FLRx Drug Policy

SUBJECT: Chronic Hepatitis C (Pegasys, Peg-Intron, ribavirin, Victrelis, Incivek, Olysio, Sovaldi) Updated: 5/27/2014	EFFECTIVE DATE: 6/03 REVIEW DATE: 5/14, 3/14, 1/14, 12/13, 10/13, 9/09,10/08 Page 1 of 16
If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial SafetyNet, and Health Care Reform products only when a contract benefit for the specific service exists.	

DESCRIPTION:

Chronic infection with hepatitis C virus (HCV) is the most common cause of cirrhosis and hepatocellular carcinoma and the most frequent indication for liver transplant in the United States.

Certain terms have been defined in multiple ways in different studies and treatment guidelines. Below is a list of terms and their meanings for the purposes of this policy:

Rapid virologic response (RVR) - undetectable HCV at week 4

Sustained virologic response (SVR) - undetectable HCV at time of test (12, 24, 48 weeks)

Relapser- a person who has achieved an undetectable level of virus during a prior treatment course of PEG/RBV and relapsed after treatment was stopped

Non-responder- patient who fails to achieve undetectable HCV levels at any point during therapy. Non-responders include both **null-responders** and **partial responders**.

- **Null-responders** describe patients who experience a minimal viral suppression (serum HCV RNA levels declined less than 2 log10 IU/mL by week 12 during a prior treatment course)
- **Partial responders** are patients with a ≥ 2 log10 IU/mL response whose virus remained detectable up to 24 weeks or the end of treatment

Slow-responder- patient who has detectible HCV at weeks 4 and 12, but has undetectable HCV by week 24.

Undetectable (or negative) viral load – viral load is below the limit of detection for the specific test. e.g., a Branched-chain DNA (bDNA) test can only detect viral loads greater than 615 IU/mL.

Detectable (or positive) viral load - the presence of virus is above the limit of detection. This can be expressed as IU/mL, virus/mL, and in logarithmic format.

Aviremic- undetectable HCV RNA on quantitative test (less than 10 IU/mL on Taqman/TMA testing)

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General Policy Criteria

Based upon our criteria and assessment of the peer-reviewed literature, **ribavirin, Peg-Intron, Pegasys, Victrelis, Incivek, Olysio and Sovaldi** have been medically proven to be effective and therefore **medically necessary** in the treatment of Chronic Hepatitis C if the request meets **ALL** of the following criteria:

1. Treatment must be prescribed by a gastroenterologist, hepatologist, infectious disease specialist, or HCV/HIV specialist.
    a. Treatment may also be prescribed by a Primary Care Provider if they have received additional training in the treatment and management of Hepatitis C and/or are working in conjunction with one of the above specialists.
2. HCV genotype and quantitative viral load (with sensitivity <100IU/mL for all drugs except Olysio) must be performed and provided before the start of therapy.
    a. Use of a sensitive assay with a lower limit of quantification of at least 25 IU/mL for monitoring HCV RNA levels during treatment is required for treatment with Olysio. See drug specific criteria
3. Quantitative viral load tests must be performed during treatment at weeks 4, 8, 12, 24, and 36 (if applicable).
4. For patients requiring peg-interferon therapy, Pegasys will be the required product in place of Peg-Intron.
5. Coverage of Hepatitis C medications in doses that vary from the FDA- approved dosages will not be covered.
6. Patient compliance will be assessed with each recertification.
7. Patients who are POST-LIVER TRANSPLANT will be evaluated on a case-by-case basis. Clinical factors that will be considered include: genotype, baseline viral load, immunosuppressant regimen, drug interactions with requested regimen, the presence of histological evidence of recurrence (F≥2), ALT levels, and any other relevant patient-specific information.
8. Pegasys, ribavirin, and Peg-Intron have pediatric indications. Requests for protease inhibitors and Sovaldi in pediatric patients will be evaluated for off-label use.

9. Hepatitis C regimens have the potential for significant drug interactions, therefore patient-specific needs will be taken into consideration.

