JOHNS HOPKINS HEALTH PLANS	Johns Hopkins Health Plans **Medical Policy Manual** **Medical Policy**	*Policy Number*	CMS20.05
		Effective Date	08/01/2023
		Approval Date	05/16/2023
	Subject **Expanded Access and Compassionate Use**	*Supersedes Date*	08/01/2022
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This document applies to the following Participating Organizations:

EHP	Johns Hopkins Advantage MD	Johns Hopkins Health Plan of Virginia Inc. (JHHPVA)	Priority Partners
US Family Health Plan			

Keywords: clinical trial, compassionate, FDA

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I. ACTION

	New Policy	
X	Revising Policy Number	
	Superseding Policy Number	
	Retiring Policy Number	

II. POLICY DISCLAIMER

Johns Hopkins Health Plans (JHHP) provides a full spectrum of health care products and services for Advantage MD, Employer Health Programs, Johns Hopkins Health Plan of Virginia Inc., Priority Partners, and US Family Health Plan. Each line of business possesses its own unique contract, benefits, regulations, and regulators' clinical guidelines that supersede the information outlined in this policy.

III. POLICY

Cross Reference:

- ADMIN016 Handling Rare Disease Cases (USFHP)
- PHARM41 PPMCO Off-Label Use of Medications
- PHARM59 USFHP Off-Label Use of Medications

For Advantage MD refer to: Medicare Coverage Database

- National Coverage Determination (NCD) 310.1 Routine Costs in Clinical Trials
- National Coverage Determination (NCD) 110.2 Certain Drugs Distributed by the National Cancer Institute

- Local Coverage Determination (LCD) L35490 Category III Codes
- Search by topic to review for applicable Local Coverage Determination (LCD) and/or National Coverage Determination (NCD)
- Advantage MD Pharmacy Formulary & Prior Authorization procedures: https://www.hopkinsmedicine.org/

For Employer Health Programs (EHP) refer to:

- Plan specific Summary Plan Descriptions (SPD's)
- EHP Plan specific Pharmacy Formularies & Prior Authorization procedures: www.ehp.org/plan-benefits/pharmacy/

For Johns Hopkins Health Plan of Virginia Inc. (JHHPVA) refer to: Medicare Coverage Database (Effective 1/1/2024)

- National Coverage Determination (NCD) 310.1 Routine Costs in Clinical Trials
- National Coverage Determination (NCD) 110.2 Certain Drugs Distributed by the National Cancer Institute
- Local Coverage Determination (LCD) L35490 Category III Codes

For Priority Partners (PPMCO) refer to Code of Maryland Regulations

- Code of Maryland Regulations (COMAR) 10.67.06.26-1 Clinical Trial Items and Services
- PPMCO Pharmacy Formulary & Prior Authorization procedures: www.ppmco.org/pharmacy/

For US Family Health Plan refers to Tricare Policy Manuals

- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 8, Section 9.1 Pharmacy Benefits Program.
- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 1, Section 3.1 Rare Diseases.
- TRICARE Policy Manual 6010.63-M, April 1, 2021, Chapter 8, Section 5.1 Medical Devices.
- USFHP Pharmacy Formulary & Prior Authorization procedures: https://www.hopkinsmedicine.org/

IV. POLICY CRITERIA

A. This policy is applicable when a member has exhausted standard of care therapy options and is expected to progress to an End-Stage Condition within a brief period of time and provides options for when a member may not be able to obtain their provider's proposed therapy through established expanded access pathways.

B. When benefits are provided under the member's contract, JHHP uses the following guidelines for expanded access and compassionate use requests.

C. Member Eligibility

1. Member with a serious medical condition that is expected to progress to an End-Stage Condition within one year.
2. Member meets one of the following eligibility criterion:
   a. Refractory to, or an inappropriate candidate for, all standard of care treatment options including, but not limited to, indicated FDA-authorized, FDA-approved, FDA-cleared, and OTC treatment options, OR;
   b. Refractory to at least one standard of care treatment option with provider documentation of inappropriateness of remaining standard of care treatment options including, but not limited to, indicated FDA-authorized, FDA-approved, FDA-cleared and OTC options
3. There is documentation of member ineligibility for clinical trial participation following search of www.clinicaltrials.gov (see Background section for more details), AND;
4. Evidence (i.e., communication from manufacturer OR communication from FDA) of enrollment failure in Expanded Access Protocol(http://navigator.reaganudall.org/, https://www.fda.gov/) (see Background section for more details), AND;

