi Total Care℠ is a comprehensive support program that provides exceptional service to patients and healthcare providers.

A single call to your dedicated Chiesi Total Care team is all it takes, and they will guide you through the process of getting a patient started on Revcovi therapy.

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see full Prescribing Information inside.

References: 1. Revcovi® (elapegademase-lvlr) Prescribing Information. Chiesi USA, Inc.; 2020.

For more information, visit revcovi.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-RV-0101 V1.0 2023

Revcovi®
elapegademase-lvlr
injection

Physician Order/Prescription & Statement of Medical Necessity

Chiesi TOTAL care

Revcovi® elapegademase-lvlr injection 1.6 mg/mL

Please fax completed form to Chiesi Total Care℠ staff at 866-272-7079

PATIENT INFORMATION

Patient Name (Last, First) _____

Social Security # _____ - _____ - _____ Sex: ☐ Male ☐ Female Date of Birth _____/_____/_____ (mm/dd/yyyy)

Address _____ City _____ State _____ Zip _____

Primary Phone (Required) _____ Cell Phone _____ Language: ☐ English ☐ Other _____

Parent/Guardian (If applicable) _____ Relationship to Patient _____

CLINICAL INFORMATION

Diagnosis: ☐ Adenosine deaminase severe combined immune deficiency (ADA-SCID) ICD-10 code D81.31 (primary)

☐ Secondary ICD-10 _____ ☐ Other ICD-10 _____

Treatment information

☐ Initial Rx for ADA-SCID ☐ Continuation on ERT ☐ Restart after Gene Therapy ☐ Restart after HSCT

☐ New patient/returning to therapy ☐ Other _____ Allergies: ☐ None ☐ Specify _____

Height _____ inches or _____ cm Weight _____ lb or _____ kg Known Drug Allergies: _____

INSURANCE INFORMATION

Primary Prescription Insurance	**Primary Medical Insurance**	**Secondary Medical Insurance**
Policy Holder _____	Policy Holder _____	Policy Holder _____
Policy ID # _____	Policy ID # _____	Policy ID # _____
Group # _____	Group # _____	Group # _____
Phone _____	Phone _____	Phone _____

☐ Eligible for Medicare ☐ Eligible for Medicaid ☐ No Insurance

Please attach copies of patient insurance and prescription cards—front and back.

REVCOVI (elapegademase-lvlr) PRESCRIPTION/ORDER

Revcovi (elapegademase-lvlr) 2.4 mg/1.5 mL single use vial NDC 10122-502-01 QTY _____ Refills _____

Instructions: Inject _____ mg intramuscularly (IM) _____ times per week.

Provide medical supplies, including syringes and needles, to safely administer prescribed medication.

☐ Skilled nursing visits _____ times for medication administration teaching

PRESCRIBER/OFFICE INFORMATION

Prescriber's Name (Print) _____ Practice/Group Name _____

Address _____ Suite _____

City _____ State _____ Zip _____

Office Contact Person _____

Office Phone _____ Office Fax _____

License # _____ NPI # _____

By signing below, I certify that I am the prescribing provider mentioned above, that I am part of the Chiesi Total Care Program, that the therapy described above is medically necessary, and that all the medical necessity information is true, accurate, and complete. The patient's records contain supporting documentation that substantiates the utilization and medical necessity of the products marked above. I provide permission to use my personal information and the personal information of the patient provided above to facilitate this request and complete any regulatory or legal requirements associated with this request. I understand that the personal information provided herein may be shared with Chiesi, successors, and their agents and service providers as needed to support this request. I also attest that I have obtained the patient's authorization to release the above information and such other personal information as may be necessary for the Chiesi Total Care Program and/or their agents and service providers. If the patient is 18 years old or younger, I attest that I have obtained permission from the patient's legal guardian. If my patient is eligible for free product, I understand that receiving free product is not contingent on any purchase obligations. I also understand that no free product may be submitted for reimbursement to any payer, including Medicare and Medicaid; nor may I bill any payer for administration of such product. I understand that any falsification, omission, or concealment of material fact may result in criminal liability.

Prescriber's Signature _____ _____ Date _____

Substitution Permitted Dispense as Written

Revcovi is available as 2.4 mg/1.5 mL (1.6 mg/mL) intramuscular injection.

Questions? Chiesi Total Care is here to help! Please contact Chiesi Total Care at 866-272-7078 if you have questions regarding this form.

Please see Important Safety Information on the reverse side.

INDICATION

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

ADVERSE REACTIONS

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

IMPORTANT MONITORING INFORMATION

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see Full Prescribing Information for more information.

For more information, visit revcovi.com/for-healthcare-providers

PP-RV-0038 V2.0

Revcovi®
elapegademase-lvlr
injection 1.6 mg/mL

Patient Enrollment Form

Fax completed form to Chiesi Total Care℠ at 1-866-565-7794 | Phone: 1-866-758-7071

Chiesi Total Care (the "Program") provides product support to eligible patients who have been prescribed a Chiesi USA, Inc. ("Chiesi") product. Program support may include: (1) reimbursement and financial support (such as investigating insurance coverage, confirming out-of-pocket costs, and reviewing eligibility for financial assistance and copay programs); (2) working with patients and pharmacies to fill prescriptions; (3) home infusion support (if applicable); and (4) providing disease-, medication-, and adherence-related educational resources and communications, including access to a Chiesi Patient Education Liaison.

Patient Name:_____ **Date of Birth** (MM/DD/YY)**:**_____

ENROLLMENT INTO CHIESI TOTAL CARE

By signing this authorization form ("Authorization"), I confirm I would like to enroll in the Program and authorize Chiesi USA, Inc., and its affiliates, service providers, agents, and successors (together, "Chiesi") to provide me with Program support. I authorize Chiesi, my healthcare providers, and their staff, my health plan, patient assistance programs, and my pharmacies to process and share my personal health information (such as information about my diagnosis, treatment, and lab results), personal identifying information (such as contact information and program preferences), and insurance information (such as prescriptions and plans) (together my "Information") in order to enroll me in the Program, provide Program support, administer the Program, meet legal obligations, conduct other business activities, and complete government reporting activities. For example, Chiesi may use my Information to communicate with me (such as by mail, phone, email, and text message*), tailor Program-related communications and services to my needs, and share my Information with my healthcare providers to dispense Chiesi products to me. Chiesi may also de-identify my Information, combine it with information about other patients, and use the results for Chiesi's and its affiliate's business purposes. I understand that once my Information is disclosed, my Information may no longer be protected by federal privacy laws and could be re-disclosed. However, Chiesi will only process and disclose my Information as described in this Authorization. Additional information on Chiesi's privacy practices can be found at https://www.chiesiusa.com/privacy-policy/.

