MTF Formulary Management for Hepatitis C Virus (HCV) Direct Acting Antiviral (DAA) Drugs Subclass
Defense Health Agency Pharmacy Operations Division
May 2015

Bottom Line:

- **The designated Basic Core Formulary (BCF) products for the HCV Drug Class include ribavirin 200 mg generic capsules and peginterferon alfa-2a injection (Pegasys) (Non-DAAs).**
- **There are no nonformulary HCV DAA agents.**
- **Prior Authorization for sofosbuvir (Sovaldi), simeprevir (Olysio), ledipasvir/sofosbuvir (Harvoni), and ombitasvir/paritaprevir/ritonavir/dasabuvir co-packaged tablets (Viekira Pak) were maintained and reflect their FDA indications and American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) HCV guidelines (www.hcvguidelines.org).**

Uniform Formulary Decision: The Director, DHA, approved the recommendations from the May 2015 DoD P&T Committee meeting in July 20, 2015, with an implementation date upon signing.

Uniform Formulary (UF) drugs		Nonformulary (NF) drugs
BCF drugs — MTFs must have on formulary	**MTFs may have on formulary***	**MTFs must not have on formulary**
	• Sofosbuvir (Sovaldi) • Simeprevir (Olysio) • Ledipasvir / sofosbuvir (Harvoni) • Ombitasvir/paritaprevir/ritonavir/dasabuvir co-packaged tablets (Viekira Pak)	No HCV DAA drugs are designated nonformulary.
* Boceprevir (Victrelis) is no longer the standard of care, but will remain UF until withdrawal from the market in December 2015.		

Prior Authorization (PA) Criteria

- All new users are required to undergo the PA process
- Current DAA users are not affected by PA; they can continue therapy uninterrupted.
- Consult the AASLD/IDSA HCV guidelines (www.hcvguidelines.org) for the most up-to-date and comprehensive treatment for HCV. Unique patient populations are also addressed; treatment recommendations may differ from those for the general population.

Manual PA Criteria

- Age ≥ 18
- Has laboratory evidence of HCV genotype 1, 2, 3, or 4 HCV infection
  - State the HCV genotype and HCV RNA viral load on the PA form
- Is prescribed by or in consultation with a gastroenterologist, hepatologist, infectious disease physician, or liver transplant physician
- Sofosbuvir (Sovaldi) and simeprevir (Olysio) are not to be used as individual stand-alone agents. Fixed-dose combination products (e.g., Harvoni and Viekira Pak) can be used as monotherapy.

Treatment Regimens and Duration of Therapy

- Please refer to the specific PA (http://www.express-scripts.com/tricareformulary)
- These PA criteria reflect their FDA indications and AASLD/IDSA Hepatitis C guidelines.

FDA Indications and HCV Guidelines

Due to the rapidly evolving HCV field, use of the DAAs outside of their FDA-labeled indications is not uncommon. The American Association for the Study of Liver Diseases/Infectious Diseases Society of America (AASLD/IDSA) updated the HCV treatment guidelines on April 8, 2015. The AASLD/IDSA HCV treatment guidelines recommend all-oral, (interferon-free) options whenever feasible for patients with HCV. Harvoni and Viekira Pak are now prominently featured in the guidelines as recommended regimens for patients with genotype 1 and 4 chronic HCV. Sovaldi in combination with Olysio is also a recommended regimen in patients with genotype 1 HCV. Sovaldi with ribavirin is recommended for patients with non-genotype 1 chronic HCV, in most situations. Consult the guidelines for the most up-to-date recommendations at: www.hcvguidelines.org. Table 1 below summarizes the recommended treatment regimens for a variety of patient populations with HCV genotype 1

Table 1: Interferon-free Hepatitis C Genotype 1 Treatment Regimen Following FDA Indications and AASLD/IDSA HCV Guidelines

Patient population	Genotype	AbbVie Viekira ± RBV	Gilead Harvoni (SOF/LDV)	Janssen SMV/SOF
Treatment-naïve, non-cirrhotic	1a	RBV 12 wks	8/12 wks	12 wks
	1b	12 wks	8/12 wks	12 wks
Treatment-experienced, non-cirrhotic	1a	RBV 12 wks	12 wks	12 wks
	1b	12 wks	12 wks	12 wks
Treatment-naïve, cirrhotic	1a	RBV 12/24 wks	12 wks	24 wks
	1b	RBV 12 wks	12 wks	24 wks
Treatment-experienced, cirrhotic	1a	RBV 12/24 wks	24 wks	24 wks
	1b	RBV 12 wks	24 wks	24 wks
HCV/HIV co-infection	1a/1b	See above dosing	See above dosing*	Not indicated
Transplant recipients	1a/1b	RBV 24 wks	RBV 12 wks*	RBV 12 wks*

***** Not an FDA indication. Recommendation only in the AASLD/IDSA HCV guidelines

RBV: ribarivin; SOF/LDV: Harvoni; SMV/SOF: Olysio

Clinical Summary

- There are no studies directly comparing Harvoni, Sovaldi in combination with Olysio or Viekira Pak. In general, when making indirect comparisons across similar patient populations, efficacy (assessed by sustained virologic response at 12 weeks [SVR12] as the primary endpoint) appears similar among these products.
- In general, the rate of SVR12 across clinical trials in patients with genotype 1 chronic HCV treated with any DAA except Victrelis is > 90%. With Harvoni and Viekira Pak, SVR12 rates are > 95% in most instances.

Safety

- The adverse events (AEs) for Harvoni, Viekira, and Olysio with Sovaldi occurred in 79% to 92% of patients and were generally mild to moderate in severity and clinically manageable. The most frequent AEs were fatigue, headache, and nausea.
- Combinations of sofosbuvir and simeprevir (Harvoni and Olysio), sofosbuvir/ledipasvir (Harvoni), or ombitasvir paritaprevir/ritonavir/dasabuvir (Viekira) are safe and well tolerated in short-term studies.
- A recent FDA Drug Safety Board Communication found serious risk of symptomatic bradycardia with co-use of amiodarone with sofosbuvir in combination with another DAA.
- There is a potential for significant drug-drug interactions with Viekira Pak.

Overall

- In the absence of head-to-head trials, HCV treatment should be based on current AASLD/IDSA treatment guideline recommendations, individual patient characteristics, likelihood of adherence, and patient preferences, as well as cost.

References

- DoD P&T Committee minutes: http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee/Meeting-Minutes
- Current/future drug classes under review by the DoD P&T Committee: http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee
- TRICARE Formulary Search Tool: http://www.express-scripts.com/tricareformulary
- Prior Authorization/Medical Necessity forms: see TRICARE Formulary Search Tool above.
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil

Hepatitis C Virus Direct Acting Antiviral Drugs Price Comparison at MTF

Drug	MTF cost/month (May 2015)
Uniform Formulary	
Ombitasvir/paritaprevir/ritonavir/ dasabuvir tablets (Viekira Pak)	$ **Most Cost-Effective**
Ledipasvir/sofosbuvir (Harvoni)	$ **Most Cost-Effective**
Sofosbuvir (Sovaldi)	$$ **Cost-Effective**
Simeprevir (Olysio)	$$ **Cost Effective**

Legend:

$ = "Most Cost-Effective" represents Rxs with the lowest cost and best clinical efficacy

$$ = "Less Cost-Effective" represents higher cost Rxs with similar clinical efficacy

$$$ = "Less Cost-Effective" represents next higher cost Rxs with similar clinical efficacy

$$$$ = "Least Cost-Effective" represents Rxs with the highest cost with similar clinical efficacy