5. Documentation of Hospice Care discussion with member, or member's parent, guardian, or healthcare proxy, or documentation of inappropriateness of a Hospice Care discussion

D. Therapy Eligibility:
   1. General Considerations:
      a. Requests are considered on a case-by-case basis within the scope of Plan specific regulations (*Refer to Policy Section III*)
      b. The following resources are available for information on rare diseases
         i. National Organization for Rare Disorders (NORD) https://rarediseases.org/
         ii. National Institute of Health (NIH), Genetic and Rare Diseases Information Center (GARD) https://rarediseases.info.nih.gov/
         iii. Orphanet (International portal for rare diseases and orphan drugs) https://www.orpha.net/
   2. Non-Pharmaceutical Therapy (e.g., Surgical Therapy, Radiologic Therapy, Medical Device Therapy): The evidence requirements below will inform evaluation of the proposed therapy
      a. A minimum of two published clinical studies that demonstrate efficacy and safety of the therapy for the intended use. Evidence level must be consistent with evidence grade I or II and demonstrate statistically-significant and clinically-meaningful improvement in the primary outcome, OR;
      b. Abstracts and poster presentations from a professional association addressing a breakthrough treatment or rare disease, in the absence of published clinical studies for the intended use. Evidence level must be consistent with evidence grade I or II and demonstrate statistically-significant and clinically-meaningful improvement in the primary outcome, OR;
      c. Therapy is consistent with recommended treatment guidelines published by a professional medical association or, for oncology therapies, inclusion in National Cancer Network (NCCN) treatment guidelines for the relevant condition.
   3. Pharmaceutical Therapy: Refer to *Policy Section III* for Plan specific guidance, applicable polices, and links to Pharmacy Formularies & Prior Authorization procedures.
      Note: For USFHP, off-label use of pharmaceuticals for treatment of rare diseases should be reviewed using TRICARE criteria for rare diseases (*Refer to Policy Section III).*

E. Authorization Process:
   1. Request may be initiated by the prescriber, member or authorized member representative.
   2. Upon member request, JHHP will contact the prescriber to obtain information to process the request.
   3. Requests will be accepted in the form of a letter of medical necessity and should include the following information, where applicable:
      a. Member demographic information, first name, last name, date of birth, and ID number
      b. Prescriber information, including name, phone number and fax number
      c. Diagnosis
      d. Explanation of medical necessity reason for the request
      e. Documentation of previous therapeutic failures, if any
      f. Documentation of adverse effects of first-line therapy, if any
      g. Clinical progress notes to support authorization requests
      h. Time-based prognosis
   4. No singular person can approve compassionate use/expanded access coverage. The following parties will discuss and determine the final outcome:
      a. CMO or designee
      b. Line of Business Head or designee
      c. AVP/Director of Pharmacy or designee
   5. All decision and notification timeframes will be met as per designated regulation.
   6. Decision will be communicated to the requesting party and the member/provider according to established policies.

7. Appeal rights are granted according to established policies and regulatory requirements.

V. DEFINITIONS

Expanded Access: Use of an investigational [therapy] when the primary purpose is to diagnose, monitor, or treat a patient rather than to obtain the kind of information about the [therapy] that is generally derived from clinical trials1. Expanded access (or compassionate use) provides access to investigational products (drug, biologic, or medical device) outside a clinical trial for members with a life-threatening condition or serious disease or condition when no comparable or satisfactory alternative therapy options are available (FDA, Miller, 2017).

End-Stage Condition: An advanced, progressive, irreversible condition caused by injury, disease, or illness: (1) That has caused severe and permanent deterioration indicated by incompetency and complete dependency; and (2) For which, to a reasonable degree of medical certainty, treatment of the irreversible condition would be medically ineffective. (Annotated Code of Maryland, Subtitle 6: Health Care Decisions Act; 5-601)

Evidence Grade:

- Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias and flaws in research design. Studies with negative results have sufficient large samples to have adequate statistical power. (e.g., large double blind randomized controlled trial)
- Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to conclusion because of inconsistencies among results among the studies or because of minor doubts about generalizability, bias and flaws in research design, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies that are consistent with minor exceptions at most.
- Grade III: The evidence consist of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results of different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

VI. BACKGROUND

Despite recent legislation, such as the 21st Century Cures Act, enacted to accelerate FDA approvals and evidence that such approvals have hit multi-decade highs, it is important to acknowledge that there are many patients who have not directly benefited from these developments (Chambers, 2017; Jarow, 2017). For seriously ill patients who have exhausted FDA-approved therapies, opportunities do exist to expand care.