I understand that this Program is optional. I can refuse to sign this Authorization and refusing to sign will not affect my treatment, insurance coverage, or eligibility for benefits or Chiesi products. However, I understand that I need to sign this form to participate in the Program.

I understand that I may cancel this Authorization at any time or receive a copy of this Authorization by mailing a letter requesting cancellation to Chiesi Total Care, 17877 Chesterfield Airport Rd, Chesterfield, MO 63005. I may also revoke my authorization to receive automated calls or text messages by replying STOP to any text from Chiesi Total Care or by contacting Chiesi Total Care in writing at the address above. Upon cancellation, to the extent required by applicable law and personal data rights, Chiesi will no longer process my Information. I understand my cancellation will not apply to any of my Information already used or disclosed based on this Authorization prior to receipt of the cancellation. Unless canceled earlier, this Authorization expires ten (10) years from the date signed below, or as otherwise required by state or local law.

By signing below, I acknowledge that my pharmacy will receive payment from Chiesi for disclosing my Information to Chiesi. I acknowledge that if I am eligible for infusion co-pay assistance, the payment will be submitted to my healthcare facility where the infusion occurred. I acknowledge that if I am enrolled in a government-funded healthcare program, I am not eligible for and will not accept any co-pay assistance from Chiesi Total Care. I understand and agree that if my insurance information changes at any time while I am participating in the Chiesi Total Care Program, I will notify Chiesi Total Care as soon as possible, and any such change may affect my eligibility for such assistance programs.

By signing below, I also acknowledge that I have read and agree to the terms and conditions of the Chiesi Total Care support programs on page 2 of this document.

Feedback: We greatly appreciate your feedback. Please indicate whether you would like to be contacted by Chiesi about opportunities for you to provide feedback to us (such as Program feedback surveys or market research):

☐ YES, I would like to be contacted to provide feedback. ☐ NO, I would not like to be contacted to provide feedback.

TEXT: Please indicate whether you authorize Chiesi to send text messages to the number(s) you provide. Your consent to receiving text messages is not a condition of receiving medication or services from Chiesi.

☐ YES, I consent to receive text messages. ☐ NO, I do not consent to receive text messages.

Patient or Legal Guardian Signature: _____ **Signature Date** (MM/DD/YY)**:**_____

Please specify any additional contacts with whom Chiesi Total Care is allowed to discuss your Information:

Additional Contact Name:_____ **Relationship to Patient:**_____

*Additional charges may apply. I understand that my telephone provider may charge me fees for calls or texts I receive, and I agree that Chiesi Total Care will not pay those fees.

Patient Enrollment Form

Fax completed form to Chiesi Total Care℠ at 1-866-565-7794 | Phone: 1-866-758-7071

CHIESI TOTAL CARE TERMS AND CONDITIONS

Chiesi Total Care Patient Support Services Program Terms and Conditions

To enroll in Chiesi Total Care (the "Program") and to assess eligibility for patient support services of the Program, patient must complete the Program Enrollment and Authorization Form and have a valid prescription for an eligible product of the Program. Additional documentation may be required. The patient must be a resident of the United States or one of its territories. If the patient is incapable of acting on their own behalf or if the patient is under 18 years old, enrollment into the Program may be completed by another person acting on their behalf (such as a caregiver).

A patient who receives healthcare benefits under any plan or program funded in whole or in part by federal or state governments including Medicare, Medicaid, TRICARE, Veterans Affairs (VA), State Prescription Assistance Plans (SPAPs) (other than health insurance for federal government employees), or any state healthcare program such as Medicaid, Children's Health Insurance Program, programs funded under Maternal and Child Health Program, or programs funded under Social Services Block Grant (collectively, "Government-funded Plans") are not eligible for the financial patient support services of the Program. A patient covered under a commercial health plan purchased through a health insurance marketplace or exchange is not a government-funded Plan beneficiary even if the costs of such coverage are subsidized by the federal government. If a change in prescription drug coverage should occur, the patient must notify the Program; such change may affect eligibility for the support services provided in the Program. Patients who have prescribed a product for an indication that is not consistent with the US Food and Drug Administration-approved labeling will not be eligible for financial patient support services offered through the Program.

Patients residing in or receiving treatment in certain states may not be eligible for certain patient support services of the Program. Patients may not seek reimbursement for value received from the Program. The Program does not obligate the use of any specific medication or healthcare provider. Patients who receive treatment or reside in Massachusetts, Michigan, Minnesota, or Rhode Island are not eligible for co-pay assistance for infusion services or routine testing services.

Chiesi Total Care may recommend contacting an independent financial assistance foundation. Independent financial assistance foundations have their own rules for eligibility. Chiesi USA does not fund independent financial assistance foundations, nor does Chiesi Total Care have involvement or influence in independent foundation decision making or eligibility criteria and does not know if a foundation will be able to help you. Chiesi Total Care can only refer you to a foundation that supports your disease state. This information is provided as a resource for you. Chiesi Total Care does not endorse or show preference for any foundation. The foundations recommended to you may not be the only ones that might be able to help you.

Chiesi Patient Education Liaisons ("PELs") may be available to assist you with disease education, provide relative educational or informational resources, and to answer questions you may have about your disease. Chiesi Field Reimbursement Managers ("FRMs") may be available to assist you with your product prescription drug coverage, including prior authorization, appeals, and denials.

