HIGHLIGHTS OF PRESCRIBING INFORMATION

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

VOCERYQ™ (doruxapapogene ralaplasmid and lalikinogene sifuplasmid-gxfd) solution for intramuscular injection
Initial U.S. Approval: 2026

----------INDICATIONS AND USAGE----------

VOCERYQ is a plasmid DNA-based immunotherapy indicated to reduce the frequency of surgical papilloma excisions in adults with recurrent respiratory papillomatosis. (1)

This indication is approved under accelerated approval based on reduction in the frequency of surgical papilloma excisions. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory study(ies). (1, 14)

----------DOSAGE AND ADMINISTRATION----------

For single-dose intramuscular (IM) injection only. (2.1)

- VOCERYQ is to be administered only with CELLECTRA® 5PSP and by a healthcare provider trained in its use. (2.1)
- The recommended dose of VOCERYQ is 1 mL (6.25 mg/mL) administered intramuscularly with electroporation via CELLECTRA® 5PSP every three weeks for a total of four doses. (2.1)
- Prior to the initial administration of VOCERYQ, perform a surgical debulking of visible papilloma to establish minimal residual disease. (2.1)
- See Full Prescribing Information for instructions on preparation and administration of drug. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------

VOCERYQ is a solution for intramuscular injection, supplied in single-dose glass cartridges containing 1 mL (6.25 mg/ml). (3)

----------CONTRAINDICATIONS----------

- None (4)

----------WARNINGS AND PRECAUTIONS----------

- Injection-site reactions have occurred with VOCERYQ injection. Monitor patients for local site reactions for at least 30 minutes after treatment and manage accordingly. (5.1)
- Electroporation Related Adverse Reactions: Procedure-related effects including muscle contractions, transient bleeding, and vasovagal reactions may occur. Avoid administration in extremities with ipsilateral ICDs/pacemakers, metal implants or skin abnormalities at the treatment site. (5.2)

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence ≥ 5%) are injection site reactions, headache, fatigue, hypertension, nausea, and dizziness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Inovio Pharmaceuticals, Inc. **at 1-855-INOVIO1 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

See 17 for PATIENT COUNSELING INFORMATION.

Revised:10/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VOCERYQ is indicated to reduce the frequency of surgical papilloma excisions in adults with recurrent respiratory papillomatosis.

This indication is approved under accelerated approval based on reduction in the frequency of surgical papilloma excisions [See Clinical Studies (14)]. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory study(ies).

2 DOSAGE AND ADMINISTRATION

For single-dose intramuscular (IM) injection only.

2.1 Recommended Dosage

The recommended dose of VOCERYQ is 1 mL (6.25 mg/mL) administered intramuscularly (IM) with electroporation (EP) via CELLECTRA® 5PSP every three weeks for a total of four doses.

Prior to the initial administration of VOCERYQ, perform a surgical debulking of visible papilloma to establish minimal residual disease.

2.2 Preparation and Handling

- Refer to the User Manual for complete instructions on the preparation and administration of VOCERYQ with CELLECTRA® 5PSP *[see User Manual]*.
- VOCERYQ is to be administered only with CELLECTRA® 5PSP and by a healthcare provider trained in its use *[see User Manual].*

Receipt and Storage of VOCERYQ

- VOCERYQ is supplied as a clear to slightly opalescent, colorless solution in a single-dose, pre-filled clear glass cartridge that is sealed with a sterile siliconized bromobutyl plunger and combination rubber septum aluminum seal.
- Each single-dose, pre-filled clear glass cartridge of VOCERYQ is placed inside the original carton along with a Package Insert.
- VOCERYQ in the original carton is shipped and received in a thermally insulated container under refrigerated conditions.
- Store VOCERYQ refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton until ready to administer. Do not freeze *[See How Supplied/Storage and Handling (16.2)].*

