Chiesi TOTAL care℠

FILSUVEZ® (birch triterpenes) topical gel Starter Kit

Lesa, Chiesi Total Care pharmacist

Indication and Important Safety Information

Indication
FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

Warnings & Precautions
Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Filsuvez®
(birch triterpenes) topical gel

Filsuvez® (birch triterpenes) topical gel: The first treatment for both dystrophic and junctional epidermolysis bullosa

What's inside

Getting a Patient Started on FILSUVEZ
- Patient enrollment form
- Rx form
- Tube calculation worksheet

FILSUVEZ Access and Support Services

FILSUVEZ Dosing and Administration Guide

Copay Support Information
Please refer to the full Terms and Conditions in the back pocket for additional eligibility requirements.

US Prescribing Information

Contact Information Card

Filsuvez®
(birch triterpenes) topical gel

Indication and Important Safety Information

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Important Safety Information

Warnings & Precautions
Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Adverse Reactions
The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Patient Counseling Information
Please refer to Prescribing Information for administration instructions.

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.

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

For more information, visit FILSUVEZ.com/HCP

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PP-FZ-0026 V3.0 2024

Chiesi

Chiesi TOTAL care℠

Getting Started Guide

To get a patient started on FILSUVEZ® topical gel, follow 2 steps outlined in this guide

Visit chiesitotalcare.com or call 1-833-670-6464 We're ready to help!

Indication and Important Safety Information

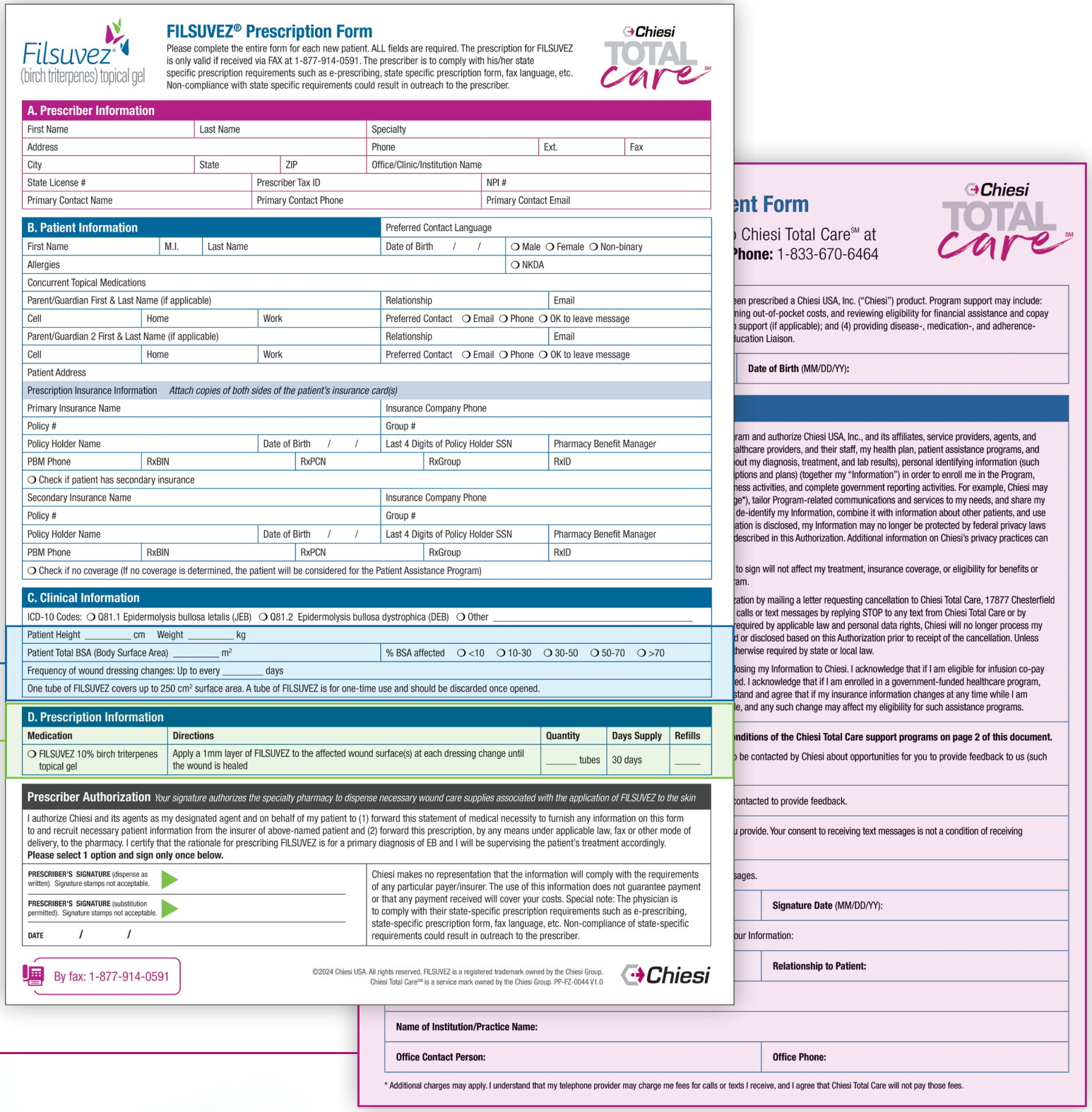
Indication
FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

Warnings & Precautions
Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Filsuvez® (birch triterpenes) topical gel

Step 1: Fill out the Prescription and Patient Consent Forms



Filsuvez® (birch triterpenes) topical gel

FILSUVEZ® Prescription Form

Please complete the entire form for each new patient. ALL fields are required. The prescription for FILSUVEZ is only valid if received via FAX at 1-877-914-0591. The prescriber is to comply with his/her state specific prescription requirements such as e-prescribing, state specific prescription form, fax language, etc. Non-compliance with state specific requirements could result in outreach to the prescriber.

