State of California—Health and Human Services Agency
Department of Health Care Services

WILL LIGHTBOURNE
DIRECTOR

GAVIN NEWSOM
GOVERNOR

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TO: All County California Children's Services Program Administrators, Medical Consultants, Integrated Systems of Care Division Staff, and Genetically Handicapped Persons Program

SUBJECT: Policy on Palynziq (pegvaliase-pqpz) for Patients with Phenylketonuria - Revised

I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to establish California Children's Services (CCS) Program and Genetically Handicapped Persons Program (GHPP) policy on the authorization of pegvaliase-pqpz (Palynziq). This drug is an enzyme substitution drug therapy that reduces phenylalanine (Phe) blood levels in with phenylketonuria (PKU). Patients with PKU are unable to maintain Phe concentrations below 600 micromol/L, despite other treatment.

The CCS Program publishes this N.L. under the program's authority to authorize services that are medically necessary to treat CCS-eligible conditions.[1,2,3]

II. BACKGROUND

PKU is an inherited disorder due to inborn error of metabolism. Affected patients do not have the ability to breakdown Phe, an amino acid found in protein foods, due to a deficiency of the enzyme phenylalanine hydroxylase (PAH). Phe accumulates in the blood and becomes toxic to the brain when it crosses the blood brain barrier. The signs and symptoms vary between individuals, but may include intellectual disability, developmental delay, seizures, and behavioral conditions. Affected individuals require lifelong treatment, generally with low protein foods and sapropterin, a synthetic analog of PAH. Individuals often have neurocognitive impairment and high levels of Phe, despite treatment.

Palynziq is a PAH enzyme replacement therapy for patients who have been diagnosed with PKU. Palynziq can be self-administered through subcutaneous

injection. Palynziq is indicated for clients who have blood Phe > 600 micromol/L. It was approved by the Food and Drug Administration (FDA) on May 24, 2018, to reduce phenylalanine concentrations in the blood.

The most serious adverse reaction in the Palynziq trials was anaphylaxis, which occurred most frequently during upward titration of the dose. Because of this risk, the product is available only through a restricted program called the Palynziq Risk Evaluation and Mitigation Strategy (REMS) Program. Prescribers and pharmacies must be certified by the REMS program. The REMS program requires providers to prescribe auto-injectable epinephrine with Palynziq so that patients can self-administer epinephrine to treat anaphylaxis. Patients must also enroll in the REMS program to be educated about the risk of anaphylaxis, and be able to self-administer auto-injectable epinephrine at any time while taking Palynziq.

III. POLICY

A. Effective the date of this letter, pegvaliase[4] is a CCS Program/GHPP benefit when the following criteria are met:

1. The client is receiving medical care from a CCS Program/GHPP approved Metabolic Special Care Center (SCC).

2. Client meets the current FDA age requirement (Attachment 1).

3. Client has been diagnosed with PKU.

4. The SCC provider who prescribed pegvaliase and the dispensing pharmacy are certified by the REMS program.

5. The treating SCC provides medical documentation showing that the client has previously been placed on sapropterin as a treatment for PKU[5], but the sapropterin treatment was ineffective or contraindicated to the client.

6. The treating SCC provides medical documentation showing that the client has attempted to manage PKU symptoms through dietary management (by restricting phenylalanine and protein intake), by eating low protein therapeutic foods (medical foods), and using specific PKU enteral nutrition products, but they have been ineffective.

7. The client has documented chronic Phe levels greater than 600 micromol/L, despite the therapies listed in section III.A.5-6.

8. Client has a prescription for auto-injectable epinephrine to treat anaphylaxis.

9. The request for pegvaliase follows the FDA approved and recommended dosing regimen (see Attachment 1). Slight deviations are acceptable based on patient response to titration treatment.

B. For initial authorization:

1. The SCC must submit all of the following, documented within the past 12 months:

a. Prescription.

b. Multiple Phe levels, documenting levels greater than 600micromol/L.

c. Metabolic SCC physician's written plan of PKU treatment, including plans for monitoring Phe levels.

d. For CCS Program clients, a CCS Program/SCC-paneled registered dietitians (RD) medical nutrition therapy plan.

2. Provider has provided documentation that the initial dose will be administered under supervision of healthcare providers equipped to manage anaphylaxis.

3. Provider has provided documentation that if client is currently on sapropterin dihydrochloride, client will discontinue its use at least 14 days prior to first dose of pegvaliase.

4. Provider has provided documentation that the client has and be willing to carry an auto-injectable epinephrine, with them at all times.

C. For re-authorizations of pegvaliase, a SCC must provide documentation confirming one of the following:

1. There is at least a 20 percent reduction in Phe levels from pre- pegvaliase treatment baseline.

2. Phe level less than or equal to 600 micromol/L after 16 weeks of pegvaliase treatment at maximum dose of 40mg once daily.