Preparing for VOCERYQ Administration

1. Assemble supplies needed for administration including:
    - CELLECTRA® 5PSP Base Station and Handset
    - Sterile CELLECTRA® 5PSP Array
    - VOCERYQ original carton with single-dose, pre-filled glass cartridge
    - Alcohol wipes (for cartridge septum and injection site)
    - Gauze and bandage
    - Sharps container
    - CELLECTRA® 5PSP User Manual (should be read before use and available during use)
2. Ensure CELLECTRA® 5PSP Base Station and Handset are set up and charged per the User Manual.
3. Ensure patient height and weight are available and current, prior to beginning administration, as the device uses patient height and weight to recommend needle depth.
4. Remove the VOCERYQ original carton from the refrigerator and without removing the single-dose, pre-filled glass cartridge from the original carton, allow VOCERYQ to reach room temperature (approximately 30 minutes).
5. VOCERYQ in original carton should be used within 24 hours of removal from the refrigerator and may be re-refrigerated if not used; do not freeze. Upon re-refrigeration, refer to the expiry listed on the carton for shelf-life. Once removed from carton, VOCERYQ should be used within 8 hours or discarded.
6. Inspect packaging and verify expiration date for both the VOCERYQ single-dose, pre-filled glass cartridge and CELLECTRA® 5PSP Array.
7. Remove VOCERYQ single-dose, pre-filled glass cartridge from original carton and inspect for damage. Inspect VOCERYQ single-dose, pre-filled glass cartridge sterile solution for particulate matter and discoloration prior to administration. VOCERYQ is a clear to slightly opalescent colorless solution. Do not use if there are particles present or if the solution is discolored or cloudy.
8. Enter patient height and weight into the Base Station and confirm needle depth. Set the needle depth on the Handset based on the recommendation and clinical judgement regarding needle length required to safely administer at the selected injection site.
9. Assemble the single-dose, pre-filled glass cartridge as described in the User Manual [*see User Manual, "Preparing and Assembling the Array"*].
10. Clean the septum of the VOCERYQ cartridge with an alcohol swab and allow to dry for at least 30 seconds.
11. Remove the sterile Array from its packaging and inspect for damage.
12. Insert the VOCERYQ cartridge into the center of the Array and firmly push until you hear an audible »click« to indicate that the cartridge is fully inserted.
13. Confirm treatment is ready to begin on the Base Station then lift the Handset off of the Base Station.
14. Attach the assembled Array with the VOCERYQ cartridge to the Handset by aligning the blue arrows on top of the Array and Handset. Ensure that the Array sits flush on the Handset on both sides. You should hear or feel a »click« when the Array locks onto the Handset.

2.3 Administration

- Reference the CELLECTRA® 5PSP User Manual for complete instructions on administration of VOCERYQ.

- Administer VOCERYQ in the thickest part of the deltoid muscle in the upper arm. If the deltoid muscle is not suitable, administer VOCERYQ to the anterolateral quadricep.
- Avoid injecting directly into areas where the skin is tender, bruised, erythematous, indurated or affected by any lesions. Do not inject within 2 cm of a tattoo, keloid or hypertrophic scar. If there is implanted metal or an implanted device, administer VOCERYQ in an alternate injection site *[see Warnings and Precautions (5.2)]*.
- There is no need to rotate injection sites during the course of treatment.

Administration of VOCERYQ

Reference the CELLECTRA® 5PSP User Manual for complete instructions on administration of VOCERYQ.

Preparing the Injection Site

1. Select an injection site in the thickest part of the deltoid muscle in the upper arm (Figure A).
    - The anterolateral quadriceps may be selected if neither deltoid is suitable.