Chiesi TOTAL care℠

A. Prescriber Information

First Name	Last Name		Specialty		
Address			Phone	Ext.	Fax
City	State	ZIP	Office/Clinic/Institution Name		
State License #	Prescriber Tax ID		NPI #		
Primary Contact Name	Primary Contact Phone		Primary Contact Email		

B. Patient Information

First Name	M.I.	Last Name	Preferred Contact Language		
			Date of Birth / /	❍ Male ❍ Female ❍ Non-binary	
Allergies				❍ NKDA	
Concurrent Topical Medications					
Parent/Guardian First & Last Name (if applicable)			Relationship	Email	
Cell	Home	Work	Preferred Contact ❍ Email ❍ Phone ❍ OK to leave message		
Parent/Guardian 2 First & Last Name (if applicable)			Relationship	Email	
Cell	Home	Work	Preferred Contact ❍ Email ❍ Phone ❍ OK to leave message		
Patient Address					
Prescription Insurance Information *Attach copies of both sides of the patient's insurance card(s)*					
Primary Insurance Name			Insurance Company Phone		
Policy #			Group #		
Policy Holder Name		Date of Birth / /	Last 4 Digits of Policy Holder SSN	Pharmacy Benefit Manager	
PBM Phone	RxBIN	RxPCN	RxGroup	RxID	
❍ Check if patient has secondary insurance					
Secondary Insurance Name			Insurance Company Phone		
Policy #			Group #		
Policy Holder Name		Date of Birth / /	Last 4 Digits of Policy Holder SSN	Pharmacy Benefit Manager	
PBM Phone	RxBIN	RxPCN	RxGroup	RxID	
❍ Check if no coverage (If no coverage is determined, the patient will be considered for the Patient Assistance Program)					

C. Clinical Information

ICD-10 Codes: ❍ Q81.1 Epidermolysis bullosa letalis (JEB) ❍ Q81.2 Epidermolysis bullosa dystrophica (DEB) ❍ Other _____

Patient Height _____ cm Weight _____ kg	
Patient Total BSA (Body Surface Area) _____ m^2	% BSA affected ❍ <10 ❍ 10-30 ❍ 30-50 ❍ 50-70 ❍ >70
Frequency of wound dressing changes: Up to every _____ days	
One tube of FILSUVEZ covers up to 250 cm^2 surface area. A tube of FILSUVEZ is for one-time use and should be discarded once opened.	

D. Prescription Information

Medication	Directions	Quantity	Days Supply	Refills
❍ FILSUVEZ 10% birch triterpenes topical gel	Apply a 1mm layer of FILSUVEZ to the affected wound surface(s) at each dressing change until the wound is healed	_____ tubes	30 days	_____

Prescriber Authorization *Your signature authorizes the specialty pharmacy to dispense necessary wound care supplies associated with the application of FILSUVEZ to the skin*

I authorize Chiesi and its agents as my designated agent and on behalf of my patient to (1) forward this statement of medical necessity to furnish any information on this form to and recruit necessary patient information from the insurer of above-named patient and (2) forward this prescription, by any means under applicable law, fax or other mode of delivery, to the pharmacy. I certify that the rationale for prescribing FILSUVEZ is for a primary diagnosis of EB and I will be supervising the patient's treatment accordingly.
Please select 1 option and sign only once below.

PRESCRIBER'S SIGNATURE (dispense as written). Signature stamps not acceptable.

PRESCRIBER'S SIGNATURE (substitution permitted). Signature stamps not acceptable.

DATE / /

Chiesi makes no representation that the information will comply with the requirements of any particular payer/insurer. The use of this information does not guarantee payment or that any payment received will cover your costs. Special note: The physician is to comply with their state-specific prescription requirements such as e-prescribing, state-specific prescription form, fax language, etc. Non-compliance of state-specific requirements could result in outreach to the prescriber.

By fax: 1-877-914-0591

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Chiesi

A

B

C

ent Form

Chiesi Total Care℠ at
Phone: 1-833-670-6464

Chiesi TOTAL care℠

een prescribed a Chiesi USA, Inc. ("Chiesi") product. Program support may include: ning out-of-pocket costs, and reviewing eligibility for financial assistance and copay n support (if applicable); and (4) providing disease-, medication-, and adherence- ducation Liaison.