PELs and FRMs are employees of Chiesi USA, Inc. PELs and FRMs are not healthcare providers and are not part of your healthcare team. PELs or FRMs will not provide medical care or advice. All treatment decisions should be made by you and your treating healthcare professional. To assist you, PELs and FRMs may need your Information. If you choose to opt out of services by PELs and FRMs, you may do so at any time. Please see Chiesi's Privacy Policy at www.chiesiusa.com/privacy-policy/.

Program benefits may not be sold, purchased, traded, or offered for sale, purchase, or trade. The Chiesi Total Care patient support services are not valid where prohibited by law, taxed, or otherwise restricted. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. This is not health insurance.

This is a voluntary program. Patients who choose not to enroll in the Program will be able to receive medication. Patients may participate in Chiesi Total Care without participating in a patient support services program of Chiesi Total Care. After enrolling in Chiesi Total Care, participants may opt out by contacting the Program, as outlined in the Chiesi Total Care Enrollment and Authorization Form. Patients must renew their eligibility by December 31 of each year to continue to receive support under the Program.

By participating in the Program, participants acknowledge that they understand and agree to comply with the Program Terms and Conditions.

PP-G-0606 V3.0

Chiesi TOTAL care℠

Revcovi® (elapegademase-lvlr) Prior Authorization and Access Guide

Visit chiesitotalcare.com or call 1-866-272-7078 – we're ready to help!

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see accompanying Prescribing Information.

Revcovi®
elapegademase-lvlr
injection

Chiesi Total Care℠ will submit for insurance reimbursement and help you navigate prior authorization (PA).

Here's a step-by-step look at the process

1 Submission

Your Chiesi Total Care Team starts the process when a new Rx form has been submitted.

The Chiesi Total Care Team helps you submit PA.

2 Monitoring PA

Chiesi Total Care monitors and tracks PA submission until an outcome is determined by payor.

3

PA is approved	• Your office and/or patient is notified
PA is denied	• Send denial documentation to Chiesi Total Care • Chiesi Total Care can help in denial situations with a high success rate **APPEAL** Based on the letter, Chiesi Total Care can submit a patient level appeal with signed patient consent. OR Your office can submit a physician level appeal. Chiesi Total Care can assist and coach on best practices.* *Chiesi Total Care assistance is neither medical guidance nor a suggestion that you submit an appeal. The resources and information provided in this guide is general in nature and is not intended to be conclusive or exhaustive. As the patient's healthcare provider, you are responsible for applying your clinical judgment regarding appropriate care and treatment of each patient.

4 PA or Appeal Approved

Pharmacy fills Rx and medication is dispensed to the patient

Contact your dedicated Chiesi Total Care program specialist with any questions you may have about your case.

PA denied? Chiesi Total Care is here to help.

It's not uncommon for the first PA submission to be denied. With a long track record of success in gaining PA and appeal approvals, Chiesi Total Care is here to provide assistance with the appeal process. Chiesi Total Care will assist in providing additional resources and/or publications depending on the reasons for denial. To request a copy of an additional resource or publication, please reach out directly to us.medical@chiesi.com.

Visit chiesitotalcare.com or call 1-866-272-7078

Chiesi TOTAL care℠

We provide updates on your patient's therapy and alert the office should there be any concerns. We also help patients with injection support for those who receive Revcovi injections at home.

We can help by:

- Provinding injection support
- Counseling patients on managing side effects
- Providing 24/7 pharmacist access
- Enrolling patients in the Revcovi Copay Program – patients may pay as little as $0 if eligible†

Lesa, Chiesi Total Care Pharmacist

† Patients participating in government-funded plans may not participate in programs that provide financial support. Please refer to the full Terms and Conditions in the back pocket for additional eligibility requirements.

Here is a checklist of best practices for Prior Authorization submission:

- ☐ Include pertinent clinical notes, dates, and laboratory findings including diagnosis confirmation
- ☐ Include prescribing practitioner NPI number and contact information
- ☐ Include medical rationale for why the patient cannot receive a bone marrow transplant
- ☐ Include therapeutic alternatives that were tried in the past, include documentation as to why it was inadequate

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see full Prescribing Information inside.

References: **1.** Revcovi® (elapegademase-lvlr) Prescribing Information. Chiesi USA, Inc.; 2020.

For more information, visit revcovi.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-RV-0102 V1.0 2023

Revcovi®
elapegademase-lvlr
injection

Sample Letter of Medical Necessity

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the steps above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing this letter of medical necessity on behalf of **[Patient Name, ID#, Group #]** to request coverage for **[Product name (generic name)].** Included in this letter of medical necessity is information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [As required]

Sample Letter of Appeal

Using this template:

- ☐ Fill in the template using the instructions highlighted in blue.
- ☐ Once you have filled in the information, remove any remaining instructions in blue.
- ☐ Select all the text and change the font to black so the whole document appears as one letter.

Use the list above as a checklist to make sure you have completed these steps prior to sending. **It is important to follow these steps to ensure the letter is clear and concise.**

[Insurance Company]
[Address]
[City, State, Zip]

Re: **[Patient Name]**
[Policy #]
[DOB]
[Address]
[City, State, Zip]

To Whom It May Concern:

I am writing to appeal the denial of benefits for the use of **[Product name (generic name)]** for services requested for **[Patient Name, ID#, Group #]**. Included in this letter of appeal are information on the treatment rationale, medical records, medical necessity data and medical studies confirming currently prescribed product as an effective treatment for the diagnosis associated with **[ICD10 Code]**.

Treatment Rationale:
[Provide information on patient response and history to past treatments and anticipated prognosis and rationale for the currently prescribed product].

Outline of Medical Studies:
[Outline a brief overview of the studies evaluating the use of the currently prescribed product in this condition and/or patient population. Remember to include the FDA approved indications and usage].

Medical Record Information:
[Highlight key dates and entries of the medical record how the currently prescribed product is used].

Per the included medical information, it is my professional opinion that the currently prescribed product is medically necessary in treating the patient and the denials for the patient's use of the drug should be reversed. Please call my office at **[Office Phone Number]** if I can provide further information or speak with a review board to appeal the denial of coverage decision. I look forward to reaching resolution of overturning the denied status of the currently prescribed product for this patient.