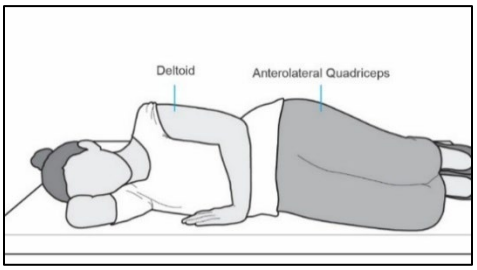


Figure A

2. Position the patient so that they can be stabilized during administration (Figure A).

3. Swab injection site with alcohol and allow at least 30 seconds to dry (Figure B).

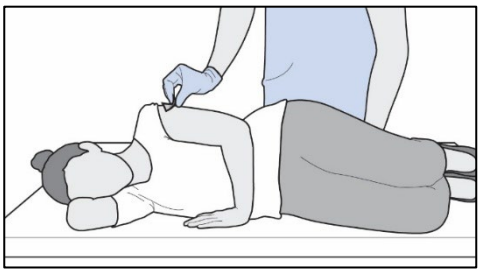


Figure B

Delivering Treatment

1. Remove the Array Cap (Figure C).

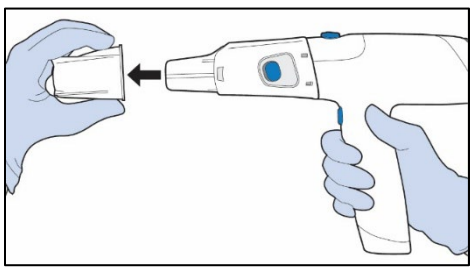


Figure C

2. Stabilize the patient as directed in User Manual (Figure D).

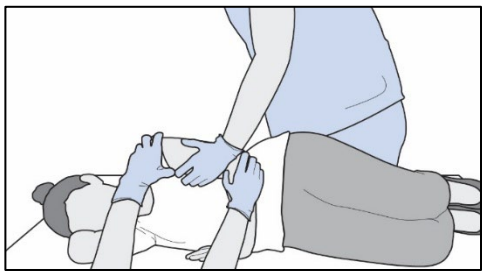


Figure D

3. Insert needles fully by firmly pushing the Handset Array straight into the injection site (Figure E).

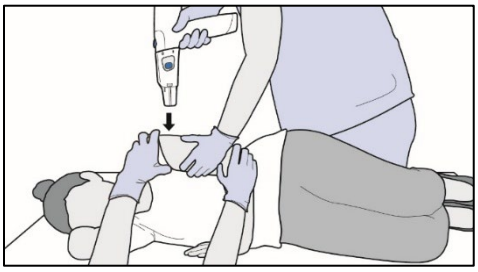


Figure E

4. Confirm the Handset displays ‘Press button to deliver treatment’. Press and release the trigger to begin treatment. Hold the Handset firmly against the muscle until the treatment is complete (Figure F).
    - The treatment takes approximately 10 seconds to complete.
    - Avoid withdrawing the Handset from the injection site before treatment is complete. Withdrawing the Handset after pressing the trigger will abort the treatment.
    - Continue to stabilize the patient’s limb and wait for the Handset to emit a confirmation sound indicating treatment is complete.

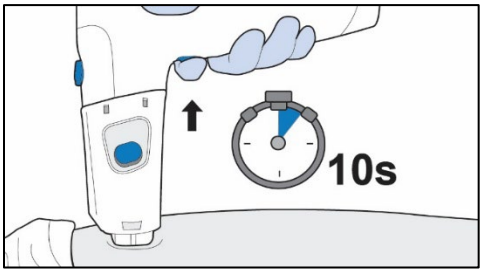


Figure F

5. Before removing the Handset, verify that “TREATMENT COMPLETE Remove array from patient” is displayed on the Handset screen.
6. Withdraw the Handset straight out from the injection site after the treatment is complete (Figure G).
    - After the Array is removed from the injection site, the shroud (cover) will retract to cover the needles.

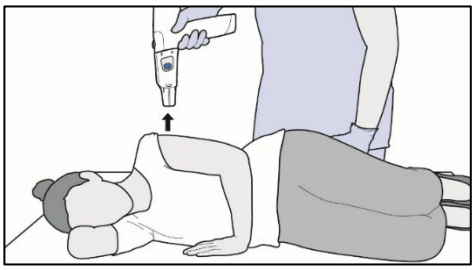


Figure G

7. Apply gauze to the injection site.

Discarding Disposables

1. Remove the used Array from the Handset by pressing and holding the blue release buttons on both sides of the Array and pulling the Array away from the Handset (Figure H).

