BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Investigational (Experimental) Services - B0005

File Name:	investigational_(experimental)_services
Origination:	1/1996
Last CAP Review:	11/2019
Next CAP Review:	11/2020
Last Review:	11/2020

Update on Investigational (Experimental) Services for COVID-19 Treatment:

In response to federal, state or local emergency declarations due to the 2019 novel Coronavirus (COVID-19) outbreak: Blue Cross Blue Shield of North Carolina (BCBSNC) recognizes the need for safe and effective, potentially life-saving treatments for COVID-19, including use of treatment approved for indications other than COVID-19 (off-label use) or investigational drugs for which data does not exist to inform clinical use in patients with COVID-19.

BCBSNC may consider coverage of investigational (experimental) services in the absence of efficacy data for patients with confirmed COVID-19 disease if the potential for benefit is felt to outweigh the risk.

BCBSNC will not provide coverage for COVID-19 treatments which the U.S. Food and Drug Administration (FDA) has deemed unsafe for use, or has prohibited use for safety reasons.

BCBSNC encourages participation in COVID-19-related clinical trials and prospective registries when possible.

The following are additional resources for COVID-19-related guidance documents and emerging treatments:

FDA COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders

FDA Emergency Use Authorization (EUA) information, and list of all current EUAs:

https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

FDA Coronavirus Treatment Acceleration Program (CTAP): https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap

CDC Healthcare Professionals FAQs: https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html

CDC Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19): https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html

ClinicalTrials.gov COVID-19 clinical trials: https://clinicaltrials.gov/ct2/results?cond=COVID-19

These changes will be effective from March 6, 2020 through June 30, 2021. We will reevaluate if an additional extension is needed as we approach June 30.

Related policies:
Clinical Trial Services
Medical Necessity
New-To-Market Specialty Drug PPA Requirements

Description of Service

BCBSNC defines the terms "investigational" or "experimental" as the use of a service that is not recognized by the Plan as standard medical care for the condition, disease, illness or injury being treated. A service includes, but is not limited to the diagnostic service, procedure, test, treatment, facility, equipment, drug or device.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will not provide coverage for Investigational (Experimental) Services, except for covered clinical trial services (see Clinical Trial Services policy). Investigational (Experimental) Services do not meet the criteria for "medically necessary services" because these services are not standard medical practice (see Medical Necessity policy).

Benefits Application

This medical policy relates only to the services described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

This policy will apply to all product lines of business unless otherwise indicated by the member's certificate/contract (e.g., self-funded groups).

When Investigational (Experimental) Services are covered

Investigational (Experimental) Services are not covered except as delineated in the Clinical Trial Services medical policy.

****NOTE: Investigational (Experimental) Services may be covered in circumstances related to treatment of the 2019 novel Coronavirus (COVID-19) as outlined above in "Update on Investigational (Experimental) Services for COVID-19 Treatment".****

When Investigational (Experimental) Services are not covered

Investigational (Experimental) Services are not covered. BCBSNC does not cover investigational (experimental) services.

A service is considered investigational (experimental) if <u>any</u> of the following criteria are met:

1. The service requiring Federal or other Governmental body approval, does not have unrestricted market approval from the Food and Drug Administration (FDA) or final approval from any other governmental regulatory body for use in treatment of a specified

condition. Any approval that is granted as an interim step in the regulatory process is not a substitute for final or unrestricted market approval.

2. There is insufficient or inconclusive evidence published in peer-reviewed medical literature to permit the Plan to evaluate the therapeutic value of the service. Evidence that permits conclusions concerning the effect on health outcomes is generally considered to be of moderate to high strength, based on well-designed and well-conducted studies.

3. There is inconclusive evidence published in peer-reviewed medical literature that the service improves net health outcomes. The services' beneficial effects on health outcomes does not outweigh any harmful effects on health outcomes.

4. The service under consideration is not as beneficial as any established alternatives.

5. There is insufficient information or inconclusive evidence that, when used in a non-investigational setting, the service has a beneficial effect on health outcomes or is as beneficial as any established alternatives.

Note: BCBSNC does not cover investigational, cosmetic or not medically necessary services and will not reimburse for any services **associated with** those investigational, cosmetic or not medically necessary services.

A requirement in a medical policy for enrollment in a patient registry to prospectively collect clinical outcomes data does not define a service as investigational.

Policy Guidelines

Determinations are made by the Plan after BCBSNC's review of available scientific data. Evidence based physician specialty societal guidelines, opinions of experts in a particular field and opinions and assessments of nationally recognized review organizations may also be considered by the Plan but are not determinative or conclusive.

Medical and Scientific Evidence is defined by BCBSNC as one of the following:

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 or biomedical compendia from such sources as the National Institute of Health's National Library of Medicine or The Cochrane Library.

3. An accepted indication for treatment in one of the following standard reference compendia:

- The American Hospital Formulary Service-Drug Information,
- The American Medical Association Drug Evaluations,
- The American Dental Association Accepted Dental Therapeutics, and
- The United States Pharmacopoeia Drug Information.