Sincerely,
[Physician Name and Signature]
[Phone Number]
Enclosure: [Original denial notification copy]

Chiesi TOTAL care℠

Revcovi® (elapegademase-lvlr) Dosing and Administration Guide

Ashley, actual Revcovi patient

Visit chiesitotalcare.com or call 1-866-272-7078 – we're ready to help!

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see accompanying Prescribing Information.

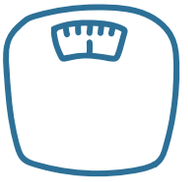
Revcovi®
elapegademase-lvlr
injection

Individualized treatment for your patients with ADA-SCID[1]

Meet each patient's unique needs with individualized dosing and careful lab monitoring.[1]

Therapeutic monitoring helps achieve appropriate dosing[1]

Recommended starting dose[1]



0.4 mg/kg/wk based on ideal body weight or actual weight, whichever is greater

Divided into 2 weekly doses for a minimum of 12-24 weeks

Until immune reconstitution is achieved

- Once immune reconstitution is achieved, dose may be gradually adjusted down to maintain trough ADA activity >30 mmol/hr/L, trough dAXP levels <0.02 mmol/L, and/or to maintain adequate immune reconstitution based on the clinical assessment of the patient[1]
- Improvement in the general clinical status of the patient may be gradual but should be apparent by the end of the first year of therapy[1]

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

Monitoring schedule[1]

	First 3 months of treatment: monitor patients **every 2 weeks**	4-12 months of treatment: monitor patients **every 1-2 months**	1 year+ of treatment: monitor patients **every 3-6 months**
ADA Activity Target trough plasma ADA activity ≥30 mmol/h/L[a]	Every 2 weeks	Every 3-6 months	Every 3-6 months
Erythrocyte dAXP Target trough dAXP levels <0.02 mmol/L	At week 8	Every 6 months	Every 6 months
Total & Subset Lymphocytes Target general improvement[b]	At weeks 4, 8, and 12	Every 1-2 months	Every 3-6 months

a A decrease of ADA activity below 30 mmol/hr/L might suggest noncompliance or a development of antibodies (anti-drug, anti-PEG, and neutralizing antibodies). Test for antibodies to Revcovi if pre-injection trough plasma ADA activity falls below 15 mmol/hr/L consistently. If there is a decline in ADA activity levels, monitor immune function and clinical status more closely and take precautions to minimize the risk of infection.[1]

b Immune function, including the ability to produce antibodies, generally improves after 2-6 months of therapy, and matures over a longer period. Improvement in the general clinical status of the patient may be gradual (as evidenced by improvement in various clinical parameters) but should be apparent by the end of the first year of therapy.[1]

Chiesi TOTAL care℠

Visit chiesitotalcare.com or call 1-866-272-7078 – we're ready to help!

Chiesi Total Care℠ is a comprehensive support program that provides exceptional service to patients and healthcare providers.

A single call to your dedicated Chiesi Total Care team is all it takes, and they will guide you through the process of getting a patient started on Revcovi therapy.

Indication

Revcovi® (elapegademase-lvlr) is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

Important Safety Information

Warnings and precautions

- Injection site bleeding in patients with thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe.
- Delay in improvement of immune function: Protect immune deficient patients from infections until improvement in immune function.

Adverse reactions

The most commonly reported adverse reactions were cough (50%) and vomiting (33%).

In addition, the following post-marketing reports for the same class of enzyme replacement therapy used in the treatment of ADA-SCID may also be seen with Revcovi treatment:

- Hematologic events: hemolytic anemia, autoimmune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological events: injection site erythema, urticaria
- Lymphomas

Important monitoring information

Treatment with Revcovi should be monitored by measuring trough plasma ADA activity and trough dAXP levels for maintenance of therapeutic targets. If a persistent decline in plasma ADA activity occurs, immune function and clinical status should be monitored closely, and precautions should be taken to minimize the risk of infection.

Please see full Prescribing Information inside.

References: 1. Revcovi® (elapegademase-lvlr) Prescribing Information. Chiesi USA, Inc.; 2020.

For more information, visit revcovi.com.
Chiesi Total Care℠ Program offered through EVERSANA Life Science Services Specialty Pharmacy

PP-RV-0103 V1.0 2023

Revcovi® elapegademase-lvlr injection

Chiesi Total Care℠ Patient Support Services Program Terms and Conditions

These terms and conditions apply to the patient support services offered through the Chiesi Total Care Patient Support Program (the "Program") for REVCOVI, unless otherwise noted. These patient support service programs may include affordability solutions support, appeals support, benefit verification, Clinical Nurse support, copay assistance, patient assistance, Pharmacist support, and prior authorization support. Patient support services offered through the Program are subject to change.

A patient who receives health care benefits under any plan or program funded in whole or in part by federal or state governments including Medicare, Medicaid, TRICARE, Veterans Affairs (VA), State Prescription Assistance Plans (SPAPs) (other than health insurance for federal government employees) or any state health care program such as Medicaid, Children's Health Insurance Program, programs funded under Maternal and Child Health Program or programs funded under Social Services Block Grant (collectively, "Government-funded Plans") are not eligible for patient support services that provide financial support through the Program. A patient covered under a commercial health plan purchased through a health insurance marketplace or exchange is not a government program beneficiary even if the costs of such coverage are subsidized by the federal government. Only patients with commercial insurance who have a valid prescription for a US Food and Drug Administration-approved indication for REVCOVI are eligible for patient support services that provide financial support through the Program.

To enroll in any of the patient support services of the Program, the patient must also enroll in Chiesi Total Care. The patient must be a resident of the US or one of its territories. **If the Patient is incapable of acting on their own behalf or if the Patient is under 18 years old, enrollment into the Program may be completed by another person acting on their behalf (such as a caregiver).**

If at any time a patient begins receiving prescription drug coverage under any Government-funded Plan, patient will no longer be able to participate in the patient support services programs that provide financial support through the Program and patient must notify the Program to stop participation.

Patients residing in or receiving treatment in certain states may not be eligible for the Copay Assistance Program. Copay assistance is not available in California or Massachusetts when a generic equivalent to the product is commercially available. Patients may not seek reimbursement for value received from Copay Programs. The Copay Programs do not obligate the use of any specific medication or health care provider. Participation in a Copay Program is not conditioned on any past, present, or future purchase.

