

<p>SUBJECT: CLINICAL POLICIES – INJECTABLE MEDICATIONS MEDICARE</p> <p>POLICY NUMBER: HS-CP-MA 13</p> <p>EFFECTIVE DATE: September 24,2025</p> <p>SERVICE/PRODUCT LINE: MEDICARE – MEDICAL & BEHAVIORAL HEALTH</p>	<p>Product Line (check all that apply):</p> <p><input type="checkbox"/> All</p> <p><input type="checkbox"/> Group HMO</p> <p><input type="checkbox"/> Individual HMO</p> <p><input type="checkbox"/> PPO</p> <p><input type="checkbox"/> POS</p> <p><input checked="" type="checkbox"/> Medicare</p> <p><input type="checkbox"/> N/A</p>
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These guidelines are used in conjunction with the independent judgment of a qualified licensed physician and do not constitute the practice of medicine or medical advice. This Clinical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of members. This Clinical Policy is not intended to recommend treatment for members. Members should consult with their treating provider in connection with diagnosis and treatment decisions.

When coverage criteria are not fully established by Medicare including but not limited to National Coverage Decisions (NCD), Local Coverage Decisions (LCD), Medicare Manuals and National Coverage Articles, Sharp Health Plan develops Clinical Policies that serve as recommendations for medical necessity decisions. Sharp Health Plan utilizes evidence-based guidelines from nationally recognized professional organizations, peer reviewed medical and scientific literature and evidence-based consensus statements, which are all based on generally accepted standards of care.

I. BENEFIT STATEMENT: Any service reviewed and approved by this Sharp Health Plan Clinical Policy must be a covered benefit according to the member’s evidence of coverage (EOC). Since benefit plans vary in coverage and some plans may not provide coverage for certain services discussed in this clinical policy, decisions are subject to all terms and conditions of the applicable benefit plan. Benefit determinations should be based in all cases on the member’s contract benefits in effect at the time of service.

All reviewers must first identify member eligibility, and all decisions of this clinical policy are subject to current state and/or federal law. This Clinical policy does not constitute plan authorization, nor is it an explanation of benefits. In the event of a conflict, a member’s benefit plan, EOC, always supersedes the information in the Clinical Policies.

II. REGULATORY

A. Refer to the following:

1. Medicare Part D regulations in 42 CFR § 423.120(b)(1).
2. Prescription Drug Benefit Manual Chapter 9 – Part D Program to Control Fraud, Waste and Abuse, section 50.2.1.2. rev2, 04-25-2006

III. DESCRIPTION

This policy defines the Sharp Health Plan (Plan) criteria for coverage of medications with a parenteral (IM, SubQ, IV) route of administration. These are also referred to as a “medical benefit” pharmacy item. Separate policies govern medications administered through the pharmacy benefit.

