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Next Review Due By: 7/2024
Policy Number: C7067-A

Kuvan (sapropterin dihydrochloride)

PRODUCTS AFFECTED

Kuvan (sapropterin dihydrochloride), Javygtor (sapropterin dihydrochloride), sapropterin dihydrochloride

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-(BH4-) responsive phenylketonuria

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. HYPERPHENYLALANINEMIA:
1. Documented diagnosis of phenylketonuria (PKU)
AND

2. Documentation that baseline phenylalanine level (prior to initiation of therapy with sapropterin) is above the recommended Phe levels [All ages: 2-6 mg/dL (120-360 mcmol/L)]. Phenylalanine lab test report dated within 30 days of request is required. [DOCUMENTATION REQUIRED]
   AND
3. Prescriber attests that dietary management will be maintained (phenylalanine-restriction) while on sapropterin dihydrochloride therapy.
   AND
4. Prescriber attests that sapropterin will be used as monotherapy. [Sapropterin dihydrochloride must be used as monotherapy and will not be authorized for use in combination with Palynziq (pegvaliase-pqpz)]
   Note: There is no data available to support the concomitant use of Palynziq and sapropterin. In the Palynziq pivotal studies, patients were required to discontinue use of Kuvan at least 14 days prior to the first dose of Palynziq.
   AND
5. IF THIS IS A NON-FORMULAR/NON-PREFERRED PRODUCT: Documentation of trial/failure of or intolerance to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Documentation of medication(s) tried, dates of trial(s) and reason for treatment failure(s) is required.

CONTINUATION OF THERAPY:

A. HYPERPHENYLALANINEMIA:

1. Prescriber attests that sapropterin is still being used as monotherapy
   AND
2. Prescriber attests to compliance/adherence to a phenylalanine-restricted diet in conjunction with sapropterin therapy
   AND
3. (a) Documentation that member's blood Phe decreased (at least a 20% reduction in Phe levels) after 1 month of treatment at 20mg/kg/day (responders to treatment with sapropterin) [DOCUMENTATION REQUIRED]
   OR
   (b) If member has not been titrated to appropriate max dose for effect within 2 months: prescriber must provide treatment plan of titration, revaluation, and monitoring [DOCUMENTATION REQUIRED]
   OR
   (c) Member has adequate blood Phe level control with continued use (monitored for hyper- and hypo-phenylalaninemia)

DURATION OF APPROVAL:

ADULTS (18 years of age and older):
Initial authorization: If dose is 5-10mg/kg/day authorize 2 months to allow titration to 20mg/kg/day

If initial dose is 20mg/kg/day authorize 1 month. Treatment should be discontinued if phenylalanine levels do not decrease after 1 month of treatment at 20 mg/kg/day (non-responder).

Member should have dosage adjusted after 1 month based on blood phenylalanine levels (if phenylalanine levels do not decrease from baseline after initiating 10 mg/kg, increase dose to 20 mg/kg once daily);
Maintenance range: 5 to 20 mg/kg once daily
Reauthorization: 6 months

PEDIATRIC (6 years of age and younger):
Initial authorization: 2 months
[10 mg/kg/dose once daily; check phenylalanine level 1 week after starting and periodically during the first month; adjust dose after 1 month based on phenylalanine levels; if phenylalanine levels have not decreased from baseline after 1 month of therapy, increase dose to 20 mg/kg/dose once daily; if still no

response after 1 month of therapy at the higher dose (20 mg/kg/day) then discontinue sapropterin (nonresponder).]
Reauthorization: 6 months

PEDIATRIC (7 years of age and adolescents):
Initial authorization: if dose is 5-10mg/kg/day authorize 2 months to allow titration to 20mg/kg/day [Oral: 10 to 20 mg/kg/dose once daily; check phenylalanine level 1 week after starting and periodically during the first month; adjust dose after 1 month based on phenylalanine levels:
For initial dose 10 mg/kg/dose: If phenylalanine levels have not decreased from baseline after 1 month of therapy, increase dose to 20 mg/kg/dose once daily; if still no response after 1 month of therapy at the higher dose (20 mg/kg/day) then discontinue sapropterin (nonresponder).

If initial dose is 20mg/kg/day authorize 1 month. Treatment should be discontinued if phenylalanine levels do not decrease after 1 month of treatment at 20 mg/kg/day (nonresponder).