To determine financial eligibility for participation in the Patient Assistance Program, patient will be asked to provide the size of the household, annual household income, and proof of income. Proof of income may include W2 form(s), paycheck stubs, and/or prior year tax returns.

Program benefits may not be sold, purchased, traded, or offered for sale, purchase, or trade. The Chiesi Total Care patient support services are not valid where prohibited by law, taxed, or otherwise restricted. Offer subject to change or discontinuance without notice. Restrictions, including monthly maximums, may apply. This is not health insurance.

This is a voluntary program. Patients who choose not to enroll in any of the support programs will still be able to receive medication. Patients may participate in Chiesi Total Care without participating in a support program. After enrolling in Chiesi Total Care, participants may opt out by contacting Chiesi Total Care, as outlined in the Chiesi Total Care Enrollment and Authorization Form. Patients must renew their eligibility by December 31 of each year to continue to receive support under the Program.

By participating in the Program, participants acknowledge that they understand and agree to comply with these Terms and Conditions.

PP-G-0834 V1.0

Chiesi TOTAL care
Revcovi® elapegademase-lvlr injection 1.6 mg/mL
Chiesi global rare diseases

Chiesi

TOTAL care℠

BY PHONE
1-866-272-7078

BY FAX
1-866-272-7079

HOURS OF OPERATION
Monday to Friday 7:00am – 6:00pm
(Central Time)

For more information, visit chiesitotalcare.com

SCAN THE QR CODE FOR THE DIGITAL RX FORM

PP-RV-0104 V1.0 2023

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

REVCOVI (elapegademase-lvlr) injection, for intramuscular use
Initial U.S. Approval: 2018

----------RECENT MAJOR CHANGES----------
Dosage and Administration, Recommended Dosage 12/2020

----------INDICATIONS AND USAGE----------
REVCOVI is a recombinant adenosine deaminase indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients. (1)

----------DOSAGE AND ADMINISTRATION----------
- Patients transitioning from Adagen to REVCOVI: The starting dose of REVCOVI is 0.2 mg/kg weekly, intramuscularly. See Full Prescribing Information (FPI) for conversion formula from Adagen to REVCOVI. (2.1)
- Adagen-naïve patients: The starting dose of REVCOVI is 0.4 mg/kg weekly based on ideal body weight or actual weight whichever is greater, divided into two doses (0.2 mg/kg twice a week), intramuscularly. (2.1)
- For complete information, maintenance dosing and therapeutic monitoring, see FPI. (2.1, 2.3)
- REVCOVI is for intramuscular injection only. See FPI for administration instructions. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
Injection: 2.4 mg/1.5 mL (1.6 mg/mL) in a single-dose vial. (3)

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

----------WARNINGS AND PRECAUTIONS----------
- Injection Site Bleeding in Patients with Thrombocytopenia: Increased risk of local bleeding in patients with thrombocytopenia; should not be used if thrombocytopenia is severe. (5.1)
- Delay in Improvement of Immune Function: Protect immune deficient patients from infections until improvement in immune function. (5.2)

----------ADVERSE REACTIONS----------
The most common adverse reactions reported were cough (50%) and vomiting (33%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Chiesi USA, Inc. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION

Revised: 12/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

REVCOVI is indicated for the treatment of adenosine deaminase severe combined immune deficiency (ADA-SCID) in pediatric and adult patients.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

Patients transitioning from Adagen to REVCOVI

If a patient's weekly Adagen dose is unknown, or a patient's weekly Adagen dose is at or lower than 30 U/kg, the recommended minimum starting dose of REVCOVI is 0.2 mg/kg, intramuscularly, once a week.

If a patient's weekly Adagen dose is above 30 U/kg, an equivalent weekly REVCOVI dose (mg/kg) should be calculated using the following conversion formula:

$$REVCOVI\ dose\ in\ mg/kg = \frac{Adagen\ dose\ in\ U/kg}{150}$$

Subsequent doses may be increased by increments of 0.033 mg/kg weekly if trough ADA activity is under 30 mmol/hr/L, trough deoxyadenosine nucleotides (dAXP) are above 0.02 mmol/L, and/or the immune reconstitution is inadequate based on the clinical assessment of the patient. The total weekly dose may be divided into multiple intramuscular (IM) administrations during a week.

Adagen-naïve patients

The starting weekly dose of REVCOVI is 0.4 mg/kg based on ideal body weight or actual weight whichever is greater, divided into two doses (0.2 mg/kg twice a week), intramuscularly, for a minimum of 12 to 24 weeks until immune reconstitution is achieved. After that, the dose may be gradually adjusted down to maintain trough ADA activity over 30 mmol/hr/L, trough dAXP level under 0.02 mmol/L, and/or to maintain adequate immune reconstitution based on clinical assessment of the patient.

The optimal long-term dose and schedule of administration should be established by the treating physician for each patient individually and may be adjusted based on the laboratory values for trough ADA activity, trough dAXP level, and/or on the treating physician's medical assessment of the patient's clinical status.

2.2 Administration Instructions

REVCOVI is for IM injection only. Follow sterile IM administration technique guidelines appropriate to the patient's age and anatomy (i.e. choice of needle gauge and length, site of administration). Take precautions not to inject into or near an artery or nerve. Alternate the injection site periodically.

Preparation of Injection and Procedure Instructions

- REVCOVI should not be diluted nor mixed with any other drug prior to administration.

- Visually inspect REVCOVI for particulate matter and discoloration prior to administration. REVCOVI is a clear, colorless solution; discard if solution is discolored, cloudy or contains particulate matter.
- Do not freeze or shake. REVCOVI should not be used if there are any indications that it may have been frozen. Once removed from refrigeration, allow REVCOVI to equilibrate to room temperature for 30 minutes.
- REVCOVI is to be administered using polypropylene syringes. Draw the solution from the vial with a 25- gauge needle or larger.
- Change the needle to a size and gauge appropriate for the patient's intramuscular administration.
- REVCOVI should be administered immediately after syringe preparation.
- Any remaining medication in the vial must be discarded immediately.

