June 28, 2016

Dear Provider:

Anthem Blue Cross is pleased to provide you with our updated and new Medical Policies and Clinical UM Guidelines. The updated polices listed below are effective for service dates on and after October 1, 2016.

The major new policies and changes are summarized below. Please refer to the specific policy for coding, language, and rationale updates and changes that are not summarized below. Attachment A summarizes other minor changes and clarifications.

New Medical Policies effective October 1, 2016:

- **DRUG.00082 Daratumumab (Darzalex™)**: This document addresses the use of daratumumab (DARZALEX), a human anti-CD38 monoclonal antibody (mAb) used for the treatment of multiple myeloma (including plasma-cell leukemia) resistant to other therapies.

- **DRUG.00083 Elotuzumab (Empliciti™)**: This document addresses elotuzumab (Empliciti), a humanized IgG1 monoclonal antibody that targets the signaling lymphocytic active molecule (SLAM) family member F7 (SLAMF7) protein that is expressed on myeloma cells and natural killer cells.

- **DRUG.00084 Interferon gamma-1b (Actimmune®)**: This document addresses the indications for interferon gamma-1b (Actimmune), a biologic response modifier used in the management of chronic granulomatous disease, severe malignant osteopetrosis, and oncologic conditions.

- **DRUG.00085 Ixabepilone (Ixempra®)**: This document addresses ixabepilone (Ixempra), a non-taxane chemotherapy agent which blocks cells in the mitotic phase of the cell division cycle, leading to cell death. Ixabepilone is used as a second or subsequent line of therapy, alone or in combination with oral capecitabine, to treat breast cancer resistant or refractory to other therapies.

- **DRUG.00086 Mecasermin (Increlex®)**: This document addresses the use of mecasermin (Increlex), a recombinant human insulin-like growth factor-1 (rhlGF-1) drug, proposed for the treatment of conditions related to IGF-1 deficiency (IGFD) and other forms of growth hormone insensitivity.

- **GENE.00045 Detection and Quantification of Tumor DNA Using Next Generation Sequencing in Lymphoid Cancers**: This document addresses next generation sequencing (which includes, but is not limited to high-throughput and deep sequencing) of tumor DNA to assist in determining the success of the treatment, forming a prognosis, monitoring disease progression and choosing therapies for individuals with lymphoid cancer.

- **SURG.00143 SpaceOAR® System**: This document addresses the use of SpaceOAR, an injectable liquid hydrogel product intended to create distance and serve as a spacer between the prostate and the anterior rectal wall in individuals undergoing radiotherapy for prostate cancer.
New Clinical UM Guidelines for Individual Members Only

Effective October 1, 2016, outpatient hip replacement, knee replacement and cervical spine fusion will be added to the precertification list for our Commercial Individual members. California individual members can currently be identified by prefixes JQL, JQM, JQN, JQO, JQP, JQR, VXB and VXD on the member’s identification card.

- **CG-SURG-42 Cervical Fusion**: This document addresses the clinical indications for anterior and posterior cervical fusion.

- **CG-SURG-53 Elective Total Hip Arthroplasty**: This document addresses elective total hip arthroplasty (THA) for hip damage severe enough to require replacement, when performed as an elective, non-emergent procedure and not as part of the care of a congenital, acute or traumatic event such as fracture (excluding fracture of implant and periprosthetic fracture).

- **CG-SURG-54 Elective Total Knee Arthroplasty**: This document addresses elective total knee arthroplasty (TKA) for knee damage severe enough to require replacement, when done as an elective, non-emergent procedure and not as part of the care of a congenital, acute or traumatic event such as fracture (excluding periprosthetic fracture).

Revised Adopted Clinical UM Guidelines and Medical Policies:

- **CG-DRUG-16 White Blood Cell Growth Factors**: This document addresses white blood cell growth factors, also known as colony stimulating factors (CSF), which are administered to enhance recovery of blood related functions in neutropenia (low white blood count) including febrile neutropenia (FN).
  - Revised medically necessary criteria addressing primary prophylaxis of developing FN when greater than or equal to 10% and less than 20% for all products
  - Added pegfilgrastim (Neulasta) as medically necessary after accidental or intentional total body radiation of myelosuppressive doses (greater than 2 Grays [Gy]) (such as Hematopoietic Syndrome of Acute Radiation Syndrome)
  - Added tbo-Filgrastim (Granix) as medically necessary:
    - After a hematopoietic progenitor stem cell transplant (HPCT/HSCT) when criteria are met
    - To mobilize progenitor cells into peripheral blood for collection by leukapheresis, as an adjunct to peripheral blood/hematopoietic stem cell transplantation (PBSCT/PHSCT)
  - Reformatted medically necessary clinical indications
  - Defined abbreviations in clinical indications