For initial dose 20 mg/kg/dose: If no response after 1 month of therapy, discontinue sapropterin (nonresponder).
Reauthorization: 6 months

PRESCRIBER REQUIREMENTS:
Prescribed by, or in consultation with, a board-certified medical geneticist or physician experienced in the management of metabolic disorders or phenylketonuria (PKU). [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
1 month of age or older

QUANTITY:
Infants and children up to 6 years of age: Initial dose of 10mg/kg once daily. Maintenance dose of 5 to 20mg/kg once daily.
Ages 6 and older: Initial dose of 10 to 20mg/kg once daily. Maintenance dose of 5 to 20mg/kg once daily.

Maximum Quantity Limits – 20mg/kg once daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Phenylketonuria Treatment - Agents

FDA-APPROVED USES:
Indicated to reduce blood phenylalanine (Phe) levels in adult and pediatric patients one month of age and older with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin- (BH4-) responsive Phenylketonuria (PKU). Kuvan, Javygtor is to be used in conjunction with a Phe-restricted diet.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Illinois (Source: Illinois General Assembly)
"(215 ILCS 200/60) Sec. 60. Length of prior authorization approval. *A prior authorization approval shall be valid for the lesser of 6 months after the date the health care professional or health care provider receives the prior authorization approval or the length of treatment as determined* by the patient's health care professional or the renewal of the plan, and the *approval period shall be effective regardless of any changes, including any changes in dosage for a prescription drug* prescribed by the health care professional. All dosage increases must be based on established evidentiary standards and nothing in this Section shall prohibit a health insurance issuer from having safety edits in place. This Section shall not apply to the prescription of benzodiazepines or Schedule II narcotic drugs, such as opioids. Except to the extent required by medical exceptions processes for prescription drugs set forth in Section 45.1 of the Managed Care Reform and Patient Rights Act, nothing in this Section shall require a policy to cover any care, treatment, or services for any health condition that the terms of coverage otherwise completely exclude from the policy's covered benefits without regard for whether the care, treatment, or services are medically necessary.
(Source: P.A. 102-409, eff. 1-1-22.)"
"(215 ILCS 200/65) Sec. 65. Length of prior authorization approval for *treatment for chronic or long-term conditions*. If a health insurance issuer requires a prior authorization for a recurring health care service or maintenance medication for the treatment of a chronic or long-term condition, *the approval shall remain valid for the lesser of 12 months from the date the health care professional or health care provider receives the prior authorization approval or the length of the treatment as determined by the patient's health care professional*. This Section shall not apply to the prescription of benzodiazepines or Schedule II narcotic drugs, such as opioids. Except to the extent required by medical exceptions processes for prescription drugs set forth in Section 45.1 of the Managed Care Reform and Patient Rights Act, nothing in this Section shall require a policy to cover any care, treatment, or services for any health condition that the terms of coverage otherwise completely exclude from the policy's covered benefits without regard for whether the care, treatment, or services are medically necessary.
(Source: P.A. 102-409, eff. 1-1-22.)"

Kentucky (Source: Kentucky Revised Statutes)
KY304.17A-167 Time span of authorizations
(Subsection 2) "Unless otherwise provided in subsection (3) of this section or prohibited by state or federal law, if a provider receives a prior authorization for a drug prescribed to a covered person with a condition that requires ongoing medication therapy, and the provider continues to prescribe the drug, and the drug is used for a condition that is within the scope of use approved by the United States Food and Drug Administration or has been proven to be a safe and effective form of treatment for the patient's specific underlying condition based on clinical practice guidelines that are developed from peer-reviewed publications, the prior authorization received shall: (a) Be valid for the lesser of: 1. One (1) year from the date the provider receives the prior authorization; or 2. Until the last day of coverage under the covered person's health benefit plan during a single plan year; and (b) Cover any change in dosage prescribed by the provider during the period of authorization." (Subsection 3) "Except as provided in paragraph (b) of this subsection, the provisions of subsection (2) of this section shall not apply to: 1. Medications that are prescribed for a non-maintenance condition; 2. Medications that have a typical treatment period of less than twelve (12) months; 3. Medications where there is medical or scientific evidence that does not support a twelve (12) month approval; or 4. Medications that are opioid analgesics or benzodiazepines. (b) Paragraph (a) of this subsection shall not apply to any medication that is prescribed to a patient in a community-based palliative care program."
Re-authorization (approved authorization previously issued by Molina Healthcare) for maintenance

medications within this policy shall be approved for a 12 month duration when request meets policy requirements, unless exceptions noted above have been met.