2.3 Therapeutic Monitoring Schedule

The treatment of ADA-SCID with REVCOVI should be monitored by measuring trough plasma ADA activity, trough dAXP levels, and/or total lymphocyte counts. Monitoring should be more frequent if therapy was interrupted or if an enhanced rate of clearance of plasma ADA activity develops. Collect blood samples for the analysis of trough plasma ADA activity and trough dAXP level prior to the first administration of REVCOVI for the week.

ADA Activity

Once treatment with REVCOVI has been initiated, a target trough plasma ADA activity should be at least 30 mmol/hr/L. In order to determine an effective dose of REVCOVI, trough plasma ADA activity (pre-injection) should be determined every 2 weeks for Adagen-naïve patients and every 4 weeks for patients previously receiving Adagen therapy, during the first 8 - 12 weeks of treatment, and every 3 - 6 months thereafter.

A decrease of ADA activity below this level suggests noncompliance to treatment or a development of antibodies (anti-drug, anti-PEG, and neutralizing antibodies). Antibodies to REVCOVI should be suspected if a persistent fall in pre-injection levels of trough plasma ADA activity below 15 mmol/hr/L occurs. In such patients, testing for antibodies to REVCOVI should be performed.

If a persistent decline in trough plasma ADA activity occurs, immune function and clinical status should be monitored closely and precautions should be taken to minimize the risk of infection. If antibodies to REVCOVI are found to be the cause of a persistent fall in trough plasma ADA activity, then adjustment in the dosage of REVCOVI and other measures may be taken to induce tolerance and restore adequate ADA activity.

Erythrocyte dAXP

Two months after starting REVCOVI treatment, trough erythrocyte dAXP levels should be maintained below 0.02 mmol/L, and monitored at least twice a year.

Immune Function

The degree of immune function may vary from patient to patient. Each patient will require appropriate monitoring consistent with immunologic status. Total and subset lymphocytes should be monitored periodically as follows:

- Adagen-naïve patients: every 4 – 8 weeks for up to 1 year, and every 3 – 6 months thereafter
- Other patients: every 3 - 6 months

Immune function, including the ability to produce antibodies, generally improves after 2 - 6 months of therapy, and matures over a longer period. In general, there is a lag between the correction of the metabolic abnormalities and improved immune function. Improvement in the general clinical status of the patient may be gradual (as evidenced by improvement in various clinical parameters) but should be apparent by the end of the first year of therapy.

3 DOSAGE FORMS AND STRENGTHS

Injection: 2.4 mg/1.5 mL (1.6 mg/mL) clear and colorless solution of elapegademase-lvlr in a single-dose vial.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Injection Site Bleeding in Patients with Thrombocytopenia

Since REVCOVI is administered by IM injection, it should be used with caution in patients with thrombocytopenia and should not be used if thrombocytopenia is severe.

5.2 Delay in Improvement of Immune Function

Maintain precautions to protect immune deficient patients from infections until improvement in immune function has been achieved. The timing and degree of improvement in immune function may vary from patient to patient.

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.

REVCOVI was administered intramuscularly in two prospective, open-label, single-arm, multi-center studies to evaluate efficacy, safety, tolerability, and pharmacokinetics in patients with ADA-SCID: Study 1 was performed in the US and Study 2 was performed in Japan *[see Clinical Studies (14)]*. Overall, 10 patients were treated and adverse reactions reported are summarized below.

Study 1

Study 1 is a one-way crossover study, conducted in the US, to evaluate the safety, efficacy, and pharmacokinetics of REVCOVI in patients with ADA-SCID who were receiving therapy with Adagen. Six patients, 8 to 37 years of age enrolled in the study. Patients' exposure to REVCOVI ranged from 2 weeks to 146 weeks. No deaths were reported and one patient discontinued treatment due to injection site pain associated with an earlier drug product formulation that was consequently modified.

The most common adverse reactions were cough (3/6 patients) and vomiting (2/6 patients). Other adverse reactions that were reported in one patient each were: abdominal pain upper, arthralgia, asthenia, cerumen impaction, conjunctivitis, convulsion, dental caries, diarrhea, ear canal irritation,

ear lobe infection, epistaxis, fatigue, fungal skin infection, gait disturbance, gastrointestinal infection, groin abscess, hematochezia, haemophilus infection (pulmonary), hemoptysis, influenza, injection site discomfort, laceration, lymphadenopathy, migraine, nasal edema, nausea, nephrolithiasis, oral candidiasis, oropharyngeal pain, otitis externa, productive cough, rash, stoma site infection, swelling face, tooth abscess, tooth extraction and upper respiratory tract infection, regardless of investigator causality assessment.

Study 2

Study 2 is a single-arm clinical study that was conducted to assess the safety, efficacy and pharmacokinetics of REVCOVI in patients with ADA-SCID. Four patients 3.4 months to 25 years of age, all Asian, were enrolled in the study and received REVCOVI. Three patients received REVCOVI for 21 weeks and one patient received REVCOVI for 15 weeks. One death due to CMV pneumonitis and respiratory failure was observed in an infant, who had also experienced pulmonary hemorrhage, respiratory failure and upper respiratory tract infection that represented serious adverse events. Neutropenia was a serious adverse reaction reported by one of the patients. There were 22 reported adverse events for four patients. Most common adverse events were respiratory infections (2/4 patients).

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The immunogenicity results from Study 1 and Study 2 suggest that patients who previously received Adagen may present an immunologic response to REVCOVI. Therefore, monitoring for changes in ADA levels during REVCOVI treatment is recommended. *[see Dosage and Administration (2.3)]*

The observed incidence of antibodies (including neutralizing antibodies) is dependent on assay sensitivity and specificity, assay methodology, and concomitant medications. Therefore, the comparison of the incidence of antibodies to REVCOVI with the incidence of antibodies to other products may be misleading.