Date of Birth (MM/DD/YY):

ram and authorize Chiesi USA, Inc., and its affiliates, service providers, agents, and althcare providers, and their staff, my health plan, patient assistance programs, and out my diagnosis, treatment, and lab results), personal identifying information (such ptions and plans) (together my "Information") in order to enroll me in the Program, ness activities, and complete government reporting activities. For example, Chiesi may ge*), tailor Program-related communications and services to my needs, and share my de-identify my Information, combine it with information about other patients, and use ation is disclosed, my Information may no longer be protected by federal privacy laws described in this Authorization. Additional information on Chiesi's privacy practices can

to sign will not affect my treatment, insurance coverage, or eligibility for benefits or am.

zation by mailing a letter requesting cancellation to Chiesi Total Care, 17877 Chesterfield calls or text messages by replying STOP to any text from Chiesi Total Care or by required by applicable law and personal data rights, Chiesi will no longer process my d or disclosed based on this Authorization prior to receipt of the cancellation. Unless herwise required by state or local law.

losing my Information to Chiesi. I acknowledge that if I am eligible for infusion co-pay ed. I acknowledge that if I am enrolled in a government-funded healthcare program, stand and agree that if my insurance information changes at any time while I am le, and any such change may affect my eligibility for such assistance programs.

nditions of the Chiesi Total Care support programs on page 2 of this document.

be contacted by Chiesi about opportunities for you to provide feedback to us (such

contacted to provide feedback.

u provide. Your consent to receiving text messages is not a condition of receiving

sages.

Signature Date (MM/DD/YY):

our Information:

Relationship to Patient:

Name of Institution/Practice Name:

Office Contact Person: **Office Phone:**

* 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.

Indication and Important Safety Information

Adverse Reactions

The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Specify clinical information related to patient body surface area

A

Patient Total BSA (Body Surface Area) _____ m^2

% BSA affected ☐ <10 ☐ 10-30 ☐ 30-50 ☐ 50-70 ☐ >70

Frequency of wound dressing changes: Up to every _____ days

One tube of FILSUVEZ covers up to 250 cm^2 surface area.
A tube of FILSUVEZ is for one-time use and should be discarded once opened.

Specify prescription information

B

Use the specified clinical information from the section above to calculate the quantity of tubes required.

Medication	Directions	Quantity	Days Supply	Refills
❍ FILSUVEZ 10% birch triterpenes topical gel	Apply a 1mm layer of FILSUVEZ to the affected wound surface(s) at each dressing change until the wound is healed	_____ tubes	30 days	_____

Ask each patient to sign the Patient Consent Form

C

Please ask each patient to sign the Patient Consent Form before they leave the office and fax it along with the Enrollment Form for each patient.

Participation in the Chiesi Total Care program is optional.

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 **1-877-914-0591. PLEASE COMPLETE ONE FORM PER PATIENT.**
3. **Subsequent prescriptions:**
   After the initial script is filled, future prescriptions can be made via telephone or e-script. If you wish to send additional forms via e-script please search for “PANTHERx" 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.

Chiesi TOTAL care℠

Filsuvez®
(birch triterpenes) topical gel

If you have questions, visit chiesitotalcare.com or call 1-833-670-6464 – we're ready to help!

Indication and Important Safety Information

Indication

FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

Important Safety Information

Warnings & Precautions

Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Adverse Reactions

The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Patient Counseling Information

Please refer to Prescribing Information for administration instructions.

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.

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

For more information, visit FILSUVEZ.com/HCP

References: 1. FILSUVEZ® (birch triterpenes) Prescribing Information. Amryt, December, 2023

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PP-FZ-0028 V2.0 2024

Chiesi
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Chiesi TOTAL care℠

Access and Support Services

Chiesi Total Care℠ (CTC) is a dedicated team committed to the individualized needs of every patient.

Visit chiesitotalcare.com or call 1-833-670-6464 We're ready to help!

Indication and Important Safety Information

Indication
FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

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Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Filsuvez® (birch triterpenes) topical gel

Access to FILSUVEZ and support services for your patients happens in 4 easy steps:

1

Step 1: Enrollment

Complete the FILSUVEZ prescription form to get started with Chiesi Total Care℠

2

Step 2: Connection

The Chiesi Total Care Team will then reach out:

a. To your office to make an introduction

b. To your patient/caregiver to obtain patient consent, if not previously provided

3

Step 3: Assessment

Chiesi Total Care conducts a Benefits Investigation and Prior Authorization

a. The team will conduct an assessment of your patient's health insurance benefits to provide an individualized overview of pharmacy coverage information and out of pocket costs

b. Tailored access support will be provided by a team of dedicated Field Reimbursement Managers, including support with payer prior authorizations and any appeals process that may be required

4

Step 4: Delivery

Chiesi Total Care will work with the patient and caregiver to set up delivery of FILSUVEZ

Important Safety Information

Warnings and Precautions

Hypersensitivity: Local hypersensitivity, including rash and contact dermatitis has occurred in patients treated with FILSUVEZ. If signs and symptoms of local or systemic hypersensitivity occur, discontinue FILSUVEZ immediately and initiate appropriate therapy.

Squamous Cell Carcinoma: Patients with EB may be at increased risk of development of squamous cell carcinoma of the skin (SCC). Cases of SCC have been reported in patients treated with FILSUVEZ. A causal association has not been established. If a patient treated with FILSUVEZ is diagnosed with SCC, discontinue treatment with FILSUVEZ to the affected area.

Accidental Eye Exposure: In case of accidental contact, irrigate eyes with water.