- **DRUG.00028 Intravitreal Treatment for Retinal Vascular Conditions**: This document addresses the following medications used to treat retinal vascular conditions of the eye: pegaptanib (Macugen®); bevacizumab (Avastin®); ranibizumab (Lucentis®); and aflibercept (Eylea®).
  - Title revised
  - Added choroidal neovascularization associated with myopic degeneration as medically necessary indication for ranibizumab
  - Added diabetic retinopathy, with or without diabetic macular edema, as medically necessary indication for bevacizumab
  - Revised the medically necessary indication of diabetic retinopathy to include the words “or without” before “diabetic macular edema” for both ranibizumab and aflibercept
  - Added radiation retinopathy as medically necessary indication for bevacizumab, ranibizumab and aflibercept
  - Clarified the medically necessary criteria to state that the treatment of proliferative diabetic retinopathy with or without diabetic macular edema is a medically necessary indication for bevacizumab, ranibizumab, and aflibercept
• **MED.00119 High Intensity Focused Ultrasound (HIFU) for Oncologic Indications:** This document addresses the use of high intensity focused ultrasound (HIFU) or magnetic resonance-guided focused ultrasound (MRgFUS) for the treatment of oncologic conditions.
  o Title, category and number revised (Previous category & number: SURG.00094; Previous title: High Intensity Focused Ultrasound (HIFU) for the Treatment of Prostate Cancer).
  o Expanded scope of document to include all oncologic conditions
  o Added the use of HIFU for pain palliation in individuals with localized metastatic bone pain as medically necessary when criteria are met
  o Revised investigational and not medically necessary statement to include when criteria are not met and for all other indications, including but not limited to, prostate cancer
  Added the biosimilar infliximab-dyyb (Inflectra™) as medically necessary for the same indications for use as infliximab (Remicade®)

• **SURG.00037 Treatment of Varicose Veins (Lower Extremities):** This document addresses various modalities for the treatment of valvular incompetence (reflux) of the great saphenous vein (GSV) or small saphenous vein (SSV) (also known as greater saphenous vein or lesser saphenous vein, respectively) and associated varicose tributaries as well as telangiectatic dermal veins.
  o Added coil embolization as a treatment of lower extremity veins as investigational and not medically necessary

• **SURG.00098 Mechanical Embolectomy for Treatment of Acute Stroke:** This document addresses the use of intra-arterial mechanical embolectomy devices, also known as endovascular thrombectomy, for the treatment of acute thrombotic or embolic stroke.
  o Removed requirement for the treated individual to be 18 years of age or older
  o Added criteria that the procedure is done with a stent retriever device

Anthem Blue Cross Medical Policies and Clinical UM Guidelines are developed by our Medical Policy and Technology Assessment Committee. The Committee, which includes Anthem medical directors and representatives from practicing physician groups, meets quarterly to review current scientific data and clinical developments. Medical Policies and Clinical UM Guidelines are subject to the approval of the Physician Relations Committee.

All coverage written or administered by Anthem Blue Cross excludes from coverage services or supplies that are investigational and/or not medically necessary. A member’s claim may not be eligible for payment if it was determined not to meet medical necessity criteria set forth in Anthem Blue Cross’ Medical Policies. Review procedures have been refined to facilitate claim investigation.

The complete list of our Medical Policies and Clinical UM Guidelines may be accessed on the Anthem Blue Cross Web site at [www.anthem.com/ca](http://www.anthem.com/ca) (select “Provider”, then select “Medical Policies and Clinical UM Guidelines” listed under “Learn More”. Recent changes to Medical Policies can be found under “Recent Updates”. We thank you for your continued efforts on behalf of our members and your partnership toward improved access to quality health care for Californians.