6.3 Postmarketing Experience with ADAGEN

The following postmarketing adverse reactions were voluntarily reported for Adagen, the same class of enzyme replacement therapy used in the treatment of ADA-SCID, and may also be seen with REVCOVI treatment:

- Hematologic: hemolytic anemia, auto-immune hemolytic anemia, thrombocythemia, thrombocytopenia and autoimmune thrombocytopenia
- Dermatological: injection site erythema, urticaria
- Lymphomas

Since these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

7 DRUG INTERACTIONS

The drug interaction potential of REVCOVI is not known.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Adequate and well-controlled studies with REVCOVI have not been conducted in pregnant women to inform a drug-associated risk. Animal reproduction studies have not been conducted with REVCOVI. It is not known whether REVCOVI can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human

No pregnancy was reported for any patients receiving REVCOVI. There are two reports of confirmed cases of successful pregnancy and delivery in ADA-SCID patients treated with Adagen (the same class of enzyme replacement therapy used in the treatment of ADA-SCID). No teratogenic effects of Adagen were reported.

For patients treated with REVCOVI, more frequent monitoring of the health status for both the mother during pregnancy and the development of the offspring is recommended.

8.2 Lactation

Risk Summary

Human or animal lactation studies have not been conducted to assess the presence of REVCOVI in breast milk, the effects on the breastfed infant, or the effects on milk production for the mother.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for REVCOVI and any potential adverse effects on the breastfed infant from REVCOVI or from the underlying maternal condition.

8.4 Pediatric Use

The safety and efficacy of REVCOVI have been established in pediatric patients *[see Clinical Studies (14)].*

8.5 Geriatric Use

REVCOVI was not studied in patients 65 years and older.

10 OVERDOSAGE

There are no reports of administration of REVCOVI in excess of the prescribed doses. The highest weekly prescribed dose administered in the clinical studies was 0.4 mg/kg. In nonclinical studies, there was no evidence of toxicity related to study drug at doses up to 1.8-fold the clinical dose (based on mean human AUC normalized to the dose of REVCOVI administered per patient), except for a slight increase in activated partial thromboplastin time (APTT).

11 DESCRIPTION

Elapegademase-lvlr is a recombinant adenosine deaminase (rADA) based on bovine amino acid sequence, conjugated to monomethoxypolyethylene glycol (mPEG). rADA is manufactured in *E.coli* and is covalently conjugated to mPEG with a succinimidyl carbamate linker to produce methoxypolyethylene glycol recombinant adenosine deaminase (SC-PEG rADA). The approximate molecular weight of elapegademase-lvlr (SC-PEG rADA) is 113 KDa.

REVCOVI (elapegademase-lvlr) injection is a sterile, preservative free, clear, colorless solution for intramuscular use supplied in single-dose vials. Each vial provides 1.5 mL of solution containing 2.4 mg elapegademase-lvlr (1.6 mg/mL), sodium chloride (12.75 mg), sodium phosphate dibasic heptahydrate (12.7 mg), sodium phosphate monobasic monohydrate (3.81 mg), and Water for Injection, USP. The pH is 6.9.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

SCID associated with a deficiency of ADA enzyme is a rare, inherited, and often fatal disease. ADA enzyme is involved in purine metabolism, catalyzing the irreversible hydrolytic deamination of adenosine or deoxyadenosine to inosine or deoxyinosine, respectively, as well as several naturally occurring methylated adenosine compounds. Maintaining a low level of 2'-deoxyadenosine and adenosine is crucial for proper number and function of immune cells as well as decreasing the frequency of opportunistic infections. Elevated adenosine levels, as occurring in ADA deficiency, contribute to apoptosis and a block in the differentiation of thymocytes, causing severe T-lymphopenia.

Elapegademase-lvlr provides an exogenous source of ADA enzyme that is associated with a decrease in toxic adenosine and deoxyadenosine nucleotides levels as well as an increase in lymphocyte number *[see Clinical Studies (14)].*

12.2 Pharmacodynamics

The effect of REVCOVI on the QT interval is not known.

12.3 Pharmacokinetics

The pharmacokinetics (PK) of REVCOVI were evaluated based on steady state plasma ADA activity in six patients with ADA-SCID (five adults and one pediatric) from two studies (Study 1 and Study 2) who received weekly IM injections at doses ranging from 4.99 to 19.6 mg *[see Clinical Studies (14)]*. The PK results are summarized in Table 1.

Table 1 Individual Estimates of Steady State Plasma Pharmacokinetic Parameters of REVCOVI Following Weekly IM Administration in ADA-SCID Patients

Study	Patient's Age (yrs), Sex, Race	Weekly Dose (mg) [mg/kg]	T_{max} (hr)	DN $AUC_{0\text{-}168hr}$ (hr*mmol/hr/L) /(mg/kg)[b]	DN C_{max} (mmol/hr/L) /(mg/kg)[b]	C_{trough} (mmol/hr/L)[c]
Study 1[a]	19, Male, Hispanic/Latino	10.0 [0.188]	47.7	32710	237	29.0
	21, Male, Hispanic/Latino	10.2 [0.224]	71.9	31343	219	37.7
	37, Male, Black/African American	19.6 [0.2]	48.2	42400	292	46.2
	30, Female, White/Caucasian	10.0 [0.209]	72.0	24564	166	23.5
Study 2[a]	25, Male, Asian	10.0 [0.167]	48.0	37605	251	33.5
	16, Female, Asian	4.99 [0.233]	27.2	19013	150	20.2

[a] PK data calculated over the dosing interval after weekly IM administration of REVCOVI at a stable REVCOVI dose for at least five consecutive weeks
[b] Dose-normalized (DN) $AUC_{0\text{-}168hr}$ and C_{max} estimates based on mg/kg/week dose of REVCOVI
[c] Non-dose normalized steady state C_{trough} ADA activity in plasma at Day 7 prior to administration of next weekly dose

In Study 1, steady state ADA activity levels were reached following seven consecutive once weekly IM doses of REVCOVI. In addition, dAXP activity levels in all patients at the majority of all sampling timepoints in Study 1 were less than 0.02 mmol/L.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential and impairment of fertility have not been performed with REVCOVI.