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

Financial Assistance and Support

Chiesi TOTAL care℠

Chiesi Total Care will provide information on financial assistance options based on the individualized needs of your patients.

Access made easy with:

- Financial assistance for out-of-pocket expenses including copay assistance and referrals to other sources of support
- Copay program helps eligible commercially insured patients with their out of pocket cost. Patients pay as little as $0
- Patient Assistance Program (PAP) for individuals without insurance or who meet other eligibility criteria
- Additional financial services may be available for eligible patients experiencing a coverage delay and/or lapse in insurance coverage

Dedicated Medication Support

PantheRx is the dedicated specialty pharmacy ensuring patients have access to FILSUVEZ as a part of their daily routine and prevent gaps in therapy.

If you have questions, visit chiesitotalcare.com or call 1-833-670-6464 – we're ready to help!

Filsuvez® (birch triterpenes) topical gel

Filsuvez®
(birch triterpenes) topical gel

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Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Adverse Reactions

The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Patient Counseling Information

Please refer to Prescribing Information for administration instructions.

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Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

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PP-FZ-0029 V3.0 2024

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Dosing and Administration Guide

Visit chiesitotalcare.com or call 1-833-670-6464 We're ready to help!

Indication and Important Safety Information

Indication
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Warnings & Precautions
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Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Filsuvez®
(birch triterpenes) topical gel

Starting your patients on FILSUVEZ® (birch triterpenes) topical gel

Apply to Every Wound.*
At Every Wound Dressing Change.

*FILSUVEZ is for junctional and dystrophic EB wounds.

HOW TO APPLY FILSUVEZ

- Clean wounds before applying FILSUVEZ
- Apply FILSUVEZ with a clean or gloved hand

Step 1

Apply a generous layer of FILSUVEZ to a sterile nonadhesive wound dressing so that the gel is in direct contact with the wound. FILSUVEZ can also be applied directly to the wound.

Step 2

As you spread the layer of FILSUVEZ on the dressing, make sure the layer is about the **same thickness as a credit card.**

If you apply FILSUVEZ directly to the wound, **do not** rub in the gel.

Step 3

Apply the dressing to the wound.

Reapply FILSUVEZ each time your dressing is changed until the wound is completely healed.

A tube of FILSUVEZ contains enough gel to cover about two 5x4-inch bandages, **nearly the same area as a business-sized envelope.**

Apply a layer of FILSUVEZ about the thickness of a credit card

- FILSUVEZ should not be used on full-thickness wounds.
- Patients treated with FILSUVEZ have experienced local hypersensitivity, including rash and contact dermatitis. If signs and symptoms of local or systemic hypersensitivity occur, discontinue FILSUVEZ immediately and start appropriate therapy.
- If a FILSUVEZ-treated wound becomes infected, discontinue treatment to that wound until the infection has resolved.

Indication and Important Safety Information

Adverse Reactions

The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

Easy to use, sterile, single-use tubes

PRESCRIBING NOTES

Available through specialty pharmacy

Across the Phase 3 study population, patients used an average of 27 tubes per month (median 19 tubes)*

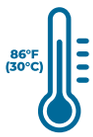
Apply a layer of FILSUVEZ about the thickness of a credit card (1mm)

1 tube covers same area as a business envelope

*Data on file, Amryt Pharmaceuticals, Inc.

USING FILSUVEZ

The tube of FILSUVEZ should only be used once. Once the tube has been opened, apply the gel to wounds immediately and then **discard the tube and any remaining gel.**



Store FILSUVEZ below 86°F (30°C) and do not freeze.

Do not use FILSUVEZ in or around the eyes or mucous membranes (mouth, vagina, or anus). If accidental contact does occur, patients should be instructed to immediately wash with clean water and contact their doctor if they have any discomfort.

Patients will receive a starter kit with guidance on how to use FILSUVEZ once their prescription has been shipped.

Visit chiesitotalcare.com
or call 1-833-670-6464
We're ready to help!

Filsuvez®
(birch triterpenes) topical gel

If you have questions, visit chiesitotalcare.com or call 1-833-670-6464 – we're ready to help!

Indication and Important Safety Information

Indication

FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

Important Safety Information

Warnings & Precautions

Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis. If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy.

Adverse Reactions

The most commonly reported adverse reaction in clinical trials was pruritus and pain at the wound application site (7.3%).

Patient Counseling Information

Please refer to Prescribing Information for administration instructions.

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.

Please see accompanying full Prescribing Information for FILSUVEZ topical gel.

