

***Title: interferon alfa-2b (Intron A)***

<b>Origination:</b> 09/28/06	<b>Revised:</b> 03/10/10	<b>Annual Review:</b> 12/15/11
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**Purpose:**

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

**Background Information:**

***Reference Statement***

- Guidelines are compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

***Medication Summary***

- **Intron A** is a recombinant alpha interferon that exerts its cellular activity by binding to specific membrane receptors causing induction of various enzymes, suppression of cell proliferation, enhancement of phagocytic activity of macrophages, augmentation of the cytotoxicity of lymphocytes, and inhibition of virus replication in virus infected cells similar to the group of interferon alpha subtypes produced by human leukocytes.
- **Intron A** is indicated for:
  - The treatment of hairy cell leukemia;
  - As an adjuvant to surgical treatment for malignant melanoma in Members who are free of disease, but at high risk for recurrence (within 56 days of surgery);
  - As initial treatment of clinically aggressive follicular Non-Hodgkin's Lymphoma in conjunction with anthracycline-containing combination chemotherapy;
  - The intralesional treatment of condylomata acuminata involving external surfaces of the genital and perianal areas;
  - The treatment of AIDS-Related Kaposi's Sarcoma;
  - The treatment of chronic hepatitis C virus (HCV) with compensated liver disease in Members who have a history of blood or blood product exposure and/or are HCV antibody positive;
  - The treatment of chronic hepatitis B virus (HBV) with compensated liver disease.
- Certain cancer-related diagnoses require calculation of body surface area (m<sup>2</sup>), which will require height and weight (refer to BSA calculator at <http://www.globalrph.com/bsa.htm>).

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**Background Information, continued:**

***Exclusion Criteria***

- Member less than 18 years of age for all indications other than chronic hepatitis B or C virus;
- Member less than three (3) years of age, or over three (3) years of age and not on concurrent ribavirin, for indication of chronic hepatitis C;
- Member less than one (1) year of age for indication of chronic hepatitis B;
- Hypersensitivity to interferon alfa or any of its components;
- Organ transplant recipients with chronic hepatitis B or C and immunosuppression;
- Diagnosis of autoimmune hepatitis;
- Hepatic decompensation (Child-Pugh class B and C) before, or during, treatment;
- History of severe uncontrolled depression or severe psychiatric disorder (i.e., bipolar disorder, mania, psychosis).

***Eligibility Criteria***

- Member must be eligible and have applicable benefit coverage (i.e., self-injectable rider) within the specified date(s) of service.
- **Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.**
- For all Members, Intron A will be a:
  - Medical benefit (authorization to be loaded in Amisys) when diagnosis is secondary to:
    1. Malignant melanoma for the first four (4) weeks of treatment ONLY (IV infusion);
    2. Bladder Cancer (bladder intravesically or instillation);
    3. All other covered indications if injections are given intramuscularly (IM);
    4. Peyronie's Disease (intralesional administration).
  - Pharmacy benefit (authorization to be loaded by PBM) with applicable copay, when diagnosis is secondary to:
    1. Malignant melanoma after the first four (4) weeks of therapy;
    2. All other covered indications if injections are given subcutaneously (SC) (self-injections).

***Additional Information***

- Requests received **for Medicare Members** will be reviewed using Center for Medicare & Medicaid Services (CMS) "LCD for Interferon (Intron-A – L29202)" – Refer to Attachment A or view on-line at:  
[http://www.cms.hhs.gov/mcd/results\\_index.asp?from=%27lmpcontractor%27&contractor=197&name=First+Coast+Service+Options%2C+Inc%2E+%2809102%2C+MAC+%2D+Part+B%29&letter\\_range=4&retired](http://www.cms.hhs.gov/mcd/results_index.asp?from=%27lmpcontractor%27&contractor=197&name=First+Coast+Service+Options%2C+Inc%2E+%2809102%2C+MAC+%2D+Part+B%29&letter_range=4&retired)

**Procedure:**

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1.0 Request for *initial therapy* with **Intron A** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying **one (1)** of the following:

1.1 Diagnosis of hairy cell leukemia:

1.1.1 Approve up to 2 million IU/m<sup>2</sup> given IM or SC three (3) times a week for six (6) months;

**OR**

1.1 Diagnosis of bladder cancer:

1.1.1 Approve up to 80 million IU intravesically weekly for two (2) months;

**OR**

1.1 Malignant melanoma:

1.1.1 Approve induction therapy only: 20million IU/m<sup>2</sup> IV infusion for five (5) consecutive days per week for four (4) weeks;

**OR**

1.1 Diagnosis of AIDS-related Kaposi's sarcoma:

1.1.1 Approve up to 30 million IU/m<sup>2</sup> either IM or SC three (3) times a week for four (4) months (#16 weeks total);

**OR**

1.1 Diagnosis of follicular Non-Hodgkin's lymphoma (NHL) **AND** on concurrent anthracycline-containing chemotherapy (i.e., daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone):

1.1.1 Approve 5 million IU SC three (3) times a week for six (6) months;

**OR**

1.1 Diagnosis of condylomata acuminata (external genital and perianal warts):

1.1.1 **For Commercial Members only—excludes Medicare or Miami Dade County:** need to show inadequate response to an adequate trial of both of the following topical agents (verify through pharmacy claims or progress notes):

1.1.1.1 Podofilox (Condylox); **AND**

1.1.1.2 Imiquimod (Aldara);

1.1.2 Approve 25 million IU multi-dose vial (5 million IU/0.5ml) up to two (2) vials for one (1) month only. [Dosing: Inject 1 million IU (0.1 ml) into each lesion, up to a maximum of five (5) lesions per treatment course, three (3) times per week on alternating days for three (3) weeks];

**OR**

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**Procedure, continued:**

- 1.0 Request for *initial therapy* with **Intron A** requires documentation from the Member's medical records maintained by the independent practitioner verifying **one (1)** of the following, continued:

**OR**

- 1.1 Diagnosis of chronic hepatitis C virus (HCV);
- 1.1.1 Detectable (out of range) HCV RNA viral load (confirmed via quantitative measurement, labs usually 50,000 up to 5+ million IU/ml); **AND**
  - 1.1.2 Elevated ALT (liver enzyme) levels or liver biopsy that indicates either portal or bridging fibrosis, or at least moderate degrees of inflammation and necrosis; **AND**
  - 1.1.3 Viral genotype (1 thru 6); **AND**
  - 1.1.4 Member has failed peginterferon (Pegasys); **AND**
  - 1.1.5 Member is on concurrent ribavirin, and/or has one of the following contraindications to such therapy that prevents its use:

<b>Contraindication for use of ribavirin:</b>
Member has a drug allergy to ribavirin
Member is pregnant or unwilling to comply with adequate contraception
Member with renal impairment (CrCl < 50ml/min) or on dialysis
Member has a diagnosis of autoimmune disease or hemoglobinopathy (e.g., thalassemia major, sickle-cell anemia)
Member has a history of significant anemia or neutropenia due to ribavirin

- 1.1.6 Approve 3 million IU either IM or SC three (3) times a week for four (4) months (16 weeks total);

**OR**

- 1.1 Diagnosis of chronic hepatitis B virus (HBV);
- 1.1.1 HBsAg positive for at least six (6) months; **AND**
  - 1.1.2 Member (HBeAg-positive **or** HBeAg-negative) has a quantitative HBV DNA greater than 20,000 IU/mL; **AND**
  - 1.1.3 Elevated ALT (liver enzyme) greater than two (2) times the upper limit of normal, or a liver biopsy that indicates moderate to severe inflammation or significant fibrosis and necrosis;
  - 1.1.4 **Adults:** approve 5-10 million IU either IM or SC three (3) times a week for four (4) months (16 weeks total). **Children:** approve 3-10 million IU SC three (3) times a week for four (4) months (16 weeks total);

**OR**

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**Procedure, continued:**

- 1.0 Request for *initial therapy* with **Intron-A** requires documentation from the Member's medical records maintained by the independent practitioner verifying **one (1)** of the following diagnoses, continued:

**OR**

- 1.1 Diagnosis of Peyronie's disease requires all of the following:
- 1.1.1 **Mandatory Medical Director review; AND**
  - 1.1.2 Progress notes identifying previous therapies tried/failed, presence of erectile dysfunction, and/or penile pain; **AND**
  - 1.1.3 Duplex penile sonography with doppler analysis that captures both of the following to determine improvement for continuation:
    - 1.1.3.1 Plaque Size; **AND**
    - 1.1.3.2 Curvature/Deviation information;
  - 1.1.4 If approved by Medical Director, dose should be approved at 5 million IU injected every other week for three (3) months (which will allow for 6 treatments).
- 2.0 Request for *continuation* with **Intron A** for one (1) of the following diagnoses requires documentation from the Member's medical records maintained by the requesting provider verifying the following:
- 2.1 Hairy cell leukemia:
    - 2.1.1 Member is responding to therapy with decrease in symptoms or lack of disease progression;
    - 2.1.2 Approve up to 2 million IU/m<sup>2</sup> IM or SC three (3) times a week for one (1) year;
  - 2.2 Bladder cancer:
    - 2.2.1 Member is responding to therapy with decrease in symptoms, or lack of disease progression;
    - 2.2.2 Approve up to 80 million IU intravesically twice a month for four (4) months, then monthly for six (6) months (#14 infusions for 1 year);
  - 2.3 Malignant melanoma (**pharmacy benefit**):
    - 2.3.1 Member is responding to therapy with decrease in symptoms or lack of disease progression;
    - 2.3.2 Approve 10 million IU/m<sup>2</sup> SC three (3) times a week for 48 weeks;

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**Procedure, continued:**

- 2.0 Request for *continuation* with **Intron A** for one (1) of the following diagnoses requires documentation from the Member's medical records maintained by the requesting provider verifying the following, continued:
- 2.4 Non-Hodgkin's lymphoma (NHL):
- 2.4.1 Still on concurrent anthracycline-containing chemotherapy (i.e., daunorubicin, doxorubicin, epirubicin, idarubicin, mitoxantrone) or recently completed chemotherapy regimen; **AND**
- 2.4.2 Member is responding to therapy with decrease in symptoms, or lack of disease progression;
- 2.4.3 Approve 5 million IU SC three (3) times a week for up to one (1) year;
- 2.5 Condylomata acuminata (external genital and perianal warts):
- 2.5.1 At least 12 to 16 weeks have passed since the last treatment course;
- 2.5.2 Approve 25 million IU multi-dose vial (5 million IU/0.5ml) up to two (2) vials for one (1) additional month only. [Dosing: Inject 1 million IU (0.1 ml) into each lesion, up to a maximum of five (5) lesions per treatment course, three (3) times per week on alternating days for three (3) weeks];
- 2.6 Chronic hepatitis C virus (HCV):
- 2.6.1 Repeat HCV RNA viral load (drawn 12-weeks after initiation of treatment) was undetectable (lab usually < 50 IU/ml) **OR** decreased at least 100-fold (2 log 10) from pre-treatment HCV RNA viral load (ex. if initial viral load was 5,910,000 IU/ml and new lab is 59,100 IU/ml—this is exactly a 2 log 10 drop, basically just remove 2 zeros from the original number = a 2 log reduction); **AND**
- 2.6.2 ALT (live enzyme) value has normalized and/or improved from baseline; **AND**
- 2.6.3 Member has been adherent to the previous 16 weeks of therapy and continues with concurrent ribavirin if no contraindications are present (confirm fills through pharmacy claims);
- 2.6.4 **Genotype 1:** approve 3 million IU either IM or SC three (3) times a week for an additional 32 weeks. **Genotypes 2 or 3:** approve 3 million IU either IM or SC three (3) times a week for an additional eight (8) weeks (total of 24 weeks);