IV. DEFINITIONS

- A. A Qualified Individual is a Sharp Health Plan (Plan) member.
- B. Experimental and Investigational drugs and devices:
 - 1. Considered experimental if the FDA has not issued a specific indication or NDC number for the specific drug or device AND they are currently under investigation in a registered Clinical Trial.
 - 2. The Off-Label Use of an FDA approved prescription drug, or device is not considered an experimental/investigational service if this off-label use is not currently being investigated in a registered Clinical Trial.
- C. Injection: The introduction of a medicinal substance into the body; either subcutaneous, intramuscular, intravenous, intravenous, intra-arterial or into other canals or cavities of the body. For purposes of this medical policy, a medication is provided either by a member (self-injectable) or by a medical provider. It is a “shot” or a dosage of medication given by way of a syringe and needle, though not to be given as part of a procedure.
- D. Infusion: The slow diagnostic, prophylactic, or therapeutic introduction of fluid or medicinal substance into a vein or tissue given over a period of time.
- E. Part B Medications: Drugs that are given in a doctor’s office as part of their service, outpatient facility or hospital infusion center. Drugs include antigens, blood clotting factors, Durable medical equipment drugs such as insulin through an insulin pump or respiratory drugs through a nebulizer, injectable and infused drugs, injectable osteoporosis drugs, Intravenous Immune globulin (IVIG) given in the home, oral anti-nausea drugs used as part of cancer treatment, oral cancer drugs, immunosuppressive drugs if you were enrolled in Part A at time of organ transplant, parenteral and enteral nutrition, renal dialysis drugs including erythropoiesis stimulating agents and immunosuppressive drugs for end stage renal disease (ESRD) or Acute kidney injury (AKI), oral renal dialysis drugs, vaccines including COVID-19 vaccine, flu shots, pneumococcal shots and hepatitis shots.
- F. Part D Medications: Generally oral or self-administered medications prescribed by a provider not on Exclusion or preclusion list, drugs available only by prescription, drugs used and sold in the United States, drugs used for a medically accepted indication that is either approved by the Food and Drug Administration (FDA) or supported by compendium, not covered under part A or part B for that person, and included on the plan’s Part D list (formulary) or coverage approved through the exceptions or appeals process. Also includes vaccines on the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practice chart.
- G. Step Therapy: “Step therapy” is a process specifying the sequence in which different prescription drugs for a given medical condition and medically appropriate for a particular patient are prescribed. The health plan may require the enrollee to try one or more drugs to treat the enrollee’s medical condition before the health plan will cover a particular drug for the condition pursuant to a step therapy request. If the enrollee’s prescribing provider submits a request for step therapy exception, the health plans shall make exceptions to step therapy when the criteria is met.

- H. **Biosimilars:** A biosimilar is a biologic that is highly similar to, and has no clinically meaningful differences from, another biologic that is already approved by the FDA (known as the original biologic or reference product). Biosimilars are made with the same types of natural sources as the original medication they were compared to; they are given the same way, have the same strength and dosage, and have the same potential side effects. A biosimilar provides the same treatment benefits as the original biologic.

V. MEDICAL NECESSITY

- A. To be eligible for coverage under this policy, the member must be a Qualified Individual with active Plan membership, and
- B. An appropriate oral alternative drug does not exist, and
- C. The medication must be medically necessary and appropriate to the member's needs or condition, and
- D. Medical Injectable must be Food and Drug Administration (FDA) approved for indication.
- E. Specialty medications must be prescribed by or in consultation with an appropriate specialist (i.e., Behavioral Health by Behavioral Health, Rheumatology by Rheumatologist, Dermatology by Dermatologist, etc.), and
- F. Use of the organization's (SHP/SHC) non-preferred product including non-preferred biosimilars requires a trial of preferred product and a medical rationale documenting why the preferred product cannot be used. and
- G. The provision of physician samples does not guarantee coverage.

VI. NOT MEDICALLY NECESSARY

- A. Any injectable medication that does not meet the medical necessity of this policy.
- B. The cost of services provided out of network when a qualified health professional or facility is available within network.
- C. Certain classes of injectable medications are excluded from coverage e.g., immunizations for travel, anabolic steroids for performance enhancement. (See Medicare law)
- D. High impact drugs that have cost-effective, safe, and efficacious in class counterparts.

VII. PROCESS/PROCEDURE

- A. All requests for coverage of Injectable medications will be reviewed by the delegated Plan Medical Group (PMG) or by the Plan according to its regular and appropriate utilization management process and administered consistently with the Plan benefit.
- B. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this guideline. This Policy aids in determining coverage under the member's benefit plan.
- C. The terms of a member's benefit plan summary defined in the evidence of coverage document may differ from the standard benefit plans upon which this guideline is based. In the event of a conflict, the member's specific benefit document supersedes these guidelines.
- D. The hierarchy of guidelines are:

1. National Coverage Determinations (NCDs)
 2. Local Coverage Determinations (LCDs), Nonidian Policies (DME only if no NCD) including articles and CMS Manuals
 3. Sharp Health Plan Medicare Clinical Policy
 4. MCG, NCCN for Oncology
 5. Plan Pharmacy guidelines (PBM)
 6. Up to Date
 7. Food and Drug Administration (FDA) Package Monograph(www.accessdata.fda.gov)
 8. Articles meeting requirements of level of evidence described below
- E. To be considered Medical and Scientific evidence for the purposes of this policy, documents must meet one or more of the criteria below:
1. Peer-reviewed scientific studies published in or accepted for publication by medical journals that meet nationally recognized requirements for scientific manuscripts and that submit most of their published articles for review by experts who are not part of the editorial staff.
 2. Peer-Reviewed literature that meet the criteria of the NIH National Library of Medicine for Index Medicus, Medline, etc.
 3. Medical journals recognized by the Secretary of HHS under Section 1861(t) (2) of the Social Security Act.
 4. Any of the reference compendia approved in California Health and Safety Code Section 1370.4, such as the National Comprehensive Cancer Network Drug and Biologics Compendium or the Thomson Micromedex Drugdex.
 5. Findings, studies, or research conducted by or under the auspices of federal government agencies and nationally recognized federal research institutes, and any national board recognized by the National Institutes of Health for the purpose of evaluating the medical value of health services.
 6. Peer-reviewed abstracts accepted for presentation at major medical association meetings.

VIII. ATTACHMENTS

SHP Principles for Evidence Appraisals

OVERVIEW

Medical evidence for decision-making is appraised according to the following:

1. **Level of evidence**, using the Cook et al 1991 rules of evidence.
2. **Quality of evidence**, using the "good," "fair," or "poor" rating based on the USPSTF criteria for assessing individual studies
3. **Assessment of net benefit**, based upon principles outlined in the USPSTF criteria for net benefit.
4. **Off-Label compendia assessment**

DESCRIPTIONS

1. **LEVELS OF EVIDENCE FOR EVALUATING EFFICACY**

[Cook DJ, et al. Rules of evidence and clinical recommendations on the use of antithrombotic agents. Chest 1992;4 (suppl):305S-311S.]

Level 1:	Randomized trials that had enough power to demonstrate a statistically significant health outcome. (Preferred basis for decision-making)
Level 2:	Randomized trials with results that were not statistically significant but where a larger trial might have shown a clinically important difference.
Level 3:	Nonrandomized concurrent cohort comparisons between contemporaneous patients.
Level 4:	Nonrandomized historical cohort comparisons between current patients and former patients (from the same institution or from the literature).
Level 5:	Case series without control subjects.

2. QUALITY OF EVIDENCE

[USPSTF Criteria for Assessing Internal Validity of Individual Studies - USPS Task Force. Procedure Manual. December 2015.]

Randomized Controlled Trials and Cohort Studies

Good: Meets all criteria: well-designed and well-conducted trials; all important outcomes are considered. In addition, for RCTs, intention to treat analysis is used. **Fair:** Studies will be graded “fair” if any or all of the following problems occur, without the fatal flaws noted in the “poor” category below: some question remains whether some (although not major) differences between groups occurred with follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention to treat analysis is done for RCTs.

Poor: if any of the following fatal flaws exists: Groups are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. For RCTs, intention to treat analysis is lacking.

Systematic Reviews

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions. **Fair:** Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies.

Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

3. ASSESSMENT OF NET BENEFIT

[USPSTF Levels of Certainty Regarding Net Benefit - USPS Task Force. Procedure Manual. December 2015.]

- **Magnitude of net benefit:** substantial, moderate, small, or zero/negative. May also be expressed in quantitative terms.

- **Certainty of net benefit:**

Level of Certainty of Net Benefit	Description
High	Consistent results from well-designed, well-conducted studies in representative populations. Studies assess the effects of the intervention on health outcomes.
Moderate	Evidence is sufficient to determine the effects of the intervention on health outcomes, but confidence in the estimate is constrained by factors such as: <ul style="list-style-type: none"> • Power, design, or quality of individual studies. • Inconsistency of findings across individual studies • Limited generalizability of findings to routine practice
Low	Evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: <ul style="list-style-type: none"> • Limited number or size of studies. • Important flaws in study design or methods. • Inconsistency of findings across individual studies • Findings not generalizable to routine practice

4. OFF LABEL COMPENDIA

SHP off-label compendia assessment table (for drugs in both the Pharmacy and Medical benefits)