For more information, visit FILSUVEZ.com/HCP

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PP-FZ-0030 V2.0 2024

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SCAN THE QR CODE
FOR THE DIGITAL RX FORM

BY PHONE
1-833-670-6464

BY FAX
1-877-914-0591

HOURS OF OPERATION
Monday to Friday
8:00 am to 8:00 pm (Eastern Time)

For more information, visit chiesitotalcare.com

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PP-FZ-0027 V1.0 2024

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

FILSUVEZ® (birch triterpenes) topical gel
Initial U.S. Approval: 2023

INDICATIONS AND USAGE

FILSUVEZ topical gel is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa in adult and pediatric patients 6 months of age and older. (1)

DOSAGE AND ADMINISTRATION

- Apply a 1 mm layer of FILSUVEZ to the affected wound surface and cover with wound dressing or apply FILSUVEZ directly to dressing so that the topical gel is in direct contact with the wound. Do not rub in the topical gel. (2)
- Apply FILSUVEZ at wound dressing changes until the wound is healed. (2)
- Each tube of FILSUVEZ is for one-time use only. (2)
- For topical use; not for oral, intravaginal, intra-anal, or ophthalmic use. (2)

DOSAGE FORMS AND STRENGTHS

Topical gel: 10% birch triterpenes w/w supplied in 25 mL sterile tubes (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

- *Hypersensitivity Reactions:* If signs or symptoms of hypersensitivity occur, discontinue use immediately and initiate appropriate therapy. (5.1)

ADVERSE REACTIONS

The most common (incidence ≥2%) adverse reactions are application site reactions. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Amryt Pharmaceuticals DAC at 1-855-303-2347 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Revised: 12/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FILSUVEZ is indicated for the treatment of wounds associated with dystrophic and junctional epidermolysis bullosa (EB) in adult and pediatric patients 6 months of age and older.

2 DOSAGE AND ADMINISTRATION

- Wash hands before and after applying FILSUVEZ or wear gloves for application.
- Apply a 1 mm layer of FILSUVEZ to the affected wound surface only. Do not rub in the gel. Cover the wound with a sterile non-adhesive wound dressing. Alternatively, apply FILSUVEZ directly to the dressing so that the topical gel is in direct contact with the wound.
- Apply FILSUVEZ to cleansed wounds with wound dressing changes until the wound is healed.
- If a FILSUVEZ-treated wound becomes infected, discontinue treatment to that wound until the infection has resolved.
- Each tube of FILSUVEZ is for one-time use only. Once the tube is opened, use the product immediately. Discard the tube after use in household trash or through a drug take back site, if available.
- Avoid contact of FILSUVEZ with eyes and mucous membranes (e.g., mouth, vagina, anus). In case of accidental contact, irrigate the area with water.
- FILSUVEZ is for topical use only. Not for use on mucous membranes (oral, intravaginal, or intra-anal). Not for ophthalmic use.

3 DOSAGE FORMS AND STRENGTHS

Topical gel: 10% birch triterpenes w/w in a colorless to slightly yellowish, opalescent, non-aqueous gel supplied in 25 mL sterile tubes.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Local hypersensitivity and skin reactions have been reported in patients treated with FILSUVEZ, including urticaria and dermatitis.

If signs and symptoms of local or systemic hypersensitivity occur, discontinue FILSUVEZ immediately and initiate appropriate therapy.

6 ADVERSE REACTIONS

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

- Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of FILSUVEZ was evaluated in EASE, a randomized, double-blind, multicenter, placebo-controlled trial in 223 adult and pediatric subjects with inherited EB. During the double-blind phase of EASE, subjects received topical treatment with either FILSUVEZ or a placebo gel on partial-thickness wounds every 1 to 4 days for a total of 90 days. Treated wounds were covered with non-adhesive dressings. Following completion of the double-blind phase, all subjects received FILSUVEZ for a total of 24 months during the open-label phase *[see Clinical Studies (14)]*.

Table 1 presents adverse reactions that occurred in at least 2% of subjects treated with FILSUVEZ during the 90-day double-blind phase of EASE and at a greater frequency than in the placebo gel group.

Table 1: Number (%) of Subjects with Adverse Reactions Occurring in ≥ 2%

Adverse Reaction	**FILSUVEZ (N=109) n (%)**	**Placebo Gel (N=114) n (%)**
Application site reaction[a]	8 (7.3)	7 (6.1)

[a] Includes: application site pruritus, administration site pain, administration site pruritus.

Squamous cell carcinoma of the skin (SCC) was reported as an adverse event in the double-blind and open-label periods of EASE. Four subjects with recessive dystrophic EB each reported one SCC: a 20-year-old male on day 1 of the double-blind period; three female subjects ages 22, 46, and 49 years during the open-label period. Two of the four subjects had applied FILSUVEZ to the area which developed the SCC.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data with use of FILSUVEZ in pregnant women to evaluate for drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In an animal reproduction study, oral administration of birch triterpenes to pregnant rats during the period of organogenesis had no effects on reproductive or fetal parameters *(see Data)*.

Systemic absorption of FILSUVEZ in humans is low following topical administration of FILSUVEZ, and maternal use is not expected to result in fetal exposure to the drug *[see Pharmacokinetics (12.3)]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. 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.

Data

Animal Data

In an embryofetal development study, birch triterpenes were orally administered to pregnant rats at doses of 10, 30, or 100 mg/kg/day during the period of organogenesis. Birch triterpenes did not cause maternal toxicity or fetal malformations at doses up to 100 mg/kg/day. In a prenatal and postnatal development study, birch triterpenes were orally administered to pregnant rats at doses of 10, 30, or 100 mg/kg/day from gestation day 5 through lactation day 20. Birch triterpenes did not affect development at doses up to 100 mg/kg/day. The available data do not support relevant comparisons of systemic birch triterpenes exposures achieved in the animal studies to exposures observed in humans after topical use of FILSUVEZ.