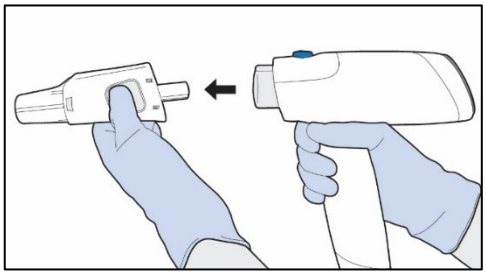


Figure H

2. Dispose of the used Array (containing the empty VOCERYQ cartridge) into a sharps disposable container.

Incomplete Treatment

Table 1 provides guidance on how to appropriately complete treatment when the patient did not receive the VOCERYQ injection and electroporation (EP).

Table 1. Managing Incomplete Treatment

Was the Array (with VOCERYQ cartridge inserted) attached to the Handset?	Was the Array fully inserted into tissue?	Was the trigger button pressed?	Action
Yes	Yes	No	Follow the device prompts to complete the procedure. Reschedule the procedure if a new Array and VOCERYQ cartridge are needed to complete the procedure.
Yes	No, but the array was locked out	No	Follow the device prompts to complete the procedure. Reschedule the procedure if a new Array and VOCERYQ cartridge are needed to complete the procedure.
Yes	Yes, but the Array was dislodged from tissue	No	Follow the device prompts. Reschedule the procedure if a new Array and VOCERYQ cartridge are needed to complete the procedure.
Yes	No	Yes	Follow the device prompts to complete the procedure
Yes	Yes	Yes	If the Handset does not display 'Treatment Complete', contact Inovio

3 DOSAGE FORMS AND STRENGTHS

VOCERYQ is supplied as a clear to slightly opalescent, colorless solution for intramuscular (IM) injection with a concentration of 6.25 mg/mL. Each single-dose, pre-filled clear glass cartridge delivers a volume of 1 mL [*see How Supplied/Storage and Handling (16)*].

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Injection-Site Reactions

Injection-site reactions have occurred with VOCERYQ injection. Monitor patients for local site reactions for at least 30 minutes after treatment and manage accordingly.

5.2 Electroporation Related Adverse Reactions

Electroporation related adverse reactions may occur with VOCERYQ administration.

Procedure-related effects associated with electroporation include brief muscle contractions or tetany, temporary bleeding at the administration site, anxiety, vasovagal reactions including lightheadedness and dizziness, and transient changes in creatine phosphokinase. Injection site erythema and injection site pain are also associated with the electroporation procedure.

To minimize risk, avoid the following during administration:

- Cardioverter-defibrillator (ICD) or pacemaker that is located *ipsilateral to* the intended deltoid injection site.
- Metal implants or implantable medical devices within the intended treatment site.
- Skin that is irritated, damaged, or has bruises, scars, or tattoos at the intended treatment site.
- Do not administer VOCERYQ to patients with any medical condition, laboratory abnormality, or clinical circumstance that, in the judgment of the treating healthcare provider, may increase the risk of treatment-related complications when administered in combination with electroporation.

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.

The safety data described in this section reflects exposure to VOCERYQ in one clinical study (Study RRP-001). A total of 32 patients with recurrent respiratory papillomatosis received a VOCERYQ dose of 1 mL (6.25 mg/mL) delivered intramuscularly (IM) followed by electroporation (EP) on Day 0, Weeks 3, 6, and 9 *[see Clinical Studies (14)]*. The most common adverse reactions (≥ 5%) are summarized in Table 2.

Table 2. Adverse Reactions Occurring in ≥ 5% of Patients in Study RRP-001 (N=32)

Adverse Reactions	RRP-001 (N=32) n (%)
Injection site reaction	11 (34%)
Headache	6 (19%)
Fatigue	5 (16%)
Hypertension	4 (13%)
Nausea	2 (6%)
Dizziness	2 (6%)

Other clinically significant adverse reactions occurring in <5% of patients included localized edema (3%), malaise (3%), lethargy (3%), flank pain (3%), jaw pain (3%), procedural anxiety (3%), flushing (3%) neutropenia (3%), cholecystitis (3%) and myalgia (3%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on VOCERYQ use in pregnant patients to evaluate a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Administration of a total of 4-5 doses of 6.23 mg VOCERYQ via intramuscular (IM) injection followed by electroporation (EP) in New Zealand White rabbits prior to mating and during gestation did not produce any significant maternal, fetal, or developmental toxicities *[see Nonclinical Toxicology (13.1)]*.