Drug Specific Criteria

VICTRELIS
INITIAL review for triple therapy 1. Therapy will only be authorized for Genotype 1 2. Triple therapy will **not** be authorized for patients who have received previous treatment with a protease inhibitor. 3. **The initial authorization period will be for 12 weeks** for the combination of Pegasys, Ribavirin, and Victrelis. 4. **Victrelis requires a 4-week lead in period of treatment with Pegasys and ribavirin.** The abbreviation **TW** is used throughout the policy section to represent Treatment Week. In the case of Victrelis: **TW4**= patient has received 4 weeks of peg-interferon alfa and ribavirin, but no boceprevir **TW8**= patient has received 4 weeks of peg-interferon alfa and ribavirin, and an additional 4 weeks of triple-drug therapy with boceprevir **TW12**= patient has received 4 weeks of peg-interferon alfa and ribavirin, and an additional 8 weeks of triple-drug therapy with boceprevir **TW24**= patient has received 4 weeks of peg-interferon alfa and ribavirin, and an additional 20 weeks of triple-drug therapy with boceprevir.

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RECERTIFICATION for Triple Therapy with Victrelis:

At Victrelis TW12:

1. If **ANY** patient type has a **DETECTABLE** viral load of >100IU/ml, then coverage for triple therapy will not be extended.
2. If the patient is **treatment naïve without cirrhosis** and the viral RNA is UNDETECTABLE, then coverage will be extended with triple therapy until TW24.
3. If the patient has **previously relapsed** or **partially-responded** in the past, does not have cirrhosis, and the viral RNA is UNDETECTABLE, then coverage will be extended with triple therapy until TW24.
4. If the patient is a **slow-responder,** UNDETECTABLE OR DETECTABLE AT TW4 AND TW12 but <100IU/ml, then coverage will be extended with triple therapy until TW24.
5. If the patient is **treatment naïve with TW4 viral load < 1 $\log_{10}$ decrease from baseline**, has **compensated cirrhosis**, or is a **null responder with TW4 undetectable or detectable <100IU/ml** then coverage will be extended with triple therapy until TW24.

At Victrelis TW24:

1. If **ANY** patient type has a **DETECTABLE** viral load of >100IU/ml, then coverage for triple therapy will not be extended.
2. If the patient is **treatment naïve without cirrhosis** and the viral RNA is UNDETECTABLE, then coverage will be extended with triple therapy until **completion** of regimen at TW28.

3. If the patient has **previously relapsed** or **partially-responded** in past, does not have cirrhosis, and the viral RNA is UNDETECTABLE, then coverage will be extended with triple therapy until **completion** of regimen at TW36.

4. If the patient is a **slow-responder** and viral RNA is UNDETECTABLE, then coverage will be extended with triple therapy until **completion** of regimen at TW36.

   If the patient is a **slow-responder** and viral RNA is **DETECTABLE**, then coverage for triple therapy will not be extended.

5. If the patient is **treatment naïve with TW4 viral load < 1 log_{10} decrease from baseline**, has **compensated cirrhosis**, or is **a null responder with TW4 undetectable or detectable <100IU/ml**, and viral load is UNDETECTABLE, then coverage will be extended with triple therapy until TW36.

If the patient is **treatment naïve with TW4 viral load < 1 log_{10} decrease from baseline** has **compensated cirrhosis**, or is a **null responder with TW4 undetectable or detectable <100IU/ml**, and the viral load is **DETECTABLE,** then coverage for triple therapy will not be extended.

6. If the patient is **African American**, *regardless of RNA viral loads at TW8*, and has an UNDETECTABLE viral load, then coverage for triple therapy will be extended until the completion of regimen at TW48.

7. If the patient is **co-infected with HIV and HCV** and is UNDETECTABLE at TW24, then coverage for triple therapy will be extended until the completion of regimen at TW48.

At Victrelis TW36:

1. If the patient is a **slow-responder** and UNDETECTABLE, coverage for peg- interferon/ribavirin will be extended to completion

of regimen at TW48. Coverage for Victrelis will not be extended past 36 weeks.

2. If the patient is **treatment naïve with TW4 viral load < 1 log_{10} decrease from baseline** has **compensated cirrhosis**, or is **a null responder with TW4 undetectable or detectable <100IU/ml**, and viral load is UNDETECTABLE, then coverage will be extended with triple therapy until TW48.

At Victrelis TW48: Coverage for all patient types will not be extended.

INCIVEK
INITIAL review for triple therapy 1. Therapy will only be authorized for Genotype 1 2. If clinically appropriate to receive triple therapy with peg-interferon, ribavirin and a protease inhibitor, Incivek will only be authorized if there is documentation of a serious adverse reaction to Victrelis, which resulted in therapy interruption. 3. **The initial authorization period will be for 4 weeks** for the combination of Pegasys, Ribavirin, and Incivek.
RECERTIFICATION for Triple Therapy with Incivek: **At Incivek TW4:** 1. A short-term extension can be granted for providers to obtain TW4 viral load. 2. If **ANY** patient type has a **DETECTABLE** viral load of >1000IU/ml, then coverage for triple therapy will not be extended.