8.2 Lactation

Risk Summary

There are no data on the presence of birch triterpenes or metabolites in human milk, the effects on the breastfed infant, or the effect on milk production.

No effects on the breastfed infant are anticipated since the systemic exposure of the breastfeeding woman to FILSUVEZ would be low. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for FILSUVEZ and any potential adverse effects on the breastfed infant from FILSUVEZ or from the underlying maternal condition *[see Pharmacokinetics (12.3)]*.

8.4 Pediatric Use

The safety and effectiveness of FILSUVEZ for the treatment of wounds associated with dystrophic and junctional EB have been established in pediatric patients 6 months of age and older. Use of FILSUVEZ in this age group is supported by evidence from a single randomized, placebo-controlled trial in 156 subjects 6 months to 17 years of age *[see Clinical Studies (14)]*.

The safety and effectiveness of FILSUVEZ have not been established in pediatric patients younger than 6 months of age.

8.5 Geriatric Use

Clinical studies of FILSUVEZ did not include sufficient numbers of EB subjects 65 years of age and older to determine whether they respond differently from younger subjects.

11 DESCRIPTION

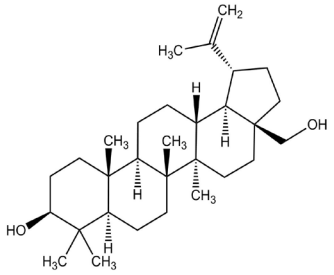
FILSUVEZ (birch triterpenes) topical gel is a sterile botanical drug product for topical use and contains birch triterpenes in an oil base. FILSUVEZ is a colorless to slightly yellowish, opalescent, non-aqueous gel.

Birch triterpenes is a botanical drug substance composed of a mixture of pentacyclic triterpenes. The botanical drug substance is a dry extract, refined, from birch bark from *Betula pendula* Roth, *Betula pubescens* Ehrh., as well as hybrids of both species, quantified to 72-88% (w/w) betulin, 2.4-5.7% (w/w) lupeol, 2.6-4.2% (w/w) betulinic acid, 0.5-1.2% (w/w) erythrodiol, 0.3-0.8% (w/w) oleanolic acid.

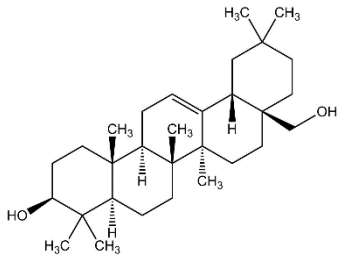
The structural formulae of the main triterpene constituents are shown in Figure 1.

Figure 1: Structure of Triterpene Constituents

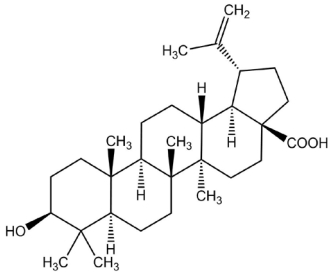
Betulin



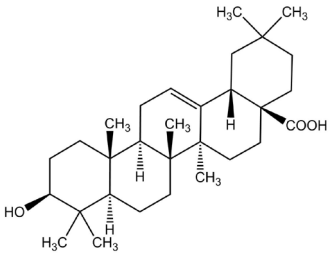
Erythrodiol



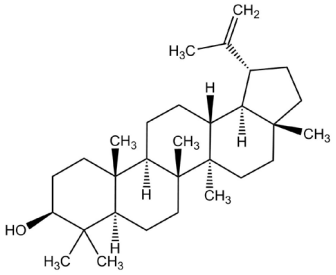
Betulinic acid



Oleanolic acid



Lupeol



Each gram of FILSUVEZ topical gel 10% (w/w) contains 100 mg of birch triterpenes in an oil base of refined sunflower oil. FILSUVEZ contains no additional excipients.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of FILSUVEZ in the treatment of wounds associated with epidermolysis bullosa is unknown.

12.2 Pharmacodynamics

Pharmacodynamics of FILSUVEZ are unknown.

12.3 Pharmacokinetics

Absorption

Systemic exposure to betulin was assessed in the 66 evaluable subjects aged ≥13 months to ≤52 years with dystrophic and junctional EB in the clinical trial EASE using venous blood sampling and validated liquid chromatography with tandem mass spectrometry assay.

Following treatment with FILSUVEZ once daily (n=27), every 2 (n=33) or 3 days (n=4) or once weekly (n=2) for 90 days with a mean treatment area of 12% body surface area or affected wound surface area of 0.11 m^2 at baseline, betulin blood concentrations in 68% subjects (n=45) were below the lower limit of quantification of 10 ng/mL on Day 90. The highest concentrations of betulin in adult and pediatric subjects with a median age of 10 years (range: ≥13 months to <18 years) were 33 ng/mL and 207 ng/mL, respectively, which were observed on Day 90.

Distribution

Plasma protein binding of betulin in vitro is >99.9 %.

Metabolism

The in vitro study indicated that incubation of 1 µmol/L betulin with human hepatocytes generated several unidentified phase I and/or phase II metabolites. In vitro, betulin was mainly metabolized by cytochrome P450 (CYP)3A. The relative contribution of CYP3A and phase II metabolizing enzymes in the overall metabolism of betulin has not been fully characterized.