8.2 Lactation

Risk Summary

There are no data on the presence of VOCERYQ in human milk, the effects on the breastfed infant, or effects on milk production.

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

8.4 Pediatric Use

The safety and effectiveness of VOCERYQ have not been established in pediatric patients.

8.5 Geriatric Use

Clinical studies of VOCERYQ did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

VOCERYQ (doruxapapogene ralaplasmid and lalikinogene sifuplasmid-gxfd) is a plasmid DNA-based immunotherapy consisting of two DNA plasmids encoding antigens from human papillomavirus (HPV)-6 and -11 as well as human interleukin (IL)-12. It is administered intramuscularly (IM) with the CELLECTRA® 5PSP Device, which delivers the dose and provides electroporation (EP). EP is used to facilitate the intracellular delivery of VOCERYQ.

During the VOCERYQ manufacturing process, doruxapapogene ralaplasmid and lalikinogene sifuplasmid are produced through fermentation of recombinant *Escherichia coli* containing the respective plasmids. The fermentation is carried out in nutrient medium containing the antibiotic kanamycin. However, kanamycin is cleared in the manufacturing process and is not detectable in the final drug product.

VOCERYQ is a sterile, preservative-free, clear to slightly opalescent colorless solution in a single-dose, pre-filled clear glass cartridge containing 1 mL (6.25 mg/mL) doruxapapogene ralaplasmid and lalikinogene sifuplasmid. Each single-dose, pre-filled clear glass cartridge delivers 6 mg doruxapapogene ralaplasmid and 0.25 mg lalikinogene sifuplasmid. Inactive ingredients include sodium chloride (8.8 mg/mL), sodium citrate (4.4 mg/mL), hydrochloric acid (0.01 mg/mL/as needed), sodium hydroxide (as needed) and water for injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

VOCERYQ is a plasmid DNA-based immunotherapy administered via the CELLECTRA® 5PSP device that facilitates cellular entry of plasmids. The plasmids are designed to express HPV-6 and HPV-11 antigens present in HPV-6 and HPV-11 infected cells and IL-12 protein to enhance the immune response. VOCERYQ is designed to generate an immune response directed against HPV-6 and 11 proteins in patients with recurrent respiratory papillomatosis.

12.2 Pharmacodynamics

The pharmacodynamic effect of VOCERYQ was evaluated in the RRP-001 study [see Clinical Studies (14)]. In 32 patients evaluated at the completion of treatment, the induction of HPV-6 and HPV-11 specific T cells was observed at Week 11 (two weeks following the final dose) and at Week 52, indicating a persistent HPV-specific T cell response in RRP patients. Analysis of the functional CD8+ cytolytic component of the T cell response demonstrated expansion in the blood followed by infiltration into the airway/papilloma tissue. In the airway/papilloma tissue, at Week 52 there was a significant enrichment ($p = 0.002$) of cytolytic T cells and a median count of 4195 T cell clones in responders (defined as patients exhibiting a reduction or elimination of the requirement for surgical debulking) compared to 1218 T cell clones in non-responders.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis and Mutagenesis

Carcinogenicity and mutagenicity studies have not been conducted with VOCERYQ.

Impairment of Fertility

In an animal fertility study, New Zealand White rabbits were administered a total of 4-5 doses of 6.23 mg VOCERYQ by intramuscular (IM) injection followed by electroporation (EP) using the CELLECTRA® 5PSP device during the premating phase and the gestation phase. No adverse effects on reproduction were observed in males or females. There were no significant effects on embryo-fetal or postnatal survival, growth, or development in the F1 generation kits or malformations or variations in the F1 generation of fetuses.

13.2 Animal Toxicology and/or Pharmacology

The safety of VOCERYQ is supported by comprehensive nonclinical toxicology studies conducted with analogous DNA-based plasmids with an identical plasmid backbone to VOCERYQ. No consistent adverse product-related systemic toxicological findings were observed.

14 CLINICAL STUDIES

The efficacy of VOCERYQ was assessed in an open-label, single-arm study in adults with recurrent respiratory papillomatosis (RRP-001; NCT04398433).