Sincerely,

Jacob Asher, MD
Vice President and Chief Medical Officer
### Attachment A - 2nd Quarter 2016 Updates
Revised Medical Policies and Clinical Guidelines

<table>
<thead>
<tr>
<th>Policy Number</th>
<th>Title</th>
<th>Medical Policy / Clinical Guideline Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG-DME-01</td>
<td>External (Portable) Continuous Insulin Infusion Pumps</td>
<td>• Added microvascular or macrovascular complications (for example, diabetic retinopathy or cardiovascular disease) as medical necessary criteria for individuals with diabetes mellitus</td>
</tr>
<tr>
<td>CG-DRUG-08</td>
<td>Enzyme Replacement Therapy for Gaucher Disease</td>
<td>• Reformatted and clarified medically necessary clinical indications for adults with type 1, and adults and children with type 3 Gaucher disease • Revised medically necessary clinical indications for type 3 Gaucher disease</td>
</tr>
<tr>
<td>CG-DRUG-15</td>
<td>Gonadotropin Releasing Hormone Analogs</td>
<td>• Title revised • Clarified medically necessary statement addressing ovarian cancer and leuprolide acetate as hormonal therapy when used as a single agent for persistent or recurrent epithelial ovarian cancer, fallopian tube cancer and primary peritoneal cancer</td>
</tr>
<tr>
<td></td>
<td>(Previous title: Gonadotropin Releasing Hormone (GnRH) Analogs)</td>
<td></td>
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<tr>
<td>CG-DRUG-27</td>
<td>Clostridial Collagenase Histolyticum Injection</td>
<td>• Added the treatment of Peyronie's disease as medically necessary when criteria are met • Updated not medically necessary statement</td>
</tr>
<tr>
<td>CG-SURG-44</td>
<td>Coronary Angiography in the Outpatient Setting</td>
<td>• Title revised • Narrowed scope of document to only address coronary angiography • Removed criteria addressing heart catheterization and criteria for angiography with heart catheterization • Revised criteria addressing angiography for individuals with suspected CAD based on results of prior noninvasive stress testing to include treadmill stress test as acceptable testing method • Added the evaluation of suspected anomalous coronary arteries and preoperative assessment before open valvular surgery as medically necessary indications • Updated not medically necessary statement</td>
</tr>
<tr>
<td></td>
<td>(Previous title: Coronary Angiography and Cardiac Catheterization in the Outpatient Setting)</td>
<td></td>
</tr>
<tr>
<td>DRUG.00002</td>
<td>Tumor Necrosis Factor Antagonists</td>
<td>• Added the biosimilar infliximab-dyyb (Inflectra™) as medically necessary for the same indications for use as infliximab (Remicade*) • Updated the not medically necessary and investigational and not medically necessary statements to include infliximab-dyyb (Inflectra) when criteria are not met</td>
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| DRUG.00041    | Rituximab (Rituxan®)                    | • Removed wording "Systemic Autoimmune Disorders" from medically necessary criteria addressing cryoglobulinemia, primary Sjögren Syndrome (SS), or Systemic Lupus Erythematosus (SLE) refractory to standard therapy (that is, lack of response to corticosteroids and at least 2 immunosuppressive agents)  
• Added immunoglobulin G4-related disease (IgG4-RD) as medically necessary when criteria are met  
• Added pediatric nephrotic syndrome as medically necessary when criteria are met  
• Added thrombotic thrombocytopenic purpura (TTP), refractory or relapsing disease (i.e., lack of response to plasma exchange therapy and glucocorticoids) who meet diagnostic criteria for TTP as medically necessary  
• Reformatted and made changes to abbreviations and acronyms throughout position statement  
• Updated investigational and not medically necessary statement  
• Made minor abbreviation changes in position statement                                                                                                                                                                                                                                                                 |
| DRUG.00047    | Brentuximab Vedotin (Adcetris®)         | • Clarified medically necessary statement addressing the treatment of individuals with CD30+ T-cell lymphoma (excluding cutaneous ALCL) that is relapsed or refractory to first-line therapy  
• Added the treatment of individuals with cutaneous CD30+ T-cell lymphoma, including mycosis fungoides/Sezary syndrome which is relapsed, refractory or for advanced disease presentation (for example, folliculotropic, large-cell transformation or extracutaneous disease) as medically necessary  
• Added the treatment of individuals with refractory CD30+ lymphomatoid papulosis that is symptomatic or characterized by extensive cutaneous lesions as medically necessary  
• Updated investigational and not medically necessary statement  
• Made minor abbreviation changes in position statement                                                                                                                                                                                                                                                                 |
| DRUG.00062    | Obinutuzumab (Gazyva®)                  | • Added obinutuzumab used as a single agent for the treatment of relapsed/refractory CLL/SLL without del (17p) mutation as medically necessary  
• Added obinutuzumab, in combination with bendamustine followed by obinutuzumab monotherapy for the treatment of individuals with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen as medically necessary  