Drug Interaction Studies

Clinical Studies

No clinical studies evaluating the drug interaction potential of FILSUVEZ have been conducted.

In Vitro Studies

CYP Enzymes: Betulin inhibited CYP3A and CYP2C8 with an IC_{50} value of >0.17 µmol/L (75 ng/mL). Betulin up to 10 µmol/L (4427 ng/mL) did not induce CYP 1A2, 2B6, or 3A4. These findings suggest that FILSUVEZ has no clinically meaningful effect on the PK of drugs metabolized by CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, or 3A.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity studies have been performed with FILSUVEZ or birch triterpenes.

Birch triterpenes were not genotoxic in the in vitro bacterial mutagenicity (Ames) assay, an in vitro mammalian chromosome aberration assay using human peripheral lymphocytes, or at doses up to 500 mg/kg in an in vivo mouse micronucleus assay.

In a fertility and early embryonic development study in rats, birch triterpenes were orally administered at doses of 10, 30, or 100 mg/kg/day from 2 weeks before mating through gestation day 6. Birch triterpenes had no effects on mating or fertility in male or female rats at doses up to 100 mg/kg/day.

14 CLINICAL STUDIES

The efficacy of FILSUVEZ for the treatment of partial-thickness wounds associated with inherited EB was evaluated in a randomized, double-blind, placebo-controlled trial in adults and pediatric subjects 6 months of age and older (EASE; NCT03068780) with dystrophic EB (DEB) and junctional EB (JEB). Subjects were randomized 1:1 to receive FILSUVEZ (n=109) or placebo topical gel (n=114) and instructed to apply approximately 1 mm (0.04 inch) of the investigational product to all their wounds at each dressing change (every 1 to 4 days) for 90 days. At randomization, 1 wound was selected by the investigator as the target wound for the evaluation of the primary efficacy endpoint. The target wound was defined as a partial-thickness wound of 10-50 cm^2 in surface area and present for 21 days to 9 months prior to screening.

Of the 223 subjects randomized, the median age was 12 years (range: 6 months to 81 years), 70% were under 18 years of age, and 60% were male and 40% were female. Eighty three (83)% of subjects were White, 5% were Asian, 1% were Black or African American, and 10% were other races or did not have race recorded. For ethnicity, 35% identified as Hispanic or Latino and 65% identified as not Hispanic or Latino. Of these 223 subjects, 195 had DEB, of which 175 subjects had recessive DEB (RDEB) and 20 had dominant DEB (DDEB); in addition, there were 26 subjects with JEB and 2 subjects with EB simplex.

The primary endpoint was the proportion of subjects with first complete closure of the target wound by Day 45 of the 90-day double-blind phase of the study, based on clinical assessment by the investigator. Efficacy results from EASE are presented in Table 2.

Table 2: Efficacy Results for the Treatment of Partial-Thickness Wounds in Subjects with EB in Trial EASE (Full Analysis Set)

Efficacy Parameter	FILSUVEZ N=109	Placebo Gel N=114	95% CI for the Treatment Difference
Proportion of subjects with first complete closure of target wound within 45 days	41.3%	28.9%	(0.8, 25.6)
By EB subtype[a]			
RDEB (n=175)	44.0%	26.2%	(3.9, 31.6)
DDEB (n=20)	50.0%	50.0%	(-47.8, 47.8)
JEB (n=26)	18.2%	26.7%	(-40.4, 23.5)
Proportion of subjects with first complete closure of target wound within 90 days	50.5%	43.9%	(-6.2, 20.0)

[a] Two subjects with EB simplex are not included
CI=Confidence interval

16 HOW SUPPLIED/STORAGE AND HANDLING

FILSUVEZ (birch triterpenes) topical gel, 10% (w/w) is a colorless to slightly yellowish, opalescent, non-aqueous gel and is supplied in 25 mL white aluminum tubes containing 23.4 grams of gel per tube (NDC 76431-310-01).

Each sterile tube is for one-time use only. Once opened, the product should be used immediately and discarded after use.

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

Do not freeze.

Do not use beyond the expiration date.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (*Patient Information and Instructions for Use*).

Administration Instructions

Advise patients (and/or their caregivers or guardians) of the following *[see Dosage and Administration (2)]*:

- Wash hands before and after applying FILSUVEZ or wear gloves for application.

- Apply a 1 mm layer of FILSUVEZ to the affected wound surface. Do not rub in the gel. Cover the wound with a sterile non-adhesive wound dressing. Alternatively, apply a generous layer of FILSUVEZ directly to the dressing so that the gel is in direct contact with the wound.
- Apply FILSUVEZ to cleansed wounds at dressing changes until the wound is healed.
- FILSUVEZ is for topical use only. FILSUVEZ is not for ophthalmic use and should not be applied to mucous membranes. In case of accidental contact, irrigate eyes with water.
- The sterile tube of topical gel is for one-time use only. Once the tube is opened, use the product immediately. Discard the tube after use, even if there is some topical gel left.

Hypersensitivity Reactions

- Inform patients that local hypersensitivity and skin reactions, including urticaria and dermatitis, have been reported in patients treated with FILSUVEZ. If signs and symptoms of local hypersensitivity or skin reactions occur, instruct patients to discontinue FILSUVEZ immediately and contact their healthcare provider *[see Warnings and Precautions (5.1)]*.