One such resource is ClinicalTrials.gov, a publicly available registry and database maintained by the NIH, which offers recruitment information for many clinical trials. This resource has also been found to include numerous compassionate use and expanded access programs aimed at those for whom other clinical trials may not be appropriate. These programs have included provision of drugs, biologics, and devices to patients with a variety of serious medical conditions (Miller, 2017).

Alternatively, physicians, upon receiving manufacturer consent, can submit an expanded access application to the FDA on behalf of their patient (Reagan-Udall Foundation, 2021). Estimates of manufacturer acknowledgement time have ranged between 1-10 business days, with most answering within 3 business days (Trickett, 2018). The 2-page application [form FDA 39267] has been estimated to take 45 minutes to complete; upon submission, a median turnaround time for FDA evaluation has been estimated at 4 days for non-emergency requests and <1 day for emergency requests. 99% of such applications have

received FDA authorization (U.S. Dept of Health and Human Services, 2021), (Trickett, 2018) and (Reagan-Udall Foundation, 2021). Institutional Review Board (IRB) requirement waivers may also be available, either on a prospective basis or on a concurrent/retrospective basis for emergency requests (U.S. Dept of Health and Human Services, 2017).

All of these factors have helped facilitate the greater than 10,000 expanded access/compassionate use requests approved over the past decade (Trickett, 2018). Furthermore, the recently enacted Right to Try Act protects manufacturers and providers from adverse impacts associated with providing unapproved investigational drugs to terminally ill patients; this will presumably further encourage expanded access utilization (U.S. Dept of Health and Human Services, 2022).

VII. CODING DISCLAIMER

Note: The following CPT/HCPCS codes are included below for informational purposes and may not be all-inclusive. Inclusion or exclusion of a CPT/HCPCS code(s) below does not signify or imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member's specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee of payment. Other policies and coverage determination guidelines may apply.

Note: All inpatient admissions require preauthorization

Adherence to the provisions in this policy may be monitored and addressed through post payment data analysis and/or medical review audits
Advantage MD: Regulatory guidance supersedes JHHP Medical Policies. If there are no statutes, regulations, NCDs, LCDs, or LCAs, or other CMS guidelines, apply the Medical Policy criteria.
Employer Health Programs (EHP): Refer to specific Summary Plan Descriptions (SPD). If there are no criteria in the SPD, apply the Medical Policy criteria.
Johns Hopkins Health Plan of Virginia Inc. (JHHPVA): Regulatory guidance supersedes JHHP Medical Policies. If there are no statutes, regulations, NCDs, LCDs, or LCAs, or other CMS guidelines, apply the Medical Policy criteria.
Priority Partners (PPMCO): Regulatory guidance supersedes JHHP Medical Policy. If there are no criteria in COMAR regulations, or other State guidelines, apply the Medical Policy criteria.
US Family Health Plan (USFHP): TRICARE policy supersedes JHHP Medical Policy. If there is no policy in TRICARE, or other regulatory guidelines, apply the Medical Policy criteria.

VIII. CODING INFORMATION

MULTIPLE APPLICABLE CODES	
CPT CODES	**DESCRIPTION**
	Multiple Codes

MULTIPLE APPLICABLE CODES

HCPCS CODES	DESCRIPTION
	Multiple Codes

IX. REFERENCE STATEMENT

Analyses of the scientific and clinical references cited below were conducted and utilized by the Johns Hopkins HealthPlans (JHHP) Medical Policy Team during the development and implementation of this medical policy. The Medical Policy Team will continue to monitor and review any newly published clinical evidence and revise the policy and adjust the references below accordingly if deemed necessary.

X. REFERENCES

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XI. APPROVALS

Historical Effective Dates: 10/01/2018, 05/03/2021, 08/01/2022, 08/01/2023