3. Client has been receiving less than 20 mg/day, but will be titrated to maintenance dose or maximum dose. (see Attachment 1).

D. Additional considerations for medical necessity determination:

For clients who do not meet the criteria described in sections III.A. through III.C., SCCs may demonstrate medical necessity by submitting any other clinical

documentation and/or evidence that would support the initial or reauthorization of the client's pegvaliase treatment SCCs or pharmacies should submit this documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee.

E. Whole Child Model (WCM) Counties:

For CCS clients who are enrolled in a Medi-Cal managed care plan (MCP) and reside in a WCM county, the client's MCP shall be responsible for authorizing, coordinating, and covering pegvaliase. MCPs operating in WCM counties should use the authorization guidelines described in this N.L., or utilize the MCP's existing pegvaliase policies, whichever is less restrictive.

IV. POLICY IMPLEMENTATION

A. Pegvaliase is not covered by a Special Code Grouping Service Authorization Request (SAR) and requires separate authorization.

B. Requesting provider must submit a SAR, clinical documentation listed in section III, and a copy of the signed prescription to the county CCS Program office or the DHCS authorizations office.

1. For non-Whole Child Model (WCM) independent counties, requests for initial and continuing pegvaliase treatment will be reviewed and authorized by county CCS Programs.

2. For dependent counties, requests for initial and continuing pegvaliase treatment will be reviewed and authorized by the ISCD Special Populations Unit at CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number (916) 440-5306.

3. For WCM counties, requests for initial and continuing pegvaliase treatment will be reviewed and authorized by the Managed Care Plan.

4. Initial authorization shall be for induction and titration therapy only.

5. Reauthorization shall be for:

   a. Any deviation from titration therapy, or

   b. If there is no deviation of titration therapy, then the second authorization shall be for maintenance therapy.

6. Therapy is titrated to achieve a response to the goal of Phe blood level below 600 micromol/L. Daily doses may be titrated, up to the first 33 weeks, but

cannot be titrated up to the maximum (40g) daily dose. A maximum daily dose may be attempted after 33 weeks. After 16 weeks of maximum (40mg daily dose) therapy, pegvaliase must be discontinued if the desired treatment goal of Phe blood level below 600 micromol/L is not achieved.

Beginning April 1, 2021, all requests for prior authorization of medications billed by National Drug Code and dispensed by a Medi-Cal enrolled pharmacy provider, shall be sent from the pharmacy provider to the Medi-Cal Rx vendor, Magellan Medicaid Administration, Inc. (Magellan). The Medi-Cal RX website provides guidance: https://medi-calrx.dhcs.ca.gov/home/.

If you have any questions regarding this N.L., please email the ISCD Medical Director or designee at ISCD-MedicalPolicy@ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

Attachment 1: Recommended Dosing Regimen

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[1] 22 Cal. Code Regs. § 41515.1 et. seq. Determination of Medical Eligibility https://govt.westlaw.com/calregs/Document/I28E30090D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=%28sc.Default%29

[2] 22 Cal. Code Regs. § 41700 Availability https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)&bhcp=1&ignorebhwarn=IgnoreWarns

[3] 22 Cal. Code Regs. § 41740 Eligibility for Treatment Services https://govt.westlaw.com/calregs/Document/I2FDD8050D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=StatuteNavigator&contextData=%28sc.Default%29

[4] FDA guidelines require biologic and biosimilar products contain a four-letter suffix following the active component of the product. This four-letter FDA assigned suffix has no clinical significance and is to differentiate between competing biologic and biosimilar products. The active component name, without the four-digit suffix, will designate intent to address the active drug, not a specific brand or product.

[5] Sapropterin is sometimes used along with a restricted diet to control blood phenylalanine levels in adults and children 1 month of age and older who have phenylketonuria. Sapropterin will only work for some people who have PKU, and the only way to tell if sapropterin will help a particular patient is to give the medication for a period of time (generally at least 1 month on the maximum allowable dosage) and see whether his or her phenylalanine level decreases

	Recommended Dosing Regimen	
Treatment	Pegvaliase Dosage	Duration*
Induction	2.5 mg once weekly	4 weeks
Titration	2.5 mg twice weekly	1 week
	10 mg once weekly	1 week
	10 mg twice weekly	1 week
	10 mg four times weekly	1 week
	10 mg once daily	1 week
Maintenance	20 mg once daily	24 weeks
Maximum†	40 mg once daily	16 weeks‡

* Current FDA-approved age for use is 18 years of age or older.

* Additional time may be required prior to each dosage escalation based on patient tolerability.

† Individualize treatment to the lowest effective and tolerated dosage. Consider increasing to a maximum of 40 mg once daily in patients who have not achieved a response with 20 mg once daily continuous treatment for at least 24 weeks [see Clinical Studies (14)].

‡ Discontinue pegvaliase treatment in patients who have not achieved a response after 16 weeks of continuous treatment with the maximum dosage of 40 mg once daily.