3. If the patient is **treatment naïve without cirrhosis** or a **previous relapser** with cirrhosis and is UNDETECTABLE, coverage will be extended to TW12.

4. If the patient is **treatment naïve without cirrhosis**, a **relapser without cirrhosis**, **naïve with cirrhosis**, a **partial responder**, or **null responder** with a **DETECTABLE viral load that is <1,000IU/ml**, then coverage will be extended to TW12.

5. If the patient is **co-infected with HIV and HCV** and has an UNDETECTABLE or DETECTABLE viral load that is <1,000IU/ml, coverage for peg-interferon, ribavirin and Incivek will be extended to TW12.

At Incivek TW12:

1. If **ANY** patient type has a **DETECTABLE** viral load of >1000IU/ml, then coverage for triple therapy will not be extended.

2. If the patient is **treatment naïve without cirrhosis** or a **previous relapser** with cirrhosis and is UNDETECTABLE at TW4 and TW12, coverage for peg-interferon/ribavirin will be extended to completion of regimen at TW24. Coverage for Incivek will not be extended past 12 weeks.

3. If the patient is **treatment naïve without cirrhosis**, a **relapser without cirrhosis**, **naïve with cirrhosis**, a **partial responder**, or **null responder** with an UNDETECTABLE or DETECTABLE viral load that is <1,000IU/ml, coverage for peg- interferon/ribavirin will be extended to TW24. Coverage for Incivek will not be extended past 12 weeks.

4. If the patient is **co-infected with HIV and HCV**, then with an UNDETECTABLE or DETECTABLE viral load that is <1,000IU/ml, coverage for peg-interferon/ribavirin will be extended to TW24. Coverage for Incivek will not be extended past 12 weeks.

At Incivek TW24:

1. For those patients who had have a DETECTABLE viral load (<1,000 U/mL) at TW4 and/or TW12, but who are UNDETECTABLE at TW24, coverage for peg-interferon/ribavirin will be extended to completion of regimen at TW48.
2. For those patients who had have a DETECTABLE viral load (<1,000 U/ml) at TW4 and/or TW12, and who are still DETECTABLE at TW24, then coverage for all further therapy will not be extended.
3. If the patient is **co-infected with HIV and HCV** and the viral load is UNDETECTABLE, then coverage will be extended to completion of regimen at TW48.

If the patient is **co-infected with HIV and HCV** and the viral load is DETECTABLE, then coverage for all further therapy will not be extended.

At Incivek TW48: Coverage for all patient types will not be extended

OLYSIO (Triple Therapy with Ribavirin + Pegasys)
INITIAL review for triple therapy with Olysio
1. Therapy will only be authorized for genotype 1 2. For patients who are infected with HCV genotype 1a, an NS3 Q80K polymorphism screening is required. If the patient is positive for the NS3 Q80K polymorphism, then triple therapy with Olysio will not be authorized. 3. Use of a sensitive assay with a lower limit of quantification of at least 25 IU/mL for monitoring HCV RNA levels during treatment is

required.

4. **The initial authorization period will be for 4 weeks** for the combination of Pegasys, Ribavirin, and Olysio.

Recertification for Triple Therapy with Olysio:

At Olysio TW4:

1. A short-term extension can be granted for providers to obtain TW4 viral load.
2. If **ANY** patient type has a **DETECTABLE** viral load of **≥25IU/ml**, then coverage for triple therapy will not be extended.
3. If the patient is **treatment naïve** or a **previous relapse,** including those with cirrhosis, and viral load is UNDETECTABLE or <25IU/ml, coverage will be extended to TW12.
4. If the patient is a **partial responder** or **null responder,** including those with cirrhosis, and viral load is UNDETECTABLE or <25IU/ml, then coverage will be extended to TW12.

At Olysio TW12:

1. If **ANY** patient type has a **DETECTABLE** viral load of **≥25IU/ml**, then coverage for all future therapy will not be extended.
2. If the patient is **treatment naïve** or a **previous relapse,** including those with cirrhosis, and viral load is UNDETECTABLE or <25IU/ml at TW4 and TW12, coverage for peg-interferon/ribavirin will be extended to **completion** of regimen at TW24. Coverage for Olysio will not be extended past 12 weeks.