Study RRP-001 enrolled 32 adults with clinically and histologically diagnosed recurrent respiratory papillomatosis and a history of 2 or more surgeries to remove laryngotracheal papillomas in the 12 months preceding study enrollment. Prior to treatment with VOCERYQ (Day 0), patients underwent surgical excision of laryngotracheal papillomas as per standard-of-care. VOCERYQ was administered on Day 0, Weeks 3, 6, and 9. All 32 patients were treated with a dose of 6.25 mg per injection.

The demographic characteristics of the study population (i.e., safety dataset) were as follows: median age 46.5 years (range 25 to 82 years), 24 patients (75.0%) were male, 26 patients (81%) were white, 4 patients (13%) were African American, 1 patient (3%) was Asian, 1 patient (3%) was of “other” race, and 29 patients (91%) were non-Hispanic or Latino.

Of the 32 patients, 26 patients had required 3 or more surgeries for papilloma excision in the 12 months prior to treatment and were included in the efficacy evaluation. The median number of papilloma surgical excisions in the 12 months prior to the first dose in the efficacy population was 4.5 (range: 3 to 8). This included the single papilloma excision procedure prior to treatment. During the VOCERYQ dosing window, no additional papilloma surgical excisions were required in the protocol. The primary efficacy endpoint was assessed as the percentage of patients with a complete response to VOCERYQ treatment, defined as no requirement for surgical intervention in the 12 months after treatment.

Seven out of the 26 patients (27% [95% CI: 12,48%]) demonstrated a complete response, defined as requiring no surgical excision of papillomas, after 12 months of follow up which is not expected as part of the natural history of the disease when untreated.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

VOCERYQ (doruxapapogene ralaplasmid and lalikinogene sifuplasmid-gxfd) is supplied as a clear to slightly opalescent colorless solution in a single-dose, pre-filled clear glass cartridge.

- Each original carton of VOCERYQ contains one single-dose, pre-filled glass cartridge of VOCERYQ sterile solution that is sealed with a sterile siliconized bromobutyl plunger and combination rubber septum aluminum seal.

Each single-dose, pre-filled glass cartridge of VOCERYQ sterile solution contains 1 mL (6.25 mg/mL) doruxapapogene ralaplasmid and lalikinogene sifuplasmid-gxfd.

- Product NDC: 84348-3107- 0 (VOCERYQ cartridge)
- Package NDC: 84348-3107-1 (VOCERYQ carton)

VOCERYQ is administered by intramuscular (IM) injection followed by electroporation (EP) using the CELLECTRA® 5PSP, which is not supplied with VOCERYQ cartridges. CELLECTRA® 5PSP is provided to healthcare providers by calling the toll-free number at 1-855-INOVIO1.

16.2 Storage and Handling

VOCERYQ is shipped in a thermally insulated container under refrigerated conditions and stored at 2°C to 8°C (36°F to 46°F) in its original carton until ready to administer.

Do not freeze.

VOCERYQ in original carton should be used within 24 hours of removal from the refrigerator and may be re-refrigerated if not used. Upon re-refrigeration, refer to the expiry listed on the original carton for shelf-life.

- Total exposure of VOCERYQ to room temperature must not exceed 24 hours.

Once single-dose, pre-filled glass cartridge is removed from original carton, VOCERYQ should be used within 8 hours or discarded.

17 PATIENT COUNSELING INFORMATION

Discuss the following with patients and/or caregivers:

- Injection Site Reactions: Inform patients and/or caregiver that injection site reactions have occurred after VOCERYQ injection. Educate patients or caregiver on possible symptoms of injection site reaction, including redness, pain, swelling, itching, or warmth at the injection site. Advise patients to manage symptoms with cold compresses, over the counter pain relievers or antihistamines, if needed. Seek medical care if symptoms worsen or are accompanied by signs of a systemic allergic reaction (difficulty breathing, widespread rash, facial swelling) or infection *[see Warnings and Precautions (5.1)]*.

Manufactured by:
Alliance Medical Products, Inc. (dba Siegfried Irvine)
Irvine, CA 92618

Manufactured for:
Inovio Pharmaceuticals, Inc.
San Diego, CA 92121

U.S. license number xxxx

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