Ohio (Source: Ohio Revised Code)
Chapter 3923 Sickness And Accident Insurance Section 3923.041 Policies with prior authorization requirement provisions "(B)(6)(a) For policies issued on or after January 1, 2017, *for a prior approval related to a chronic condition*, the insurer or plan shall honor a prior authorization *approval for an approved drug for the lesser of the following from the date of the approval: (i) Twelve months*; (ii) The last day of the covered person's eligibility under the policy or plan. (b) The duration of all other prior authorization approvals shall be dictated by the policy or plan."

State Medicaid
Kentucky (Source: Kentucky Revised Statutes)
KY304.17A-167 Time span of authorizations
(Subsection 2) "Unless otherwise provided in subsection (3) of this section or prohibited by state or federal law, if a provider receives a prior authorization for a drug prescribed to a covered person with a condition that requires ongoing medication therapy, and the provider continues to prescribe the drug, and the drug is used for a condition that is within the scope of use approved by the United States Food and Drug Administration or has been proven to be a safe and effective form of treatment for the patient's specific underlying condition based on clinical practice guidelines that are developed from peer-reviewed publications, the prior authorization received shall: (a) Be valid for the lesser of: 1. One (1) year from the date the provider receives the prior authorization; or 2. Until the last day of coverage under the covered person's health benefit plan during a single plan year; and (b) Cover any change in dosage prescribed by the provider during the period of authorization." (Subsection 3) "Except as provided in paragraph (b) of this subsection, the provisions of subsection (2) of this section shall not apply to: 1. Medications that are prescribed for a non-maintenance condition; 2. Medications that have a typical treatment period of less than twelve (12) months; 3. Medications where there is medical or scientific evidence that does not support a twelve (12) month approval; or 4. Medications that are opioid analgesics or benzodiazepines. (b) Paragraph (a) of this subsection shall not apply to any medication that is prescribed to a patient in a community-based palliative care program."
Re-authorization (approved authorization previously issued by Molina Healthcare) for maintenance medications within this policy shall be approved for a 12 month duration when request meets policy requirements, unless exceptions noted above have been met.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Kuvan is indicated to reduce blood phenylalanine (Phe) levels in patients with hyperphenylalaninemia (HPA) due to tetrahydrobiopterin-(BH4) responsive phenylketonuria (PKU). The medication should be used with a Phe-restricted diet. Kuvan works by increasing phenylalanine hydroxylase (PAH). In patients with PKU who are responsive to treatment, blood Phe levels decrease within 24 hours after administration, although maximal effect on Phe levels may take up to 1 month. The recommended starting dose of Kuvan is 10 mg/kg/day taken once daily (QD) for patients 1 month to 6 years of age. For patients ≥ 7 years of age, the recommended starting dose is 10 to 20 mg/kg QD. Therapy response is determined by changes in blood Phe after treatment for a period of 1 month. Blood Phe levels should be checked after 1 week of treatment and periodically for 1 month. Patients whose blood Phe does not decrease after 1 month of treatment at 20 mg/kg/day are non-responders and treatment with Kuvan should be discontinued.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Kuvan (sapropterin dihydrochloride) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Kuvan (sapropterin dihydrochloride), Javygtor (sapropterin dihydrochloride) include: No labeled contraindications

OTHER SPECIAL CONSIDERATIONS:

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Javygtor PACK 100MG
Javygtor PACK 500MG
Javygtor TABS 100MG
Kuvan PACK 100MG
Kuvan PACK 500MG
Kuvan TABS 100MG
Sapropterin Dihydrochloride PACK 100MG
Sapropterin Dihydrochloride PACK 500MG
Sapropterin Dihydrochloride TABS 100MG

REFERENCES

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11. Singh, Rohr, Frazier, etc al, Recommendations for the nutrition management of phenylalanine hydroxylase deficiency, Genetics in Medicine, 2014, doi:101038/gim.2013.179.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy FDA-Approved Uses Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q3 2023
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Duration of Approval Prescriber Requirements FDA-Approved Uses Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file