3. If the patient is a **partial responder** or **null responder,** including those with cirrhosis, and viral load is UNDETECTABLE or <25IU/ml at TW4 and TW12, coverage for peg-interferon/ribavirin will be extended to TW24. Coverage for Olysio will not be extended past 12 weeks.

At Olysio TW24:

1. If the patient is a **partial responder** or **null responder,** including those with cirrhosis, and has a **DETECTABLE** viral load of **≥25IU/ml**, then coverage for peg-interferon/ribavirin will not be extended.
2. If the patient is a **partial responder** or **null responder,** including those with cirrhosis, and viral load is UNDETECTABLE or <25IU/ml at TW4, TW12, and TW24, coverage for peg-interferon/ribavirin will be extended to **completion** of regimen at TW48

At Olysio TW48: Coverage for all patient types will not be extended

SOVALDI

1. For **Genotype 1**, Sovaldi will be authorized as **triple therapy** in combination with peg-interferon (Pegasys) and ribavirin for **12 weeks** unless there is a contraindication to interferon (IFN) therapy.
2. For **Genotype 1**, Sovaldi will be authorized as **dual therapy in combination with ribavirin for 24 weeks** for those that are **ineligible to receive interferon (IFN)**
   a. Contraindications to interferon therapy are defined as: comorbid autoimmune hepatitis or other autoimmune disorders, decompensated hepatic disease, history of preexisting cardiac disease, a baseline neutrophil count below 1500/µL, a

baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL, severe intolerance to past IFN therapy (such as urticaria, angioedema, broncho constriction, anaphylaxis, Stevens-Johnson syndrome, ophthalmologic disorder, thyroid disorder or refractory diabetes mellitus, or a past history of depression that required medical or pharmacological intervention.

3. For **Genotype 2**, Sovaldi will be authorized as **dual** therapy in combination with ribavirin for **12 weeks**.
4. For **Genotype 3**, Sovaldi will be authorized as **dual** therapy in combination with ribavirin for **24 weeks**.
5. For **Genotype 4**, Sovaldi will be authorized as **triple** therapy in combination with peg-interferon (Pegasys) and ribavirin for **12 weeks.**
6. Sovaldi has been shown to be effective in individuals co-infected with both HCV and HIV and as such will be allowed in these populations with the same criteria as stated above
7. Sovaldi will be approved as **dual therapy** in combination with ribavirin for individuals with **hepatocellular carcinoma** fulfilling Milan criteria (awaiting liver transplant). Initial approval will be for 12 weeks or until the time of transplantation (whichever is less).
   a. Recertification will be required every 12 weeks with a maximum length of therapy of 48 weeks regardless of liver transplant status.
8. Sovaldi will not be authorized as monotherapy.

SOVALDI / OLYSIO COMBINATION (emerging therapy)

1. Based on AASLD/IDSA treatment guidelines, Sovaldi and Olysio will be authorized for **Genotype 1** as **combination therapy** for

12 weeks for

a. Those that are treatment naïve and **ineligible to receive interferon (IFN).** Contraindications to interferon therapy are defined as: comorbid autoimmune hepatitis or other autoimmune disorders, decompensated hepatic disease, history of preexisting cardiac disease, a baseline neutrophil count below 1500/µL, a baseline platelet count below 90,000/µL or baseline hemoglobin below 10 g/dL, severe intolerance to past IFN therapy (such as urticaria, angioedema, broncho constriction, anaphylaxis, Stevens-Johnson syndrome, ophthalmologic disorder, thyroid disorder or refractory diabetes mellitus, or a past history of depression that required medical or pharmacological intervention. **OR**

b. Those that were a non-responder to previous treatment with dual ribavirin and peg-interferon.

2. This regimen can be used with or without ribavirin.

3. This regimen must only be prescribed for those patients that require immediate treatment (advanced fibrosis score > 2) because it is anticipated that safer and more effective IFN-free regimens will be available in the near future.

4. Simeprevir use is limited to patients with compensated liver disease (Child-Pugh Class A). This regimen will not be authorized for individuals with moderate to severe liver impairment (Child-Pugh Class B or C).

5. For patients who are infected with HCV genotype 1a, an NS3 Q80K polymorphism screening is not required as response rates for these individuals are still high when simeprevir is used in combination with sofosbuvir.

POLICY GUIDELINES:

1. Prior-authorization is contract dependent.

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