4. An accepted indication for treatment of cancer in one of the following standard reference compendia, for drugs approved by the FDA for treatment of cancer:

- The National Comprehensive Cancer Network Drugs & Biologics Compendium
- The Thomson Micromedex ® DRUGDEX ®
- The Elsevier Gold Standard's Clinical Pharmacology
- Any other authoritative compendia as recognized periodically by the United States Secretary of Health and Human Services.

5. Findings, studies, or research conducted by or under the auspices of federal government agencies and nationally recognized federal research institutes including the:

- U.S. Department of Health and Human Services,
- Federal Agency for Healthcare Research and Quality,
- National Institutes of Health,
- National Cancer Institute,
- National Academy of Sciences,
- Center for Medicare and Medicaid Services, and
- Any national board recognized by the National Institutes of Health for the purpose of evaluating the medical value of health services.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: *See procedure code for the specific procedure or service.*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual

Specialty Matched Consultant Advisory Panel - 11/1999

Medical Policy Advisory Group - 12/2/1999

Medical Policy Advisory Group - 9/2001

Medical Policy Advisory Group - 2/2002

Medical Policy Advisory Group - 3/2002

Medical Policy Advisory Group - 10/2003

Medical Policy Advisory Group - 9/2005

Senior Medical Director review 1/2017

Medical Director review 4/2020

Policy Implementation/Update Information

1/96	Original Policy issued
8/96	Revised: Updated list with removal of the following policies: Laser Prostatectomy, Terbutaline Infusion Pump, and TIPS.
6/97	Policy revised to include non-FDA approved drugs, devices, equipment, and supplies.
11/98	Revised to remove the list of procedures considered investigational. Check specific policy for proper coverage guidelines.
9/99	Reformatted, Medical Term definitions added.
12/99	Reaffirmed, Medical Policy Advisory Group
4/01	S9990, S9991 removed from coding section.
9/01	Medical Policy Advisory Group review. No change to policy.
4/02	Medical Policy Advisory Group review 2/02 and 3/02. Policy revised based on clinical trials mandate and medical consultant recommendations. Revised the definition for Medical and Scientific Evidence to include review from The Cochrane Library.
10/03	Medical Policy Advisory Group review. Information added in Benefits Application and Billing and Coding sections of the policy. No change in criteria. Format change.
11/03	Corrected Benefit Application Section.
3/04	Policy Number changed from ADM9060 to MED1263.
10/8/05	Medical Policy Advisory Group review on 09/08/2005. No changes to policy coverage criteria.
4/9/07	Policy Number changed from MED1263 to ADM9051.
05/05/08	Policy reviewed 4/4/2008 by Vice President and Senior Medical Director of Provider Partnerships, Medical and Reimbursement Policy. No changes to policy criteria.
09/28/09	Under the section, “When Investigational (Experimental) Services are not covered” added the following: Note: BCBSNC does not cover investigational, cosmetic or not medically necessary services and will not reimburse for any services, procedures, drugs or supplies associated with those investigational, cosmetic or not medically necessary services.” for clarification purposes. Active policy, no longer scheduled for routine review.
6/22/10	Policy Number(s) removed (amw)

7/1/2014 Policy category changed from *Medical* Policy to *Reimbursement* policy. No change to current policy statement. (adn)

7/15/2014 Policy category name returned to "Corporate Medical Policy." (adn)

11/24/15 Review dates removed from policy header. No change to policy content. (adn)

1/27/17 Added Appendix to the policy on pages 5-7. Under "Medical and Scientific Evidence as defined by BCBSNC on page 3, added accepted compendia for oncology drugs statement: "An accepted indication for treatment of cancer in one of the following standard reference compendia, for drugs approved by the FDA for treatment of cancer:The National Comprehensive Cancer Network Drugs & Biologics Compendium, The Thomson Micromedex ® DRUGDEX ®, The Elsevier Gold Standard's Clinical Pharmacology, and Any other authoritative compendia as recognized periodically by the United States Secretary of Health and Human Services. Senior Medical Director review 1/2017. (lpr)

4/1/19 Added Avalon tag AHS-B0005 to policy name. (lpr)

10/15/19 Removed Avalon tag "AHS" from policy name to clarify this is a BCBSNC policy that applies to all medical coverage policies. (eel)

12/31/19 Description section updated. Definition of service added for clarity. Evidence based physician specialty societal guidelines added to Policy Guidelines. Added to when not covered section #2 "Evidence that permits conclusions concerning the effect on health outcomes is generally considered to be of moderate to high strength, based on well-designed and well-conducted studies." Added to when not covered section #3 "The services' beneficial effects on health outcomes does not outweigh any harmful effects on health outcomes." Added to when not covered section note "A requirement in a medical policy for enrollment in a patient registry to prospectively collect clinical outcomes data does not define a service as investigational." Specialty Matched Consultant Advisory Panel review 11/19/2019. No change to policy statement. (eel)