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**Procedure, continued:**

- 2.0 Request for *continuation* with **Intron A** for one (1) of the following diagnoses requires documentation from the Member's medical records maintained by the requesting provider verifying the following, continued:
- 2.7 Chronic hepatitis B virus (HBV):
- 2.7.1 Member has a reduction from baseline in quantitative HBV DNA viral load and/or a reduction ALT (liver enzymes); **AND**
  - 2.7.2 Member has been adherent to the previous 16 weeks of therapy (confirm fills through pharmacy claims);
  - 2.7.3 **Adults:** approve 5-10 million IU either IM or SC three (3) times a week for an additional eight (8) weeks (total of 24 weeks);  
**Children:** approve 3-10 million IU SC three (3) times a week for an additional eight (8) weeks (total of 24 weeks);
- 2.8 Peyronie's disease:
- 2.8.1 **Mandatory Medical Director review; AND**
  - 2.8.2 Member is responding to therapy with improvement in symptoms; **AND**
  - 2.8.3 Repeat duplex penile sonography with doppler analysis shows improvement in plaque size and curvature/deviation;
  - 2.8.4 If approved by Medical Director, dose should be 5 million IU injected every other week for three (3) additional months **only** (which will allow for an additional 6 treatments – total 12 treatment course).

**References:**

1. Intron A (interferon alfa-2b) Prescribing Information. Schering Corporation. Kenilworth, NJ. 2009.
2. Benz R, Siciliano RD, Stussi G, Fehr J. Long-term follow-up of interferon-alpha induction and low-dose maintenance therapy in hairy cell leukemia. Eur J Haematol. 2009 Mar;82(3):194-200. Epub 2008 Dec 5.
3. Potthoff A, Brockmeyer NH. HIV-associated Kaposi sarcoma: pathogenesis and therapy. J Dtsch Dermatol Ges. 2007 Dec;5(12):1091-4. Epub 2007 Oct 18.
4. Verma S, Quirt I, McCready D, Bak K, Charette M, Iscoe N. Systematic review of systemic adjuvant therapy for patients at high risk for recurrent melanoma. Cancer. 2006 Apr 1;106(7):1431-42.

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**References, continued:**

5. Garbe C, Hauschild A, Volkenandt M, Schadendorf D, Stolz W, Reinhold U, Kortmann RD, Kettelhack C, Frerich B, Keilholz U, Dummer R, Sebastian G, Tilgen W, Schuler G, Mackensen A, Kaufmann R. Evidence-based and interdisciplinary consensus-based German guidelines: systemic medical treatment of melanoma in the adjuvant and palliative setting. *Melanoma Res.* 2008 Apr;18(2):152-60.
6. Senff NJ, Noordijk EM, Kim YH, Bagot M, Berti E, Cerroni L, Dummer R, Duvic M, Hoppe RT, Pimpinelli N, Rosen ST, Vermeer MH, Whittaker S, Willemze R; European Organization for Research and Treatment of Cancer; International Society for Cutaneous Lymphoma. European Organization for Research and Treatment of Cancer and International Society for Cutaneous Lymphoma consensus recommendations for the management of cutaneous B-cell lymphomas. *Blood.* 2008 Sep 1;112(5):1600-9. Epub 2008 Jun 20.
7. Yang J, Pu YG, Zeng ZM, Yu ZJ, Huang N, Deng QW. Interferon for the treatment of genital warts: a systematic review. *BMC Infect Dis.* 2009 Sep 21;9:156.
8. Ghany MG, Strader DB, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: an update. *Hepatology.* 2009 Apr;49(4):1335-74.
9. Keeffe EB, Dieterich DT, Han SH, Jacobson IM, Martin P, Schiff ER, Tobias H. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2008 update. *Clin Gastroenterol Hepatol.* 2008 Dec;6(12):1315-41; quiz 1286. Epub 2008 Aug 23.
10. Muammer Kendirci et al. The Impact of Intralesional Interferon a-2b Injection Therapy on Penile Hemodynamics in Men with Peyronie's Disease. 2005;2:709-715.
11. Hellstrom WJ. Medical management of Peyronie's disease. *J Androl.* 2009 Jul-Aug;30(4):397-405. Epub 2008 Oct 30.
12. Hauck EW, Diemer T, Schmelz HU, Weidner W. A critical analysis of nonsurgical treatment of Peyronie's disease. *Eur Urol.* 2006 Jun;49(6):987-97. Epub 2006 Mar 20.

**Disclaimer Information:**

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.