Manufactured by:

Lichtenheldt GmbH
Pharmazeutische Fabrik
Werk 1
Industriestr. 7-11
23812 Wahlstedt
Germany

PATIENT INFORMATION

FILSUVEZ (fill-sue-vez)

(birch triterpenes) topical gel

Important information: FILSUVEZ is for use on the skin (topical use) only. Do not use FILSUVEZ in your eyes, mouth, vagina or anus.

What is FILSUVEZ?

FILSUVEZ is a prescription medicine used on the skin to treat wounds that may happen with dystrophic and junctional epidermolysis bullosa (EB) in adults and children 6 months of age and older.

It is not known if FILSUVEZ is safe and effective in children younger than 6 months of age.

Do not use FILSUVEZ if you are allergic to any of its ingredients. See the end of this leaflet for a complete list of ingredients in FILSUVEZ.

Before using FILSUVEZ, tell your healthcare provider about all of your medical conditions, including if you:

- are pregnant or plan to become pregnant. It is not known if FILSUVEZ will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if FILSUVEZ passes into your breast milk.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

How should I use FILSUVEZ?

See the detailed "Instructions for Use" that comes with FILSUVEZ for information on how to apply FILSUVEZ.

- Use FILSUVEZ exactly as your healthcare provider tells you to use it.
- Clean wounds before applying FILSUVEZ as instructed by your healthcare provider.
- Wash hands before applying FILSUVEZ or wear gloves.
- Apply FILSUVEZ at each dressing change until the wound is healed.
- Check the expiration date on the FILSUVEZ tube. Do not use FILSUVEZ if the expiration date has passed. Call your pharmacist or healthcare provider for instructions.
- The tube of FILSUVEZ is for one-time use only. After the tube has been opened, apply the gel right away. Throw away any remaining gel and the tube after use.
- Wash hands after applying FILSUVEZ and caring for wounds.
- **Do not** use around or get FILSUVEZ in the eyes, or mucous membrane areas examples are mouth, vagina or anus.
- If you get FILSUVEZ in your eyes or mucous membrane area, rinse with clean water right away. Contact your healthcare provider if you have any discomfort.
- If the wounds you are treating with FILSUVEZ become infected, **stop treatment** and contact your healthcare provider. Signs or symptoms of infection may include the wound becoming red, warm, swollen, painful or drains yellow or greenish fluid (pus).

What are the possible side effects of FILSUVEZ?

FILSUVEZ may cause serious side effects including:

- **Allergic reactions.** Allergic reactions and skin reactions to FILSUVEZ may include the following symptoms: red itchy bumps (hives), skin rash, redness or itching. If you get any of these symptoms, stop using FILSUVEZ right away and call your healthcare provider.

The most common side effect of FILSUVEZ is application site reactions, such as pain and itchy skin.

These are not all the possible side effects of FILSUVEZ.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FILSUVEZ?

- Store FILSUVEZ at room temperature between 68°F to 77°F (20°C to 25°C). Do not freeze.
- FILSUVEZ is for one-time use only. Throw away (dispose of) any remaining FILSUVEZ and the tube right away after use in household trash or through a drug take-back option, if available. Go to www.fda.gov/drugdisposal for more information on drug disposal.

Keep FILSUVEZ and all medicines out of the reach of children.

General information about the safe and effective use of FILSUVEZ

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use FILSUVEZ for a condition for which it was not prescribed. Do not give FILSUVEZ to other people, even if they have the

same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about FILSUVEZ that is written for healthcare professionals.

What are the ingredients in FILSUVEZ?

Active ingredient: birch triterpenes

Inactive ingredients: refined sunflower oil

Manufactured by: Lichtenheldt GmbH, Pharmazeutische Fabrik, Werk 1, Industriestr. 7-11, 23812 Wahlstedt, Germany.
For more information, call 1-855-303-2347 or go to www.filsuvez.com

This Patient Information has been approved by the U.S. Food and Drug Administration Issued: 12/2023

Chiesi Total Care℠ Patient Support Services 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 FILSUVEZ® (birch triterpenes) topical gel unless otherwise noted. These patient support service programs may include affordability solutions support, appeals support, benefit verification, patient education support, copay assistance, patient assistance, and Pharmacist 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, Medicare Part D, Medicare Advantage, Medigap, Medicaid, TRICARE, Veterans Affairs (VA), Department of Defense, 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. Only patients with commercial insurance who have a valid prescription for a US Food and Drug Administration-approved indication for FILSUVEZ 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 parent or legal guardian).

If at any time a patient begins receiving prescription drug coverage under any Government-funded Plan, the patient will no longer be able to participate in the patient support services programs that provide financial support through the Program and the 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. 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, the patient will be asked to provide the size of the household, annual household income, and proof of income. Proof of income may include, among other things, W2 form(s), paycheck stubs, and/or prior year tax returns.

Other programs may be offered to eligible patients from time to time. Chiesi Total Care will notify the patient of programs for which they are eligible.

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.

Chiesi

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Chiesi Total Care℠ is a service mark of CHIESI FARMACEUTICI S.p.A.
PP-FZ-0056 V1.0 2024

Chiesi TOTAL Care℠

Filsuvez® (birch triterpenes) topical gel