4/3/20 "Update on Investigational (Experimental) Services for COVID-19 Treatment" temporarily added to policy with the following statements: "BCBSNC recognizes the need for safe and effective, potentially life-saving treatments for COVID-19, including use of drugs approved for indications other than COVID-19 (off-label use) or investigational drugs for which data does not exist to inform clinical use in patients with COVID-19. BCBSNC may consider coverage of investigational (experimental) services in the absence of efficacy data for patients with confirmed COVID-19 disease if the potential for benefit is felt to outweigh the risk. BCBSNC will not provide coverage for COVID-19 treatments which the FDA has deemed unsafe for use, or has prohibited use for safety reasons. BCBSNC encourages participation in COVID-19-related clinical trials and prospective registries when possible." Added the following statement to "When Covered" section: "NOTE: Investigational (Experimental) Services may be covered in circumstances related to treatment of the 2019 novel Coronavirus (COVID-19) as outlined above in "Update on Investigational (Experimental) Services for COVID-19 Treatment." The expansion is limited to the timeframe outlined within the policy and subject to defined extensions as needed. Medical Director review 4/2020. (krc)

5/1/20 COVID-19 related changes extended "effective from March 6, 2020 until June 5, 2020, and then will be re-evaluated for extension every 30 days thereafter." (eel)

6/5/20 COVID-19 related changes extended "effective from March 6, 2020 until July 5, 2020, and then will be re-evaluated for extension every 30 days thereafter." (eel)

6/26/20 COVID-19 related changes extended "effective from March 6, 2020 until August 4, 2020, and then will be re-evaluated for extension every 30 days thereafter." (eel)

7/30/20 COVID-19 related changes extended "effective from March 6, 2020 until September 30, 2020. We will reevaluate if an additional extension is needed as we approach September 30." (eel)

9/29/20 COVID-19 related changes extended "effective from March 6, 2020 through December 31, 2020. We will reevaluate if an additional extension is needed as we approach December 31." (eel)

11/20/20 COVID-19 related changes extended "effective from March 6, 2020 through June 30, 2021. We will reevaluate if an additional extension is needed as we approach June 30." (eel)

Appendix: Evidence Standards from NCCN, DrugDex ®, and Clinical Pharmacology/Gold Standard

NCCN

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B: Based upon lower-level evidence, there is (non-uniform) NCCN consensus that the intervention is appropriate.
Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

DRUGDEX

Strength of recommendation

Class I	Recommended	The given test or treatment has been proven to be useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test, or treatment is generally considered to be useful, and is indicated in most cases.

Class IIb	Recommended, In Some Cases	The given test, or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test, or treatment is not useful, and should be avoided.

Strength of evidence

Category A	Category A evidence is based on data derived from: Meta-analyses of randomized controlled trials with homogeneity with regard to the directions and degrees of results between individual studies. Multiple, well-done randomized clinical trials involving large numbers of patients.
Category B	Category B evidence is based on data derived from: Meta-analyses of randomized controlled trials with conflicting conclusions with regard to the directions and degrees of results between individual studies. Randomized controlled trials that involved small numbers of patients or had significant methodological flaws (e.g., bias, drop-out rate, flawed analysis, etc.). Nonrandomized studies (e.g., cohort studies, case-control studies, observational studies).
Category C	Category C evidence is based on data derived from: Expert opinion or consensus, case reports or case series.

Efficacy

Class I	Effective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is effective
Class IIa	Evidence Favors Efficacy	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion favors efficacy.
Class IIb	Evidence is Inconclusive	Evidence and/or expert opinion is conflicting as to whether a given drug treatment for a specific indication is effective, but the weight of evidence and/or expert opinion argues against efficacy.
Class III	Ineffective	Evidence and/or expert opinion suggests that a given drug treatment for a specific indication is ineffective.

Clinical Pharmacology/Gold Standard

Strong recommendation: An off-label use that carries a Strong Recommendation "For" or "Against" use, with any level of evidence, should be considered binding and reflect that Elsevier recommends or does not recommend, respectively, the use of the drug for that indication in the situation described. All off-label uses with a strong level of recommendation will appear in the referential database and be clearly identified as recommended or not recommended; however, a strong recommendation "Against use" will not be found within the clinical decision support data.

Equivocal/Weak Recommendation: Off-label uses that have inconclusive data "For" or "Against" use carry a Weak Recommendation. A Weak recommendation, with any level of evidence, reflects a neutral or equivocal position (i.e., neither for or against use) by Elsevier. All off-label uses with a weak level of recommendation will appear in the referential database and be clearly identified as equivocal; however, a weak recommendation "Against use" will not be found within the clinical decision support data.

The GRADE system provides guidelines for evaluating and rating the quality of evidence and utilizes four (4) quality of evidence levels:

- High

- Moderate
- Low
- Very Low