	AHFS DI	Thompson		Clinical Pharmacology	NCCN Drug & Biologics	2 peer reviewed articles
		DrugDex	DrugPoints*			
Medicare & Commercial requirements	X	X	Medicare only,	Anticancer Chemo Regimens only		X
Medically necessary	<ul style="list-style-type: none"> • AHFS & Clinical Pharmacology = Listed as supported, indicated, recommended, or equivalent terms • NCCN = Category 1 or 2A indication • DrugDex: = Class I, Class IIa, or Class IIb • <i>Use peer reviewed literature to assess when compendia list as "inconclusive" or "equivocal"</i> 					

Not medically necessary	<ul style="list-style-type: none"> • AHFS & Clinical Pharmacology = Not listed, OR listed as unsupported, not indicated, not recommended, or equivalent terms • NCCN = Category 3 indication • DrugDex = Class III • <i>Use peer reviewed literature to assess when compendia list as “inconclusive” or “equivocal”</i>
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IX. CODES:

The following list(s) of procedure codes is provided for reference purposes only and may not be all-inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Inclusion of a code in this section does not guarantee that it will be reimbursed. The member specific benefit plan document and applicable laws that may require coverage for a specific service determine benefit coverage for health services.

CPT Code	Description
90281-90399	Immune globulins (intramuscular, intravenous, subcutaneous)
90465-90466, 90468-90472, 90474	Immunization administration for vaccines/toxoids (intradermal, intramuscular, percutaneous, subcutaneous)
90581-90658, 90666-90676, 90691-90710, 90713-90749	Vaccines, toxoids (intradermal, intramuscular, intravesicular, percutaneous, subcutaneous)
96365-96379	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

X. REFERENCES

- A. Medicare Part D regulations in 42 CFR § 423.120(b)(1)(iv) Accessed 08/21/23
- B. Medicare Part D regulations in 42 CFR § 423.120(b)(1)(v) Accessed 08/21/23
- C. Medicare Part D Attestation required by the Part D MEDICARE PRESCRIPTION DRUG BENEFIT Solicitation for Applications for Medicare Prescription Drug Plan 2023 Contracts Section 3.2.1.D.6 Accessed 08/21/23
- D. Medicare Part D regulations in 42 CFR § 423.120(b)(1), Formulary Development and Review by a Pharmacy and Therapeutics (P&T) Committee. Accessed 08/21/23
- E. Prescription Drug Benefit Manual Chapter 9 – Part D Program to Control Fraud, Waste and Abuse, section 50.2.1.2. last updated, rev16, 01-11-2013. Accessed 08/21/23.
- F. Office of Inspector General (OIG) Compliance Program Guidance for Pharmaceutical Manufacturers. Accessed 08/21/23.
- G. DRAFT GUIDANCE September 2023 US Department of Health and Human Services, Food and Drug Administration “Demonstrating Substantial Evidence of Effectiveness with ONE Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence” Guidance for Industry.

- H. Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products (December 2019) US Department of Health and Human Services, Food and Drug Administration.
- I. NCCN Drug and Biologics Compendium, Fort Washington, PA: National Comprehensive Cancer Network (NCCN); <https://www.nccn.org/compendia-templates/compendia/drugs-and-biologics-compendia>; accessed 08/21/23
- J. U.S. Preventive Services Task Force Procedure Manual April 2023 Accessed 08/21/23.

XI. REVISION HISTORY

Date	Modification (Original, Reviewed or Revised)
01/2006	Original
08/28/13	Revised – Compliance with ACA (benchmark plan)
05/28/14	Revised; Approved by QMC
11/18/15	Revised
9/21/16	Revised
12/06/17	Revised
12/05/18	Revised: Approved by QMC
12/04/19	Reformatted, updated references
12/09/20	Updated References
12/15/21	Updated References
12/21/22	Updated References
12/20/23	Updated References
03/26/25	Added definitions of part B and part D drugs, Removed Hayes Technology from criteria hierarchy, Added Guidance 2019 and draft 2023 references to evidence of effectiveness.
9/24/25	Added definitions biosimilars and step therapy

<p>Approved by: (Signature of VP /CMO)</p> 	<p>Approval date: 09/24/2025</p>
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