14 CLINICAL STUDIES

14.1 Study 1

Study 1, conducted in the US (NCT 01420627), is an ongoing Phase 3, open-label, multicenter, single-arm, one-way crossover study of REVCOVI. The purpose of this clinical study is to evaluate the safety, efficacy, and PK of REVCOVI in 6 patients with ADA-SCID, 4 males and 2 females, who are receiving therapy with Adagen. The study treatment consists of three phases: Adagen Lead-in Phase (minimum of 3 weeks), the REVCOVI Treatment Phase (weeks 1 through 21), and followed by the REVCOVI Maintenance Phase. Six patients treated in the study were 8 to 37 years of age at the start of the study. The starting weekly dose of REVCOVI was calculated based on the last Adagen dose received in the study. Weekly REVCOVI doses ranged from 0.188 mg/kg to 0.292 mg/kg *[see Dosage and Administration (2.1)].*

The efficacy endpoints assessed were as follows:

- Trough dAXP Level (metabolic detoxification was defined as a trough erythrocyte dAXP concentration equal to or below 0.02 mmol/L)
- Trough plasma ADA activity (adequate trough plasma ADA activity is defined as trough plasma ADA activity equal to or above 15 mmol/hr/L)
- Immune status (lymphocyte and B-, T-, and NK-lymphocyte subset counts as well as quantitative immunoglobulin [Ig] concentration [IgG, IgA, IgM])

A PK assessment was performed during Week 9 of the REVCOVI Treatment phase *[see Clinical Pharmacology (12.3)]*.

Five of six patients reached the 21-week endpoint of the Treatment Phase, and three of six patients received treatment with REVCOVI (elapegademase-lvlr) for over 135 weeks. These patients (except for one value in a patient at Treatment Week 47) had erythrocyte dAXP concentration equal to or below 0.02 mmol/L. These patients had trough plasma ADA activity equal to or above 15 mmol/hr/L at 88/89 timepoints and maintained metabolic detoxification for at least 2 years under REVCOVI treatment. Patients achieved trough plasma ADA activity above 30 mmol/hr/L by week 5, except for one patient who achieved this level at week 1. The mean trough plasma ADA activity for patients receiving REVCOVI at a normalized dose of 0.2 mg/kg/week were 34.3 ± 6.6 mmol/hr/L. The same patients had a mean trough plasma ADA activity of 14.2 ± 5.1 mmol/hr/L when treated with Adagen at a normalized dose of 30 U/kg/week during the Lead-in Phase of the study.

Lymphocyte and subset counts during REVCOVI treatment increased above levels observed during the Adagen Lead-in Phase (i.e., PK day 1 or before the start of REVCOVI treatment): maximum increases of approximately 3-fold at Weeks 60-73 for one patient, maximum increases of approximately 2- to 3-fold at Weeks 73-99 for one patient and approximately 1.5- to 3-fold for the third patient at several timepoints. For these three patients who completed the primary endpoint (21 weeks of treatment) and received REVCOVI for over 135 weeks, a positive trend between high trough plasma ADA activity and increased total lymphocyte counts was observed.

Observations for the other three patients in the study, indicate that these patients also achieved complete detoxification based on trough dAXP level and trough plasma ADA activity, and show stable or slightly increased lymphocyte counts during REVCOVI treatment relative to values recorded during the Adagen Lead-in Phase.

14.2 Study 2

Study 2, conducted in Japan, is a single-arm clinical study that assessed the safety, efficacy and PK of REVCOVI in patients with ADA-SCID. The study includes two phases: 1) Evaluation, consisting of a Dose Adjustment Period (5 weeks) and a Dose Maintenance Period (16 weeks); and 2) Continuous Administration (Extension) Phase, to be continued until the end of the study.

A total of four patients were enrolled in the study: two males (age 25 years and 3.4 months) and two females (age 16 years and 4.3 months). Two patients, who were on Adagen treatment within 4 weeks before entering the study, received a first dose of REVCOVI that was calculated to be equivalent to the last Adagen dose received. One patient, who did not receive Adagen within four weeks prior to entering the study, was given the first dose of REVCOVI at 0.1 mg/kg body weight, followed by second and third doses at 0.133 mg/kg body weight and weekly thereafter. Over the dose adjustment phase of the study, the dose was titrated to meet criteria for dAXP level (equal to or below 0.02 mmol/L) and adequate trough ADA activity (equal to or above 15 mmol/hr/L). These three patients received REVCOVI for at least 21 weeks (having completed the 5-week Dosage Adjustment Period and the 16-week Maintenance Period) before entering the Extension Phase. The fourth patient (newly

diagnosed Adagen-naïve patient with CMV pneumonia *[see Adverse Reactions (6.1)]*) was dosed with REVCOVI at 0.4 mg/kg weekly (divided into two IM administrations) for 16 weeks.

All four of the patients in Study 2 achieved and maintained detoxification (trough dAXP [erythrocyte or blood] ≤0.02 mmol/L) throughout their participation in the Treatment Phase of 21 weeks (Dose Adjustment and Dose Maintenance). Serum ADA activity increased after administering REVCOVI for all four patients, with three patients achieving activity level over 15 mmol/hr/L during the Dose Maintenance Period. Total lymphocyte counts and B-/T-/NK-lymphocyte subset counts for three patients increased from screening to Day 15 during dose adjustment and were stable or increasing during the Maintenance Period.

16 HOW SUPPLIED/STORAGE AND HANDLING

REVCOVI (elapegademase-lvlr) injection, 2.4 mg/1.5 mL (1.6 mg/mL), is a sterile, preservative free, clear, colorless solution for intramuscular use available as one single-dose vial per carton (NDC 10122-502-01).

The vial stopper is not made with natural rubber latex.

Single-dose vial; do not re-use the vial. Discard unused portions.

Store REVCOVI in the refrigerator between 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze or shake. REVCOVI should not be used if there are any indications that it may have been frozen.

17 PATIENT COUNSELING INFORMATION

Importance of Compliance

Counsel patients and caregivers that continuous therapy and adherence to the recommended drug schedule is important for the success of the treatment.

Manufactured by: Chiesi USA, Inc. Cary, NC 27518, USA, U.S. License No. 2150 at Exelead Inc., 6925 Guion Rd, Indianapolis, IN 46268, USA

Chiesi

CTRV-001-1120-00-W