• Revised investigational and not medically necessary statement                                                                                                                                                                                                                                                                 |
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| DRUG.00066    | Antihemophilic Factor and Clotting Factors | ● Clarified medically necessary criteria addressing measurement of factor levels throughout position statement  
● Added the following factors as medically necessary when criteria are met  
  – Antihemophilic Factor (Factor VIII) Recombinant (Kovaltry)  
  – Antihemophilic Factor (Factor VIII) Recombinant, pegylated (Adynovate)  
  – von Willebrand Factor (Recombinant) (Vonvendi)  
  – Coagulation Factor IX, Recombinant, Albumin Fusion Protein (Idelvion)  
● Added Antihemophilic Factor VIII Recombinant (Advate, Helixate FS, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha) for the treatment of bleeding episodes in an individual with von Willebrand disease (VWD) as medically necessary when criteria are met  
● Added investigational and not medically necessary statements for antihemophilic factor (factor VIII) Recombinant, pegylated and von Willebrand factor (Recombinant) |
| DRUG.00071    | Pembrolizumab (Keytruda®)            | ● Clarified medically necessary criteria addressing treatment of melanoma and non-small cell lung cancer to indicate that the individual was not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant  
● Added the treatment of individuals with relapsed or refractory Hodgkin lymphoma, except for those with lymphocyte-predominant Hodgkin lymphoma, as medically necessary indication  
● Updated investigational and not medically necessary statement |
| DRUG.00075    | Nivolumab (Opdivo®)                 | ● Clarified medically necessary criteria addressing treatment of melanoma, non-small cell lung cancer, and renal cell carcinoma to indicate that the individual was not receiving therapy for an autoimmune disease or chronic condition requiring treatment with a systemic immunosuppressant  
● Added the treatment of individuals with relapsed or refractory Hodgkin lymphoma, except for those with lymphocyte-predominant Hodgkin lymphoma, as medically necessary indication  
● Updated investigational and not medically necessary statement |
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<tbody>
<tr>
<td>DRUG.00077</td>
<td>Monoclonal Antibodies to Interleukin-17A</td>
<td>• Title revised</td>
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<tr>
<td></td>
<td>(Previous title: Secukinumab [Cosentyx®])</td>
<td>• Expanded scope of document to address both FDA approved IL-17A receptor antagonists ixekizumab (Taltz®) and secukinumab (Cosentyx®)</td>
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<tr>
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<td></td>
<td>• Added ixekizumab for the treatment of plaque psoriasis as medically necessary when criteria are met</td>
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<td></td>
<td></td>
<td>• Made minor abbreviation changes in position statement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Updated not medically necessary and investigational and not medically necessary statements</td>
</tr>
<tr>
<td>MED.00076</td>
<td>Inhaled Nitric Oxide</td>
<td>• Added INO as a method of assessing pulmonary vasoreactivity in individuals with pulmonary hypertension as medically necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Updated investigational and not medically necessary statement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Made minor abbreviation changes in position statement</td>
</tr>
<tr>
<td>SURG.00011</td>
<td>Allogeneic, Xenographic, Synthetic, and Composite Products for Wound Healing and Soft Tissue Grafting</td>
<td>• Added AlloDerm® RTU (also known as AlloDerm Ready to Use) as medically necessary for the same indications as AlloDerm® Regenerative Tissue Matrix (also known as AlloDerm RTM)</td>
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<td>• Added FlexHD® as medically necessary for breast reconstruction surgery</td>
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<td></td>
<td>• Clarified &quot;Note&quot; in medically necessary criteria</td>
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<td>• Added AlloDerm RTU, FlexHD, and fresh frozen unprocessed allograft skin products (for example, AlloSkin, TheraSkin) as investigational and not medically necessary when criteria are not met and for any use not listed as medically necessary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Added new products to the investigational and not medically necessary list</td>
</tr>
<tr>
<td>THER-RAD.00007</td>
<td>Intensity Modulated Radiation Therapy (IMRT)</td>
<td>• Added esophageal cancer as medically necessary indication</td>
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<tr>
<td></td>
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<td>• Added the treatment of mediastinal tumors for which radiation is indicated as medically necessary indication</td>
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<tr>
<td></td>
<td></td>
<td>• Revised medically necessary criteria for the treatment of lung cancer</td>
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</tbody>
</table>